



Cardiology in the Young

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Session 5: Adolescent and Adult Congenital Heart Disease

O5-1

Exercise training in adults with congenital heart disease: cheap, safe & effective!

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Introduction: A wide range of health benefits including improvement in quality of life has been associated with regular physical activity; however the influence of regular structured exercise training on exercise capacity and quality of life in adults with congenital heart disease has not been reported before.

Methods: Sixty-one patients [age 18–63, mean 31.7 ± 10.9 yrs; 36 Male] were recruited from unit database and divided into 3 sub-groups depending upon their NYHA class [Group I: NYHA class 1, N = 26; Group II: NYHA class 2, N = 18; Group III: NYHA class 3 & 4, N = 17]. Patients had a clinical examination, BP &

ECG was recorded and an echocardiogram performed. Exercise capacity was determined by walking on a treadmill. Quality of life was ascertained by 3 questionnaires: 1) Diener's Satisfaction with Life Questionnaire (DSLQ), 2) Physical Self-Perception Profile – shortened (PSPPs), and 3) Health Survey Questionnaire (SF-12). Baseline physical activity was assessed using accelerometers [Actigraph® & Caltrac®] to measure habitual activity levels and energy expenditure. This data was used to provide an individualised incremental exercise regimen consisting of walking for 5 days a week for 10 weeks, with the daily walking time being increased every week. The patients were assessed again and the differences noted. **Results:** Forty-nine patients (mean age 32.6 ± 11.8 yrs; 30 Male) completed all measures. Treadmill walking time increased from a mean of 7.87 minutes to 9.44 minutes post training. The daily activity linked Calorie usage increased from a mean of 351 to 428 Calories [p = 0.001]. Similar trend was seen in the questionnaire scores with the mean scores of all the three questionnaires going up after the exercise training implying improvement in quality of life, physical self-perception and perceived health status with the differences being statistically significant for all the questionnaire scores. There was no untoward effect of exercise noted and there were no deaths.

Conclusions: A simple regular physical activity intervention is safe, and, effective in significantly increasing the exercise capacity of adult patients with all stages of congenital heart disease. It is also helpful in improving the quality of life by improving physical self-perception, satisfaction with life, physical activity levels and general health.

	Treadmill duration (minutes)		Activity linked energy expenditure in 7 days (Calories)	
	Pre	Post	Pre	Post
'p' value	0.013		0.001	
Mean	7.57	9.44	2459	2998
Min	1.00	4.50	706	1023
Max	19.20	22.50	4832	5611

	PSPPs score		DSLQ score		Health survey SF-12 score	
	Pre	Post	Pre	Post	Pre	Post
'p' value	0.001		0.00029		0.0055	
Mean	45	50	23	26	31	35
Min	15	22	11	14	8	21
Max	66	67	33	35	47	48

Pre = Pre exercise training assessment; Post = Post 10 week exercise training assessment.

O5-2

Hepatic changes late after the Fontan operation, a radiological perspective

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Introduction: Venous hypertension and systemic hypoxia are frequent accompaniments of the Fontan circulation late after surgery,

particularly in the presence of atrio-pulmonary connections. Venous outflow from the liver demonstrates gravity dependent obstruction and deep intrahepatic reflux. Such changes may bring about profound hepatic injury. We sought to define liver changes late after the Fontan operation in patients being evaluated for total cavopulmonary conversion.

Methods: Hospital records including radiology reports (CT and abdominal ultrasound scans) and liver histology were retrospectively reviewed in patients evaluated for Fontan conversion.

Results: Among 12 (3 female) patients (9 with atrio-pulmonary connections), mean age was 24.9 years (range 16.5–42.9) and mean body surface area was 1.65 (range 1.2–1.9). Mean duration of Fontan circulation was 15 years (range 7–27). CT (n = 12) and abdominal ultrasound scans (n = 8) were grossly abnormal in all patients, demonstrating abnormal contrast enhancement patterns including “nutmeg” changes in 8, zonal changes with central preservation in hepatic inflow in 4 patients, and hypervascular nodules in 2 patients. Splenomegaly occurred in all but 4 patients with a mean diameter of 13.5 cm (normal <12 cm), range 12–17 cm. Large gastro-oesophageal varices and/or lienorenal shunts, similar in size to the descending aorta, were present in 4 patients, all with significant splenic enlargement, of whom 2 had protein losing enteropathy, and 3 had histological evidence of cirrhosis. Intrahepatic veno-venous collaterals were present in 3 patients. Gallstones (without obstruction) were present in 4 patients. Only 3 patients had biochemically detectable abnormalities in liver function, 1 of whom presented with acute upper gastrointestinal symptoms.

Conclusions: All patients with longstanding Fontan circulations demonstrate striking morphological hepatic abnormalities. These findings are consistent with pathological changes of cirrhosis, varying degrees of fibrosis and portal hypertension. Liver enhancement patterns suggest significant arterialisations of hepatic inflow presumably due to intra and extrahepatic venous hypertension. Such venous hypertension may also promote development of venous collaterals manifest as gastric and splenic varices and lienorenal shunts. The presence of large varices should alert the physician in the performance of transoesophageal procedures. Despite preservation of liver function biochemically, profound liver injury exists uniformly in patients with a Fontan circulation.

O5-3

Long term follow up of GUCH patients after modified Fontan operation

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Introduction: Since the introduction of single ventricle palliation more patients reach adulthood and need specialized supervision and therapy. We analyzed hemodynamics, physical performance and morbidity in GUCH patients after modified Fontan operation.

Methods: Twenty-nine adults with median age of 24 (range 16–43) years who underwent Fontan operation between 9/1991 and 6/2002 were analyzed regarding exercise (EC) and oxygen consumption capacity (OC), necessity for cardiac medication and the incidence of arrhythmias. Fifteen of them were operated on as adults (16–37 years). The intraatrial modification was performed in 20 patients and extracardiac Fontan operation (ECFO) in 9. All fenestrations (n = 20) were closed spontaneously or by transcatheter intervention in median 6 months after surgery.

Results: There was one late death (mortality 3.7%). Patients who underwent heart catheterization (n = 20) showed stable Fontan

hemodynamics with low pulmonary artery pressure (median 11 mmHg) and low transpulmonary gradient (median 5.5 mmHg). Cardiopulmonary exercise testing showed a mean EC of 2.2 ± 0.69 w/kg ($64.9 \pm 19.2\%$ of the norm for this age group) and an OC of 25.9 ± 6.6 ml/min/kg ($58.5 \pm 13.9\%$). Patients who were tested twice showed decreased EC and OC of 1.5 ± 0.87 w/kg ($43.7 \pm 25.3\%$) and 21.1 ± 8.5 ml/kg/min ($48.3 \pm 17.7\%$), respectively, compared to earlier postoperative testing (p = 0.015 for EC and p = 0.006 for OC). During the median follow-up of 7.0 (range 2.3–13) years, 7 patients (26%) developed tachyarrhythmias. Seven patients, all after intraatrial Fontan operation, required a permanent pacemaker due to bradyarrhythmias. Medical treatment of heart failure was necessary in 21 patients (72%). All patients were on an anticoagulation regime. No clinically relevant thromboses were noted but one thromboembolic event occurred in one patient after classic total cavopulmonary connection.

Conclusions: The circuit separation with lateral tunnel or extracardiac conduit Fontan operation allows the patients to reach adulthood with stable hemodynamics and low morbidity. Postoperative arrhythmias are one of the main drawbacks but the incidence of arrhythmias after ECFO seems to be lower. Regular checks of the patients physical exercise capacity and hemodynamics are necessary to optimize the cardiac medication for progressive heart failure and to identify candidates for later heart transplantation.

O5-4

Outcomes of congenital aortic valve stenosis – result of 1480 children of the Hungarian national survey

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Introduction: In medical care planning for grown-up congenital heart (GUCH) patients it is essential to explore the size and composition of the future patient population. Objective of this retrospective study was to determine the occurrence, severity and outcome of congenital aortic valve stenosis (CAVS) in the entire Hungarian pediatric population.

Methods: Records of all patients born with isolated CAVS between 1985 and 2003 were obtained from nation-wide pediatric heart-network. Age and severity at presentation, subsequent clinical course were studied.

Results: In July of 2003, 1480 CAVS patients were recorded and followed-up. Median age at presentation was 20 months (range 0–18 years). Median follow-up was 8.1 years (range 1–18 yrs). Stenosis was mild at presentation in 1259 patients, moderate in 102, severe in 119. 183 children required catheter or surgical intervention and further 93 children are expected to need intervention still in childhood. 126 pts required 1, 48 pts 2 and 9 pts 3 intervention. The first intervention was transcatheter balloonvalvuloplasty in 120 patients, surgical valvulotomy in 48 pts, prosthetic valve implantation 9 pts, Ross operation 6 pts. There were 2 sudden cardiac death and 8 death followed any intervention. Aortic valve insufficiency associated to stenosis in 301 cases (219 spontaneous, 82 after any intervention). 3 endocarditis and 18 heart failure occurred. Considerable progression (>50 mmHg) was detected in 64 children. In the post-interventional group 21 had excellent, 71 good, 52 fair, 30 poor, 9 unclassifiable cardiac status, while in the non-interventional group 915 had excellent, 269 good, 77 fair, 11 poor and 25 unclassifiable cardiac status.

Conclusions:

1. The study population is representative for the entire Hungarian population (10 millions).
2. Majority of the children have mild stenosis at presentation.
3. Considerable CAVS progression is rare in childhood.
4. Majority of the children who underwent any intervention are in excellent, good or fair cardiac status.
5. Children entering GUCH care most frequently have mild CAVS and good cardiac status.

O5-5**Adult patients with patent ASD: cardiopulmonary exercise test in the evaluation of exercise capacity in patients over 30 years of age**

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Adult patients (P) with atrial septal defect (ASD) describe their physical performance as normal, it may delay the decision to close the defect. Subjective perception does not fully relate to clinical status. The aim of the study was to determine exercise capacity using spirometry, in adult asymptomatic P with ASD. 36 P (25F), mean age $44,7 \pm 8,2$ years with patent ASD II were studied. The control: 25 healthy individuals (15F), mean age $45,6 \pm 6,1$ years. **Echo Examination:** End-diastolic dimensions (EDD) of left (LV) and right ventricle (RV) were measured as well as ejection fraction of left ventricle (EF), right ventricular end-systolic pressure (RVSP), pulmonary perfusion to systemic perfusion ratio Qp:Qs was calculated. Exercise test according to modified Bruce protocol was performed as well as resting spirometry, where forced vital capacity (FVC) tidal volume (TV), minute ventilation equivalent (VE), forced expiratory volume (FEV1), forced expiratory flow (FEF 25–75%), and peak oxygen consumption (peak VO_2) VE/VCO_2 slope was measured. **Results:** 30 (86%) P were NYHA I, 5 P – NYHA II. Qp:Qs mean $1,8 \pm 0,4$. RV in studied group was larger than in control $p = 0,00001$, LV and EF was smaller among ASD than in control ($p = 0,0004$, $p = 0,004$).

Spirometry: P with ASD: VO_2 was decreased compared to control ($p = 0,00001$). HR max and systolic BP was smaller than in controls ($p = 0,01$, $p = 0,001$) VE/VCO_2 slope, was higher in P ($p = 0,0001$), including 5 (14% P) higher than 34, VE was smaller than in controls ($p = 0,00003$). RQ in ASD P $-1,03 \pm 0,06$ were smaller than in controls ($p = 0,01$).

FVC and VT were smaller than in controls ($p = 0,002$, $p = 0,00008$). FEV1, FEF 25–75% were higher than in controls ($p = 0,0008$, $p = 0,01$).

Negative Correlations: VO_2 and Qp:Qs ($p = 0,004$), VE/VCO_2 slope and Qp:Qs ($p = 0,058$). VE and LV ($p = 0,03$), HR max and RV ($p = 0,02$). FEV1 vs RV and vs RVSP ($p = 0,04$, $p = 0,01$), RQ and RVSP ($p = 0,004$). HR correlated positively with VO_2 ($p = 0,005$).

Conclusions:

1. Exercise capacity was significantly reduced among P with ASD, contrary to their subjective perception.
2. Decreased exercise capacity results from decreased heart ejection due to altered anatomy and functional pathologies of lungs consequent to increased pulmonary blood flow.

O5-6**Impaired vascular endothelial function in adult patients with cyanotic heart disease: evaluation by strain gauge plethysmography**

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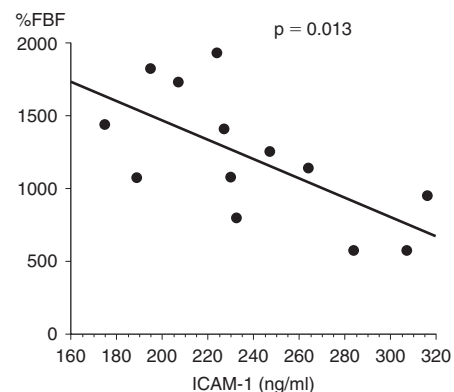
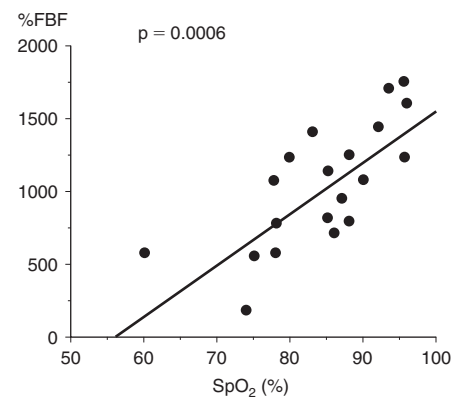
Background: Vascular endothelial function may be damaged by long-standing cyanosis or hemodynamic stress in adult patients with cyanotic heart disease.

Objective: To evaluate endothelial function and its related factors in adult patients with cyanotic heart disease.

Methods: Forearm blood flow (FBF) response to handgrip exercise or brachial arterial occlusion were assessed in 14 patients with cyanotic heart disease (mean age: 26.8 ± 6.0 years, SaO_2 : $82.1 \pm 8.4\%$) and age-matched control (mean age: 30.9 ± 8.3 years, SaO_2 : $98.1 \pm 0.9\%$) using strain gauge plethysmography. As the related factors of vascular endothelial function, red blood cell (RBC), uric acid, MDA-LDL, ICAM-1, von Willebrand factor, thrombomodulin, endothelin, erythropoietin, urine 8-hydroxy-2'-deoxyguanosine and urine NOx level were analyzed.

Results: Percent change of FBF to handgrip exercise in cyanotic patients was significantly deteriorated than that in control ($882.6 \pm 358.8\%$ vs. $1428.4 \pm 447.6\%$, $p = 0.007$). Similarly, percent change of FBF to brachial arterial occlusion in cyanotic patients was significantly deteriorated than that in control ($292.6 \pm 89.9\%$ vs. $455.6 \pm 117.8\%$, $p = 0.002$). Such percent changes were significantly correlated with oxygen saturation, RBC and ICAM-1 level (figure).

Conclusions: These findings suggested that endothelial impairment exists in cyanotic patients and closely related with severity of cyanosis or vascular shear stress. Such impaired endothelial function may influence on the long-term outcome in these populations.



Session 6: Interventions

O6-1

Endovascular stenting and subsequent removal induces stenosis of veins and not of arteries

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Objective: To investigate the effect of stent implantation and later surgical removal on the growth potential of juvenile vessels.

Methods: We implanted stents in the carotid artery and jugular vein of six 6-week old lambs (18 + 2.2 kg). After 10 weeks (animal weight 43 + 6.9 kg) the stents were excised and the vessels closed without the use of patch material. Again 10 weeks later (animal weight 55 + 6.7 kg), the animals were catheterised. Vessel sizes of the treated and untreated control side were measured. The animals were sacrificed for histological analysis. No anti-aggregants were given. Comparison of vessel sizes was done with the paired t-test.

Results: Initial arterial stent sizes varied between 4 and 5 mm. At analysis, the vessel size (9.6 + 1.5 mm) was not significantly different from the control side (11.1 + 1.1 mm). None of the vessels was occluded. Histological analysis showed a normal arterial vessel wall architecture in four cases. In two animals, the artery showed signs of partial injury of the lamina elastica interna (30% lumen reduction).

Initial venous stent size varied between 11 and 14 mm. At analysis, 2 vessels were thrombosed. Vessel size was significantly smaller as compared to the control side (8 + 8 mm vs. 14 + 5 mm; $p = 0.03$). Vessel wall architecture was conserved in all but one vessel.

Conclusion: Arterial stenting with subsequent stent removal, does not affect vessel development. However, venous stenting with subsequent stent removal results in a high risk of thrombosis.

As the vessel wall integrity remains intact, this thrombosis can be due to lower blood velocity in the venous system.

O6-2

Transcatheter closure of multiple interatrial septal defects

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Objectives: To evaluate the efficacy, safety and the follow-up results of transcatheter closure of multiple interatrial septal defects.

Methods: Between 1996 and 2004, 87 patients (pts) (mean age 43 ± 19, range 5–79 years) with multiple interatrial septal defects underwent percutaneous treatment. Indication to closure was paradoxical embolism in 64 pts, right ventricular overload in 15, decompression illness in 4 divers, platypnea-orthodeoxia syndrome in 3 pts; 1 pt was candidate to liver transplantation. An atrial septal aneurysm was associated in 73 pts (83%). The procedure was performed with the standard technique under general anesthesia with fluoroscopic and transesophageal echocardiographic guidance. Color Doppler and Contrast Echo was obtained 24 hours, 1, 6 months and every year after treatment.

Results: In 80 cases a single device was implanted: 10 Cardioseal-Starflex, 17 Amplatzer PFO, 4 Amplatzer Septal Occluder, 12 Helex and 37 Amplatzer ASD-MF "Cribriform". Seven pts were treated with 2 devices (Cardioseal-Starflex in 5, Amplatzer Septal Occluder in 2). The procedure was successful in 86 pts (99%). In one case with multifenestrated aneurysm an Amplatzer PFO occluder was removed because of residual shunt and the pt underwent surgery. There were no complications.

The mean follow-up period of 86 pts is 2 ± 2.1 years (range 1 day–7 years). No pts suffered recurrences of paradoxical embolism. Complete occlusion was demonstrated in 74/86 cases (85%). Residual shunt was detected in 5/65 pts (8%) at 6 months and in 1/45 (2.3%) at 1 year follow-up.

Conclusions: Percutaneous closure of multiple interatrial septal defects is safe and effective. With the new generation devices, even cases with complex anatomy can be successfully treated.

O6-3

Covered stents in the management of Coarctation of the aorta in special situations

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Background: Stent implantation as primary management for Coarctation of aorta in older children & adults is emerging as the preferred form of treatment. Covered stents have been used not only to decrease vascular complications but to treat co-existent conditions. We report our experience with the use of covered stents in the management of Coarctation of the aorta.

Objective: To assess the early & mid-term results of stenting as primary treatment in a tertiary referral center for paediatric & adult cardiology.

Patients and Methods: We implanted 9 covered Cheatham Platinum (CP) balloon expandable stents from NuMED with BIB balloon in 6 adolescents and adults from Dec 01–Dec 04. All were done under general anaesthesia. The median age was 21 yrs (range 12–38 yrs). The indications included critical long segment Coarctation ($n = 1$), associated PDA ($n = 2$), critical transverse arch native Coarctation ($n = 1$), Turner syndrome ($n = 1$) and aortic dissection after angioplasty & attempted stenting of a native Coarctation. **Results:** Adequate implantation was possible in all patients. The pre-stent systolic gradient was 50 mmHg (40–71) and disappeared fully in all patients. The mean diameter at the narrowest point increased from mean of 4 + 2.5 mm to 19 + 4.2 mm. The PDA was immediately closed in both patients. Patient with iatrogenic aortic dissection received two covered stents in the first instance and two more were implanted subsequently to try and seal the dissection in full. No vascular complications or thromboembolism occurred. During a median follow up of 1.3 years (0.1–3 yrs), none of the 6 pts has shown recoarctation. No adverse systemic hypertension has been noticed and 4 of the 6 patients are still on antihypertensive treatment.

Conclusions: Availability of covered stents adds to the armamentarium of interventional cardiologists in the management of Coarctation of the aorta. They decrease the potential of vascular complications in atretic/long segment Coarctation and in pts with Turner syndrome. It can be used to close the associated ductus without using a further device. They can be used to seal the aortic dissection and are an important bail out following any complication related to Coarctation intervention.

O6-4

Percutaneous closure of right-to-left shunt in patients with Ebstein's anomaly

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Background: Patients (pts) with Ebstein's anomaly may suffer from right-to-left shunt at atrial level resulting in hypoxemia, high

hematocrit and hyperviscosity syndrome. Their treatment remains controversial.

Aim: The purpose of this study was to assess the results of percutaneous closure of an atrial right-to-left shunt in pts with Ebstein's anomaly.

Methods: The records of pts were reviewed; only pts with low right ventricular and pulmonary artery systolic pressures were treated. The study focused on their condition before and after shunt closure studying clinical data, O₂ saturation and hematocrit.

Results: Since January 2002 six patients were treated. Their ages ranged from 10 to 56 years; all were male. Right ventricular systolic and/or pulmonary artery systolic pressures was under 15 mmHg in all. Three had previous episodes of stroke or transient ischemic attacks and two had severe polycythemia requiring plasmapheresis. Right-to-left shunting occurred via an ASD in four and via a PFO in two. Test occlusion of the right to left shunt was performed in all patients with a balloon catheter, revealing an increase in systemic O₂ saturation and right atrial pressures lower than 12 mmHg in all. Closure of the atrial shunt was achieved with an Amplatzer ASD or PFO device in five cases and with an Helex device in one. There were no complications.

Follow-up ranged between 2.5 and 36 months. Arterial O₂ saturations increased in all patients from 86.8% ± 1.9 to 97.8% ± 2.1 (mean ± SD). With device occlusion their hematocrit decreased from 55.2% ± 6.1 to 43.0% ± 1.2. Both plasmapheresis programs were discontinued. There were no neurological events at follow up. One patient developed signs of mild systemic venous congestion requiring diuretics for 3 months. All pts report a marked improvement in their effort tolerance.

Conclusions: Percutaneous closure of atrial right-to-left shunting in selected pts with Ebstein's anomaly may offer significant improvement, abolishing hypoxemia, hyperviscosity syndromes and preventing paradoxical embolization. This form of treatment should be considered more often in this group of pts.

O6-5

Off-pump replacement of the pulmonary valve in large right ventricular outflow tracts: a hybrid approach

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Objectives: Percutaneous pulmonary valve replacement (PVR) has recently been introduced and is under investigation in humans. This technique is, however, limited to patients with a right ventricular outflow tract (RVOT) that does not exceed 22-mm in diameter. We report our experience of off-pump PVR in animals with large RVOTs using a hybrid approach.

Methods and Results: 8 ewes were included in the protocol and equally divided into 2 groups. A left thoracotomy was firstly performed and the main pulmonary artery (PA) was banded using two radio-opaque rings with a diameter of 18-mm that allowed for further PVR. We then intended to implant a valved stent either percutaneously (group 1) or through a transventricular approach (group 2). All animals were sacrificed after valve implantation. The surgery allowed the pulmonary diameter to be reduced from 30 to 17.6-mm. The right ventricular pressure did

not significantly increase after the reduction of the PA diameter (25 vs. 36-mmHg). Subsequent PVR through a percutaneous or a transventricular approach was always possible without any requirement of extracorporeal circulation. All devices were successfully delivered inside the PA banding and were functioning perfectly at early evaluation.

Conclusions: Implantation of a pulmonary valve is possible in ewes through a hybrid approach when the RVOT exceeds 22-mm in diameter. This involves both surgeons and interventionists and allows for a staged procedure where the valvulation is performed percutaneously; or for a combined hybrid approach where the valve is implanted off-pump transventricularly during the same surgery.

O6-6

Intermediate-term outcome of neonates with critical aortic stenosis after balloon valvotomy in the Ross era

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Since 1994 we have treated critical aortic stenosis with primary balloon valvotomy (BV). Autograft replacement (Ross) is performed in patients with persistent stenosis and/or regurgitation. The purpose of this study was to (1) determine intermediate-term outcome of these patients; (2) evaluate the applicability of published criteria for stratifying to uni versus biventricular repair; (3) determine anatomic predictors of ultimate need for Ross.

Methods: Data were reviewed on all patients 1 month or younger who underwent BV between 1994 and 2004. Significance of potential outcome predictors was assessed by t or Fisher's exact test ($p < 0.05$). Survival probabilities were estimated from Kaplan-Meier curves.

Results: BV was performed in 29 newborns; 2 extremely premature infants were excluded from analysis. The 27 remaining patients underwent BV at 9 (0–31) days of age and were followed for a mean of 4.0 years (0.1–10 years). Survival was 95% at 1 and 5 years; 2 failed biventricular circulation.

Reintervention Was Common: 12 had repeat BV; 10 underwent subsequent Ross (7 after repeat BV) for stenosis (10) and regurgitation (7). Freedom from reintervention was 56% at 1 and 41% at 5 years. Both patients who failed to achieve a biventricular repair were correctly stratified by published criteria (CHSS and "Rhodes score"), but these criteria incorrectly predicted failure of biventricular circulation in 44% of cases. At last follow-up echocardiogram, all patients had normal ventricular function, the average mean gradient was 22 (0–48) mmHg, and aortic insufficiency was mild or less in 19 and moderate in 2. Measurements of aortic root, annulus, and left ventricular outflow tract (LVOT) made from baseline echo were significantly smaller in patients who had Ross compared with BV only. All patients with LVOT < 5 mm went on to Ross (7 of 10 Ross patients).

Conclusions: Primary BV followed, if necessary by a Ross procedure, allows for successful biventricular circulation, low mortality, and favorable intermediate-term outcome in critical aortic stenosis. LVOT diameter appears the most reliable predictor of subsequent Ross. New algorithms are needed for stratifying to BV versus Norwood.

Note: This Abstract was presented as a poster at the Scientific Session 2003, AHA.

Session 8: Imaging I

O8-1

Comparative study of phase-contrast magnetic resonance imaging and radionuclide lung perfusion imaging for assessing differential branch pulmonary blood flow

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Introduction: The assessment of patients with branch pulmonary artery stenosis is a frequent clinical scenario in paediatric cardiology. The functional significance of these stenoses is important, and is commonly defined using radionuclide lung perfusion scanning, and repeat investigations can be used to serially assess the affect of surgical or catheter-based interventions. However, radionuclide lung perfusion imaging is associated with a radiation dose of ~1 mSv; equivalent to approximately 50 PA chest radiographs or 6 months background radiation exposure in the UK. Magnetic resonance (MR) imaging can be used to assess both branch pulmonary artery anatomy and also pulmonary artery blood flow, in a minimally invasive fashion without exposure to x-ray radiation.

Purpose: To compare differential total right and left lung blood flow acquired with phase-contrast MR imaging with radionuclide lung perfusion measurements in children and adolescents with congenital heart disease and suspected branch pulmonary artery stenosis.

Methods and Materials: Radionuclide lung perfusion and MR imaging were performed in 12 children and adolescents with suspected unilateral branch pulmonary artery stenosis (mean age 12.1 ± 5.9 years, range 3.1–17.2 years). Radionuclide lung perfusion scanning was performed using Technetium-99m macro-aggregated albumin as part of routine clinical assessment. MR imaging was performed using a 1.5 T scanner (Symphony, Siemens, Erlangen, Germany) as part of routine MR assessment of congenital heart disease. A non-breath-hold, FLASH (Fast Low Angle Shot) gradient echo phase-contrast MR sequence was used to measure flow in the pulmonary trunk and either the right or left branch pulmonary artery. The lesser stenosed branch pulmonary artery was chosen for phase-contrast MR.

Results: Phase contrast MR imaging was successfully performed in all subjects. There was excellent correlation between the radionuclide and phase-contrast MR calculated total lung blood flow ($r = 0.98, p < 0.0001$) (Figure 1).

Conclusion: Phase-contrast MR is an accurate method for measuring differential total right and left lung blood flow. Thus, radionuclide imaging can be avoided, reducing the overall radiation burden to this group of subjects.

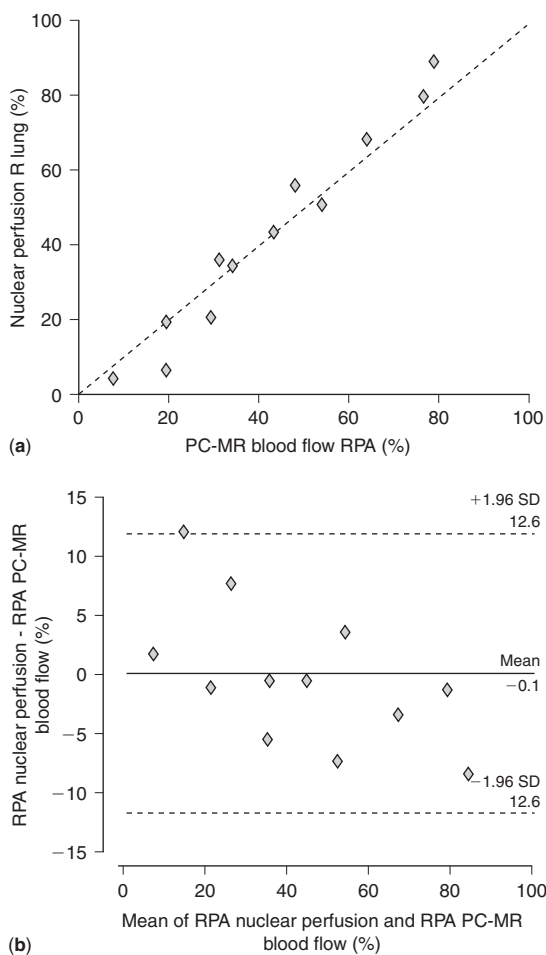


Figure 1. **a.** Plot of radionuclide vs. phase-contrast MR (PC-MR) measurement of blood flow to the right lung, showing good correlation. **b.** Bland-Altman plot for the same data.

O8-2

Remodelling of the right ventricle after early pulmonary valve replacement in children with repaired tetralogy of Fallot: assessment by cardiovascular magnetic resonance

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Background: Pulmonary regurgitation is a common residual finding after repair of tetralogy of Fallot with potential deleterious complications. Correct timing for pulmonary valve replacement (PVR) is crucial for preventing such complications. We sought to assess the remodeling of the right ventricle after early PVR in children, by using cardiovascular magnetic resonance (CMR).

Methods and Results: 20 children with severe pulmonary regurgitation and right ventricular (RV) dilatation, mean age 13.9 ± 3 years, underwent haemodynamic CMR evaluation 5.6 ± 1.8 months before and 5.9 ± 0.6 months after PVR. PVR was performed when the RV enddiastolic volume exceeded 150 ml/m², as measured by CMR. The time interval between primary repair and PVR was 12 ± 3 years. Postoperative CMR data demonstrated a significant reduction of the RV enddiastolic volume from 189.8 ± 33.4 ml/m² to 108.7 ± 25.8 ml/m² ($p < 0.0001$), of the RV endsystolic volume from 102.4 ± 27.3 ml/m² to 58.2 ± 16.3 ml/m² ($p < 0.0001$), and an improvement of the RV ejection fraction corrected for valve regurgitation, from 15.8 ± 7.2% to 32.3 ± 10.0% ($p < 0.0001$). An increase in left ventricular enddiastolic volume from 77.3 ± 10.1 ml/m² to 86.5 ± 13.4 ml/m² ($p = 0.003$), and a trend towards better left ventricular function were also observed.

Conclusions: Early PVR in childhood, performed when the RV enddiastolic volume exceeds 150 ml/m², results in prompt remodelling of the right and the left ventricles. CMR is the ideal tool for timing and assessment of the haemodynamic effects of PVR.

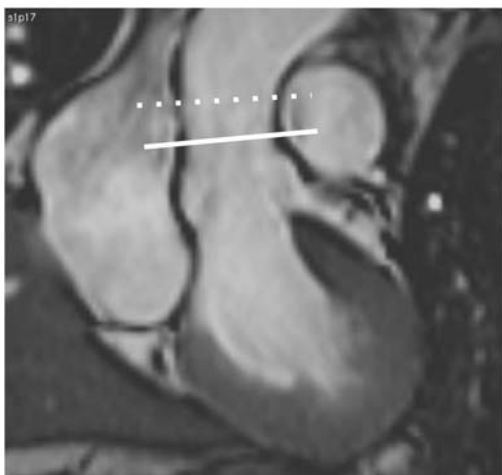
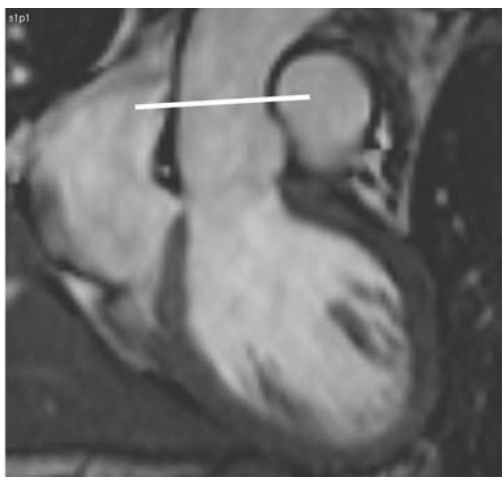
O8-3

Aortic autograft dilatation and impaired distensibility in Ross patients, assessed with MRI

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Introduction: The Ross procedure to replace a dysfunctional aortic valve is widely used in the paediatric population. However, recent reports indicate that dilatation of the autograft frequently occurs during follow-up. Therefore, we investigated the degree of dilatation and its effect on aortic root (AR) distensibility in Ross patients with MRI, with comparison to volunteers.

Methods: 10 Ross patients and 7 volunteers (matched for age and gender; mean (SD) age 18.1 (4.2) years) underwent MR-imaging on a 1.5 T scanner. Diameters of AR at the level of the annulus (ANN), sinus of Valsalva (SOV), sino-tubular junction (STJ) and the ascending aorta (AA) were assessed, with distensibility measurements at the level of the STJ. Distensibility is defined as: $\text{Dist (mmHg}^{-1}) = (A_{\max} - A_{\min}) / A_{\min} \times (P_{\max} - P_{\min})$. (With A_{\max} and A_{\min} maximal and minimal cross-sectional lumen area (mm²) respectively, and P_{\max} and P_{\min} systolic and diastolic blood pressure (mmHg) respectively.)



Two orthogonal scouts of the AR were obtained for planning of acquisition planes. Minimal lumen area was expected during isovolumetric contraction phase, while maximal area was expected

during peak of aortic flow. To determine optimal delay between R-wave and timing of acquisition of minimal and maximal area measurements, first flow-measurements at the AA were performed with a phase-contrast sequence. The acquisition planes were manually adjusted for both measurements, thus correcting for through-plane motion of the AR during contraction (Figure).

Distensibility was assessed using an SSFP-type sequence.

Results: A significantly decreased mean distensibility was observed in Ross patients compared to volunteers (Mann-Whitney U-test $p < 0.01$). Also, diameters at all levels were significantly larger in Ross patients (Mann-Whitney U-test $p < 0.05$ for all 4 levels).

Conclusion: This study demonstrated a significantly decreased distensibility of the AR as well as a significantly increased lumen diameter in Ross patients, compared to volunteers. Despite the overall good clinical results of the Ross procedure, the presence of dilatation in combination with decreased distensibility of the aortic autograft might constitute a better indication for reoperation in the future than the currently used parameter of increasing dilatation.

O8-4

Follow-up data on 100 PFO-patients after interventional occlusion with 5 different devices – a single center study based on transesophageal echocardiography

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Introduction: From 1998 to 2003 one hundred patients at the German Heart Center underwent successful interventional PFO-occlusion with 5 different devices Helex 43/100, Cardioseal 30/100, Starflex 16/100, Amplatzer ASD Occluder 11/100, Amplatzer PFO Occluder 8/100.

Aim: Purpose of this study was to evaluate the success of PFO occlusion by means of transesophageal echocardiography and look for patients neurological and cardiological sequela with a standardized questionnaire.

Patients/Methods: 100 patients (50 male and 50 female) were included in the study. Mean age at the intervention was 46 years, mean age at follow-up was 47 years. All patient records and questionnaires were included in the study.

Results: 35 patients had a simple PFO, 59 a combination of PFO and atrial septal aneurysm and 6 an ASD II. All patients had a cryptogenic cerebral stroke prior to occlusion. 1 patient died for non cardiac reason during follow up. 52/99 patients sent their questionnaire back to the clinic. Before device implantation 54 patients were on oral anticoagulation, 25 on antiplatelet therapy. After the procedure at follow-up 10 patients were still on oral anticoagulation, 30 patients were treated with antiplatelets. Cardiac dysrhythmia (atrial flutter/fibrillation) were documented in 6/100 cases. In 3/100 patients thrombotic formation on the device was suspected on TTE and proven by TEE. In all cases the therapy with oral anticoagulation/antiplatelets was proceeded. 80/99 patients had a follow-up TEE with a median of 7 month (mean 11 ± 10 m). Residual shunts could be demonstrated in 14/99 patients, right to left shunt in 5. Surgical device explantation with patch closure was done in 5/100 (2 due to recurrent

stroke and residual shunt on TEE (1 Cs, 1 Hx); 2 due to thrombotic formation on the device (2 Cs) and 1 due to multiple fractures of the device (Cs).

Conclusion: Follow-up of our patients with cerebral events after interventional PFO-occlusion was complicated in few cases by recurrence of neurologic events (2%), thrombotic formation (3%) and dysrhythmia (6%). Surgical device removal was done in 5/100. The question when interventional PFO occlusion is indicated still remains open.

O8-5

Right ventricular (RV) diastolic function after repair of tetralogy of Fallot (TOF) at rest and changes with stress: restrictive versus non-restrictive RV physiology

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Introduction: RV dysfunction is a problem in repaired tetralogy of Fallot. Diastolic dysfunction may precede systolic dysfunction. We assessed RV diastolic function in tetralogy of Fallot (TOF) at rest and during stress.

Methods: 36 patients with corrected TOF (age 16.3 ± 4.6 y) underwent MRI at rest and during dobutamine stress ($7.5 \mu\text{g}/\text{kg}/\text{min}$). Velocity encoded flowmaps were acquired of the tricuspid and pulmonary valve and time volume flow curves were derived. RV time volume change curves were reconstructed by summation of these curves. Indices of diastolic function were derived from the ventricular time-volume curves. End-diastolic forward flow (EDFF) and pulmonary regurgitation (PR) were measured on the pulmonary curve. A multi-slice, multiphase gradient echo volumetric dataset was acquired for determination of RV volumes.

Results:

Table 1. RV diastolic parameters. Changes between rest and stress.

Parameter	Rest Gr I	Stress Gr I		Rest Gr II	Stress Gr II	
AFF (%)	17.7(7.8)	25.0(12.7)	<0.01	34.5(11.0)*	33.7(9.2)**	n.s.
FF (%)	52.2(10.6)	47.2(10.0)	<0.01	38.6(6.5)*	41.6(9.2)	n.s.
PeFRc (sec^{-1})	4.2(0.7)	4.0(0.8)	<0.05	4.3(1.1)	3.9(0.9)	n.s.
PaFRc (sec^{-1})	1.9(0.7)	2.5(0.9)	<0.001	3.5(1.1)*	3.4(1.2)**	n.s.
E/A-ratio	2.6(1.2)	1.9(1.1)	<0.001	1.2(0.3)*	1.3(0.5)**	n.s.
Dtc	25.5(7.0)	33.9(10.6)	<0.001	30.0(11.8)	31.0(8.9)	n.s.

* difference between group I and II at rest

** difference between group I and II during stress

PeFRc = peak early filling rate normalised for RVSV, PaFRc = normalised peak atrial filling rate, FF = filling fraction (first third diastole), AFF = atrial filling fraction, Dtc = E-wave deceleration time normalised for RR-interval, E/A-ratio = PeFR/PaFR.

25 patients showed EDFF (restrictive RV) (group I). EDFF was $5.3 \pm 3.3\%$ of total pulmonary forward flow. Eleven patients showed no EDFF (non restrictive RV) (group II). In both subgroups E-wave deceleration time was prolonged.

Between Subgroup Differences: At rest and during stress PaFRc and AFF were higher and E/A-ratio was lower in group II.

Within Subgroup Changes During Stress: In subgroup I AFF, PaFRc and Dtc increased, while FF, PeFRc and E/A-ratio decreased. Group II showed no changes.

Furthermore EDFF (ml) was positively correlated with PR (ml) ($r = 0.60$), RVEDV (ml/m^2) ($r = 0.44$), RVESV (ml/m^2) ($r = 0.41$) and length of follow-up ($r = 0.52$).

Conclusions: Both TOF patients with restrictive and non restrictive RV physiology show signs of impaired RV relaxation at rest. During stress this impairment in restrictive patients becomes more pronounced, while non restrictive patients show no pattern change. Restrictive RV physiology becomes more pronounced (amount of EDFF increases) with follow up duration, amount of PR and RV dilatation.

O8-6

Visualization of complex pulmonary blood supply with multidetector computed tomography

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Introduction: Precise visualization of the pulmonary vasculature is basis for adequate treatment of patients with pulmonary atresia and ventricular septal defect (PA-VSD). So far major aorto-pulmonary collateral arteries (MAPCA) have been visualized by selective injections of contrast agent in the catheterization laboratory.

Methods: Eight patients (age 4 weeks to 27.8 years) with PA-VSD and MAPCAs underwent multidetector computed tomography (MDCT) and cardiac catheterization. MDCT was performed with a Somatom Sensation (16 detectors, collimation 0.75 mm, 80 kV, 98 eff. MAs, voxel size $0.5 \times 0.5 \times 0.6$ mm, $n = 6$, or 64 detectors, voxel size $0.4 \times 0.4 \times 0.4$, $n = 2$) after peripheral injection of contrast agent (Imeron 400). The thorax and upper abdomen were imaged within 8 to 15 seconds. After semiautomatic segmentation aorta, pulmonary arteries and aorto-pulmonary vessels were displayed as a 3D model by colour coding each vessel separately (DKFZ OrgaNicer, Version 1.0.3). MDCT and angiographic data were analysed independently by two observers describing origin, course, intrapulmonary anastomosis of each vessel and measuring vessel diameters independently. Using Spearman's correlation and a paired t-test interobserver variability and correlations between MDCT and angiographic data were assessed. A p-value <0.05 was considered as statistically significant.

Results: Pulmonary arteries ($n = 8$), aorto-pulmonary shunts ($n = 2$), a right ventricular to pulmonary artery conduit and origin, course and intrapulmonary connections of all MAPCAs ($n = 22$) were described correctly compared to angiographic data. Measurements of vessel diameters ($n = 67$) in MDCT datasets by two independent observers correlated well ($r = 0.96$) and were statistically not significantly different ($p = 0.29$). Comparing MDCT vessel diameter measurements and angiographic data ($n = 55$) similar results are shown ($r = 0.96$, $p = 0.73$). Bland-Altman analysis of MDCT versus angiographic data ($n = 55$) are displayed in Figure 1.

Conclusions: Using 3D imaging software complex pulmonary blood supply in infants and adults with congenital heart disease can be accurately imaged with high resolution MDCT within 8 to 15 seconds. Peripheral intravenous injection of contrast agent and radiation is necessary. As being less invasive than cardiac catheterization this technique may help to reduce the number of cardiac catheterisations in this group of patients or guide interventional or surgical therapy.

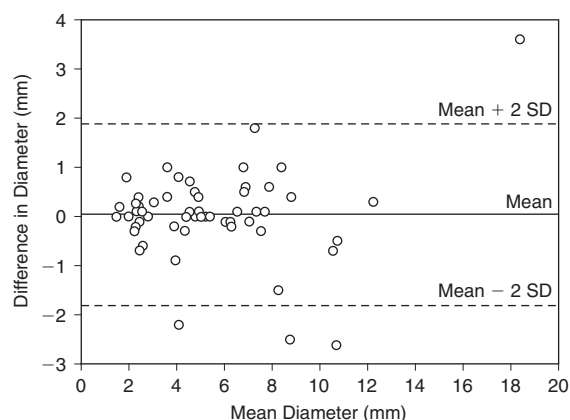


Figure 1. Bland–Altman analysis of the agreement between MDCT and X-ray angiography vessel diameter measurements ($n = 55$).

Session 9: Dysrhythmias

O9-1

Non-contact mapping and radiofrequency catheter ablation of fast and hemodynamic unstable ventricular tachycardia after surgical repair of tetralogy of Fallot

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Introduction: In patients after surgical repair of tetralogy of Fallot the electrophysiological mechanism of ventricular tachycardia (VT) are based on reentrant circuits around scars or prosthetic material. Due to hemodynamic instability during tachycardia conventional mapping techniques are not applicable in most of these patients. Aims of electrophysiological study (EPS) are identification of the arrhythmogenic substrate, induction of linear radiofrequency lesions, non-inducibility of VT and proof of conduction block along the induced lesion lines.

Patients and Methods: Since 10/2001, 9 patients after surgical repair of tetralogy of Fallot (mean age 28 years) underwent EPS and radiofrequency ablation for hemodynamic unstable VT using the non-contact mapping system (Esite 3000). The multielectrode balloon array was introduced in the right ventricle, endocardial anatomy was reconstructed using the Enguide signal and activation was recorded during sinus rhythm and induced VT (mean cycle length 280 msec).

Results: Based on the analysis of color-coded isopotential maps and unipolar virtual electrograms, individual ablation strategies were developed. Linear radiofrequency current lesion lines (70°C, 50 W) were induced during sinus rhythm between areas of residual conduction within scar tissue ($n = 5$), between scar tissue and the tricuspid valve annulus ($n = 2$), and between the VSD patch and the tricuspid valve annulus ($n = 1$). In one patient focal ablation in the right lateral outflow tract was performed. Mean duration of energy delivery was 780 sec. In all 9 patients, VT was not inducible after energy delivery. Pacing along the induced lesion lines proved complete conduction block in 8 patients. Mean fluoroscopy time was 60 min, mean duration of the study was 7.3 hours. No complications were noted. During follow-up (mean 27 months) 7 patients are in sinus rhythm, an implantable cardioverter defibrillator was implanted in one patient, and one patient had recurrence of VT with a different cycle length.

Conclusions: In patients with inducible fast and hemodynamic unstable VT after surgical repair of tetralogy of Fallot the non-contact

mapping and individual induction of linear radiofrequency lesion lines allowed for an accurate assessment of reentrant circuits and curative treatment. Indication for implantation of an implantable cardioverter defibrillator in these patients is still undetermined.

O9-2

Prevention of atrial tachycardia: cryoablation to block conduction between the right atriotomy and tricuspid annulus is feasible and safe

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Introduction: Atrial tachycardia is a serious problem after surgery for congenital heart disease. We observed that typical atrial flutter and incisional atrial tachycardia represent 79% of tachycardias after the right atriotomy. Prevention of these tachycardias has not been systematically studied.

Methods: The subjects of this prospective feasibility study are 15 consecutive adult patients undergoing corrective surgery for congenital heart disease. We perform peroperative prophylactic 1-minute cryoablation connecting the right atriotomy with tricuspid annulus anteriorly and crista terminalis posteriorly. These two lines, if complete, should make the circuits of both typical atrial flutter and incisional atrial tachycardia impossible. Conduction time between two epicardial electrodes placed on both sides of the line between the incision and tricuspid annulus is measured on the second postoperative day. Electrophysiology study and coronary angiography are performed three month after the operation.

Results: Conduction time between the epicardial electrodes could be measured in 12 out of 13 patients operated until today. Electrophysiology study has already been performed on 8 patients; it showed block of conduction in 7 and no block in 1. All patients with block had conduction time at least 120 ms and the patient without block had conduction time 90 ms. Conduction time was at least 145 ms in 3 out of 5 patients, who have not yet had catheterization; the other two patients had conduction times of 100 and 60 ms. Minimal temperature during cryoablation formation was below -155°C (until -161°C) in 8 patients and these had conduction block or conduction time of at least 145 ms. Four patients had minimal temperature above -149°C ; one of them had no block, two had conduction time of 100 and 60 ms, and only one had block. No lesion of the right coronary artery was detected either clinically or at coronary angiography. In summary, minimal temperature below -155°C and conduction time at least 120 ms was 100% predictive of block.

Conclusions: Creation of a complete line of block between the tricuspid annulus and right atriotomy is feasible without adverse effects. Experience with the device and technique is needed to achieve 100% success rate.

O9-3

Predictors of left ventricular remodeling and failure in right ventricular pacing in the young

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Introduction: Permanent right ventricular (RV) pacing may lead to significant left ventricular (LV) remodeling and failure. Risk factors for such adverse outcome in a pediatric population have not been identified yet.

Methods: Consecutive pts with either non-surgical (N = 50, group A) or surgical (N = 41, group B) complete AV block (CAVB) who underwent pacemaker implantation between 1984–2003 at a mean age of 7.7 ± 5.7 yrs were evaluated by echocardiography prior and immediately after the procedure and after a mean follow-up of 6.6 ± 4.4 yrs. All pts had 100% ventricular pacing from either RV apex (N = 56), RV septum (N = 17) or epicardial RV outflow tract (RVOT) (N = 18).

Results: LV enddiastolic diameter (LVEDD) decreased in group A (from a median of 115 to 103% of normal, $p = 0.005$) and did not change in group B (from a median of 103 to 107% of normal, $p = \text{NS}$) during follow-up. LV shortening fraction (SF) decreased in both group A (from a mean of 0.41 to 0.34, $p < 0.001$) and group B (from a mean of 0.38 to 0.31, $p < 0.001$). In groups A and B combined, percentage of pts with LV dilatation (LVEDD > normal + 2SD) and dysfunction (SF < 0.26) increased from 0% prior to implantation to 2.0% immediately after the procedure and to 13.2% (symptomatic as NYHA II–IV in 8.8%) at last follow-up ($p = 0.001$). Lower age at implantation ($p = 0.009$), RVOT pacing ($p = 0.003$), DDD pacing ($p = 0.008$), longer QRS duration ($p = 0.032$) and lower early postimplantation SF ($p = 0.037$) were significant univariate predictors and age at implantation < 2 years (OR = 23.8, CI 3.3–166.7, $p = 0.002$) and QRS duration ≥ 160 ms (OR = 27.0, CI 2.2–333.3, $p = 0.011$) multivariate predictors of LV dilatation and dysfunction. Etiology of CAVB and pacing duration did not show any significance.

Conclusions: RV based pacing leads to a significant decrease in global LV systolic function irrespective of CAVB etiology. Age at implantation < 2 years and QRS duration ≥ 160 ms are significant multivariate risk factors for LV remodeling and failure.

O9-4

Evolution of left ventricular function in pediatric patients with permanent right ventricular pacing with and without structural heart disease

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Introduction: Chronic right ventricular (RV) pacing may have detrimental effect on left ventricular (LV) function and may promote to heart failure in adults. The effect of chronic RV pacing on left ventricular performance is not well studied in a pediatric population.

Aim: The aim of this retrospective study was to assess the evolution of LV function in a pediatric pacemaker population with and without structural heart disease (HD).

Methods and Results: 98 pediatric patients (59 males) were studied retrospectively. 42 patients had pacemaker indication without structural heart disease. 25 out of the remaining 56 patients had isolated and the others complex congenital malformation. Patients were distributed in six age groups (group I: < 1 yr, group II: 1–2 yrs, group III: 3–4 yrs, group IV: 5–7 yrs, group V: 8–11 yrs, group VI: 12–15 yrs) and were followed up for an average of 58.69 ± 45.23 months (ranging: 3–188.5 months) with ECG and transthoracic echocardiography. LV fractional shortening (FS) was used as a marker of LV function. LV FS did not change statistically in the age groups (group I: 0.43 ± 0.09 , group VI: 0.39 ± 0.08 ; $p = \text{NS}$). When the progression of LV FS was assessed in the subgroups according to the presence or absence of structural HD, there could be only tendencies observed (isolated: group I: 0.51 ± 0.06 , group VI: 0.31 ± 0.09 , $p = \text{NS}$; complex: group I: 0.42 ± 0.06 , group V: 0.33 ± 0.06 , $p = \text{NS}$).

Conclusion: Chronic RV pacing in pediatric patients with and without structural HD does not necessarily results in decline of LV function.

O9-5

Fracture of epicardial pacing leads: not uncommon, and difficult to predict!

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Objective: Epicardial pacing leads in children are submitted to progressive tension during growth and to multiple cardiac and respiratory movements, leading to metal fatigue and lead fracture. Such sudden loss of paced rhythm may lead to catastrophic events, especially if there is no adequate underlying escape rhythm. This study was set to determine the incidence, time frame, predisposing factors and predictability of lead fracture.

Methods: Retrospective study. From 1969 until 2004 we implanted 235 epicardial pacing leads in 116 patients (age 0–59 yr, mean 8.0 ± 9.7 , median 4.8 yr; 1–7 leads/pt, median 2) during 127 operations (1–4 leads/operation, median 2). Twenty-seven leads were excluded as they had never been connected to a pacemaker. All patients were regularly followed with frequent pacemaker controls. All measurements and clinical events suggesting a lead fracture were recorded.

Results: In 207 leads a total of 848 years of follow-up was obtained (0–27.7 yr/pt, mean 4.2 ± 4.7 yr/pt, median 2.8 yr/pt). Fourteen lead fractures were observed. Four patients died suddenly; in these 4 patients, a lead fracture appears the probable cause of sudden death. The 18 fractures occurred 4.9 ± 4.8 years (range 0.9–18.7 yr, median 3.2 yr) after implantation. In 1 patient the fracture occurred within 10 days after a blunt abdominal trauma. Restoration of pacing was obtained in 14 patients. In 5 patients a previously implanted reserve lead could be used (through programming or surgical connection). A fractured lead was repaired in 4 cases; in the other patients a new system was implanted. No follow-up data (such as serial impedance measurements, pacing thresholds, chest XRs, patient growth, ...) could predict imminent lead fracture.

Conclusions: In our experience fracture of an epicardial lead is more common than fracture of an endocavitary lead. Prediction of lead fracture seems to be impossible.

Therefore, especially in patients without an adequate escape rhythm, if physically possible, we currently prefer implanting 2 ventricular leads connected to a biventricular DDD CRT pacemaker. In small children, where VVI pacing was the option, we have used a small size DDD pacemaker and two ventricular leads.

O9-6

Left heart atrial and ventricular epicardial pacing through a left lateral thoracotomy in children: a safe approach with excellent functional and cosmetic results

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Objectives: Left heart atrial and ventricular epicardial pacing through a left lateral thoracotomy is an alternative approach for lead insertion in children, avoiding venous access complications and right ventricular stimulation, without compromising sporting or musical activities. We analysed the survival and performance of

left atrial and left ventricular epicardial pacing leads, and present mid-term follow-up data.

Methods: Bipolar steroid eluting pacing leads (Medtronic CapSure Epi 4968) were implanted in 41 children, aged 8.6 ± 5.1 years. Pacing systems included 34 DDDR and 7 VVIR. Pacing leads were inserted through a muscle-sparing left lateral thoracotomy, and sutured to the left atrium and to the left ventricle. The generators were buried behind the abdominal muscles or between the thoracic muscle layers. Congenital heart disease with previous cardiac surgery was present in 25 children. Indications for pacing were postoperative heart block ($n = 14$), sinus node disease ($n = 13$), congenital heart block ($n = 9$), and various ($n = 5$). Threshold values and measured data were obtained at 6-month intervals. The mean follow-up was 3.8 ± 2.9 years.



Results: There was no mortality or major morbidity, with excellent functional and cosmetic results. Lead survival was 94% and 86% for atrial leads, and 97% and 86% for ventricular leads, at 1 and 5 years, respectively. There were 5 reoperations for lead fracture, and 1 patient required reprogramming for atrial lead dysfunction. In the absence of acute lead failure, mid-term follow-up shows very satisfactory and stable lead performance.

	1 year	5 years	
Atrial impedance (ohm)	636 ± 87	709 ± 103	$p = 0.01$
Atrial threshold (V @ 0.5 ms)	1.1 ± 0.6	1.3 ± 0.5	ns
Atrial sensing (mV)	3.4 ± 1.5	3.7 ± 1.7	ns
Ventricular impedance (ohm)	656 ± 168	716 ± 194	ns
Ventricular threshold (V @ 0.5 ms)	1.3 ± 0.9	1.3 ± 0.7	ns
Ventricular sensing (mV)	10.1 ± 4.8	10.8 ± 4.4	ns

Conclusions: Left heart atrial and ventricular epicardial pacing leads inserted through a left lateral thoracotomy demonstrate a high probability of survival, with favorable pacing characteristics, and optimal sensing thresholds at mid-term follow-up. Epicardial left heart pacing is reliable, and easy access can be achieved through a cosmetic and functional muscle-sparing left lateral thoracotomy.

Session 10: General Paediatric Cardiology I

O10-1

Multivariate risk analysis of early cardiovascular changes in obese children

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Introduction: Obesity in adults tends to be the most important cause of cardiovascular morbidity and mortality in the industrialized

countries. There is evidence that childhood obesity leads to adult obesity and cardiovascular disease mainly because of increased risk factors (RF). Based on impaired flow-mediated vasodilation (FMD) and increased intima-media thickness (IMT), surrogate parameters of atherosclerosis, it is possible to correlate cardiovascular RF with early vascular wall changes in children. This study investigated whether obese children already present vascular wall changes and if these relate to traditional and new cardiovascular disease RF in a multivariate regression analysis.

Methods: We examined 54 obese children (aged 10 to 17 years) versus 55 control subjects. All children underwent identical screening, with a broad RF profile, FMD/IMT and echocardiographic measurements.

Results: Obese children presented significantly impaired FMD ($4.29 \pm 2.5\%$ versus $10.2 \pm 2.9\%$, $p < 0.001$) and higher IMT values than the controls (0.49 ± 0.07 mm versus 0.36 ± 0.05 mm, $p < 0.001$). Obese children and controls showed significant differences in a number of RF (blood pressure during rest and exercise, physical fitness, left ventricular mass, size of left atrium (LA), triglycerides, fibrinogen, insulin resistance, etc.). By multivariate regression analysis abnormal vascular status (FMD $< 5\%$, IMT > 0.46 mm) was independently associated with body mass index, high body fat content, arterial hypertension, LA > 3 cm, decreased physical fitness (Wmax, anaerobic threshold), fibrinogen > 3.5 g/l, triglycerides > 1.2 g/l, birth weight > 4000 g and inadequate results in school sports activities.

Conclusions: This study documents early vascular wall changes in obese children. Arterial hypertension (during rest and exercise), low physical fitness and higher levels of fibrinogen and triglycerides seem to predict the risk in the sense of an early development of atherosclerosis in obese children. FMD and IMT combined with broad RF screening are helpful tools to identify children at high risk from atherosclerotic disease and to monitor vascular development during follow-up and therapeutic measures.

O10-2

Arterial stiffness and reactivity after successful repair of coarctation: impact of aortic arch geometry

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Introduction and Objectives: Vascular dysfunction has a high prevalence after coarctation (CoA) repair. There is, however, a wide overlap of the individual values of endothelial function and arterial stiffness parameters between patients and controls. The relationship between conduit arteries function and the development of arterial hypertension remains poorly understood. Systolic hypertension after CoA repair has been related to an abnormal gothic geometry of the aortic arch in the absence of other residual anatomic anomalies. We hypothesized that abnormal geometry of the aortic arch could promote its development through increased vascular stiffness.

Methods and Results: We studied 63 normotensive patients (age 15.9 ± 6.3 years; blood pressure $116.2 \pm 11.7/67.6 \pm 8.9$ mmHg) who had undergone CoA repair without residual obstruction. These subjects were matched sex-age and blood pressure to 63 controls (age 14.0 ± 6.0 years; blood pressure $113.8 \pm 11.9/66.6 \pm 5.7$ mmHg). Using MRI, we assessed the aortic arch shape and calculated the left ventricular mass index (LVMI). Three categories of aortic arch shape were defined based on the global geometry of the aortic arch: gothic, crenel and normal. Using a high-resolution echographic technique, we assessed the intima-media

thickness (IMT), the stiffness (Einc, beta-stiffness index) and the distensibility of the common carotid artery. Endothelium and non-endothelium brachial artery reactivity with respectively flow-mediated dilatation (FMD), and dilatation after sublingual glyceryl trinitrate (GTN) were evaluated.

Gothic arch was associated with higher IMT (0.65 ± 0.05 mm, $P < 0.0001$), higher stiffness ($E_{inc} = 2.3 \pm 0.4$ mmHg $\cdot 10^3$, $P < 0.0001$; beta stiffness index = 2.8 ± 0.52 , $P < 0.0001$), lower distensibility (4.4 ± 2 mmHg $^{-1} \cdot 10^{-3}$, $P < 0.0001$), higher LVMI (110 ± 15.5 g/m 2 , $P = 0.0007$), and lower brachial reactivity (FMD = $4.7 \pm 2.1\%$, $P < 0.01$; GTN = $14.4 \pm 5.0\%$, $P < 0.0001$), when compared to crenel and normal geometries, and to control subjects. CoA patients with normal geometry had higher stiffness ($E_{inc} = 1.3 \pm 0.37$ mmHg $\cdot 10^3$, $P < 0.0001$; beta stiffness index = 2.1 ± 0.33 , $P < 0.0001$), lower distensibility (9.6 ± 3 mmHg $^{-1} \cdot 10^{-3}$, $P < 0.0001$), and lower brachial artery reactivity (FMD = $6.9 \pm 0.9\%$, $P = 0.0002$; GTN = $22.9 \pm 5.3\%$, $P < 0.0001$) compared to control subjects. There was no difference in IMT between CoA patient with normal geometry and control subjects.

Conclusion: Endothelial dysfunction and increased vascular stiffness are common features after successful CoA repair. An abnormal gothic geometry of the aortic arch is an aggravating factor that accelerates vascular remodeling and dysfunction in this condition.

O10-3

B-type natriuretic peptide in patients with congenital heart disease

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B-type natriuretic peptide (BNP) is a cardiac hormone secreted mainly by the ventricles with diuretic, natriuretic, and vasodilatory properties. Measurement of plasma BNP levels (or the N-terminal fragment of proBNP) is increasingly used in adults with congestive heart failure. Recently, we have reported normal concentrations of both peptides from infancy to adolescence. The purpose of this study was to evaluate the impact of plasma BNP on patients with congenital heart defects.

BNP plasma concentration was measured by sandwich immunoassay (triate BNP assay, Biosite[®]) in 264 consecutive patients (aged 0–21 years) with atrial or ventricular septal defect or persistent ductus arteriosus ($n = 58$), isolated left or right heart obstruction ($n = 65$), tetralogy of Fallot ($n = 33$), functionally univentricular heart ($n = 76$), or impaired left ventricular function ($n = 32$). The BNP levels were compared to age- and gender-specific normal values from healthy subjects ($n = 195$), to hemodynamic data obtained at cardiac catheterization, and to echocardiographic data.

Plasma BNP increased significantly with decreasing left ventricular shortening fraction ($r = -0.83$; $p < 0.001$). In patients with left-to-right shunt, plasma BNP was positively correlated to shunt volume ($r = 0.66$; $p < 0.001$), systolic right ventricular pressure ($r = 0.69$; $p < 0.001$), mean pressure of the pulmonary artery ($r = 0.66$; $p < 0.001$), and pulmonary resistance ($r = 0.59$; $p < 0.001$). Patients with functionally univentricular heart had higher plasma BNP levels than normal subjects, but there was no difference between patients before and after bidirectional Glenn operation or complete cavopulmonary connection. Plasma BNP levels in patients with aortic or pulmonary valve stenosis were slightly increased (mean standard deviation score + 0.91; $p < 0.001$), but there was no correlation between BNP and invasive pressure gradient nor extent of ventricular hypertrophy. In patients with tetralogy of Fallot, BNP was in the normal range.

Plasma BNP correlates well with systolic ventricular function and increasing pulmonary pressure and resistance due to left-to-right shunt. The data on patients with tetralogy of Fallot, pulmonary or aortic valve stenosis and functionally univentricular heart indicate, however, that there is no straight correlation between plasma BNP and pressure or volume load of the ventricles.

O10-4

Predictors of spontaneous closure of secundum atrial septal defect in children – a longitudinal study

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Introduction: The natural course of secundum atrial septal defect (ASD) in children is not well described. Objective to the current study was to assess the rate of regression of ASD in children and to determine predictors of spontaneous closure.

Methods: Retrospective cohort study of consecutive children diagnosed with isolated ASD (>3 mm diameter, no additional congenital heart disease, no syndrome) at a tertiary care pediatric cardiology centre. Patients were followed by two dimensional echocardiography, performed according to a standardized examination protocol. **Results:** The study population consisted of 224 children. Median age at diagnosis was 5 months (minimum 0 months to maximum 13.9 years). Atrial septal defect diameter at diagnosis was 4 to 5 mm in 86 (38%), 6 to 7 mm in 60 (27%), 8 to 10 mm in 43 (19%), and >10 mm in 35 (16%) patients. Sixty-eight (30%) defects showed spontaneous closure at an age of median 4.2 years (7 months to 16 years) and another 60 (27%) defects decreased to a defect diameter of 3 mm or less at an age of 4.4 years (4 months to 10 years). Forty-five (20%) of ASD still had a diameter of >3 mm after an observation time of median 3.0 years (3 months to 9.4 years). Fifty-one (23%) of ASD had to be closed by surgery or device at an age of 4.5 years (8 months to 13.3 years).

Logistic regression revealed ASD diameter at diagnosis as the main predictor of spontaneous closure or regression < 4 mm. Atrial septal defects with initial diameters of 4 to 5 mm showed spontaneous closure in 53%, those with initial diameters of 6 to 7 mm in 28%, and those with initial diameters of 8 to 10 mm in 12%. Logistic regression also showed age at diagnosis to be independently associated with spontaneous ASD closure. Children of young age at diagnosis were more likely to experience spontaneous closure. Gender and observation time were not significantly associated with spontaneous ASD closure.

Conclusions: Fifty-seven percent of ASD in children showed spontaneous closure (30%) or regression < 4 mm (27%). Atrial septal defect diameter at diagnosis is the main predictor of ASD closure.

O10-5

Age-specific mortality rates in childhood hypertrophic cardiomyopathy

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Introduction: In hypertrophic cardiomyopathy (HCM) the annual mortality (sudden death) is higher in children than in adults, yet

many cardiologists recommend that screening asymptomatic children of parents with HCM need not take place until after puberty. The aim of the study was to establish the age groups at highest risk of sudden death.

Methods: Cohort study from six regional centres of paediatric cardiology, comprising children diagnosed in life as well as presenting with sudden death diagnosed at post mortem, $n = 139$.

Results: Below 20 years of age there were a total of 21 sudden deaths, but also two instances of resuscitated out-of-hospital ventricular fibrillation that were considered together with the sudden deaths, i.e. 23 in total. In addition there were 12 heart failure related deaths. All but two of the deaths occurred in children not receiving high-dose beta blockade, and as this treatment has previously been showed to reduce mortality in childhood HCM, the children receiving >4.5 mg/kg of propranolol (or corresponding doses of other beta-blockers) were not included in the calculation of age-specific mortality rates. One sudden death occurred in the first year of life, but apart from that they started to appear from age of 8 years onwards, with the highest annual mortality rate seen in 9-year-olds (10.0%). Analyzing in larger age bands highest rate is in 9–11.9-year-olds (7.4%; 95% CI 2.8 to 12.0%), intermediate in the 12–15.9 group (4.6%; 95% CI 1.5 to 7.7%), and a rate approaching that reported in young adults in the 16–19.9 years group (1.8%; 95% CI 0 to 3.95%). The mortality rate in 9–11.9-year-olds is significantly higher than in 16–19.9-year-olds ($p = 0.03$). Eight heart failure deaths occurred during the first year of life, giving an annual heart failure mortality of 27.6% during the first year of life in children not receiving high-dose beta-blockade.

Conclusions: The risk of unexpected sudden death is highest during the pre-pubertal growth spurt and in early puberty. Family screening with risk factor profile analysis ought to be carried out no later than 6–7 years of age in families with familial HCM.

O10-6

Aortic wall distensibility and stiffness index in neonates with coarctation of the aorta

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Introduction: Despite successful surgical correction morbidity of patients with coarctation of the aorta is increased. It is well known that patients even after successful surgical correction have impaired elastic properties of the prestenotic arteries, which might play a major role in the pathogenesis of these problems. To find out whether these abnormalities are primarily present in patients with coarctation or develop later on in life we studied 17 newborns before and early after surgery.

Methods: M-mode measurements of ascending and abdominal aortic diameters were performed and wall stiffness index and aortic distensibility were calculated using oscillometric blood pressure measurements of the right arm and leg. 17 patients with coarctation (mean age 20 ± 26 days, mean weight 3.6 ± 0.9 kg, mean length 52 ± 4 cm) were compared to 17 normal neonates (mean age 13 ± 7 days, mean weight 3.3 ± 0.4 kg, mean length 52 ± 2 cm) pre- and postoperatively (10 ± 6 days).

Results: Ascending aortic distensibility in the patients was significantly reduced preoperatively (79 ± 58 vs. 105 ± 36 ; $p = 0.03$) and postoperatively (65 ± 24 vs. 105 ± 36 ; $p < 0.005$). Pre- and postoperative ascending aortic stiffness index was also higher in patients (preoperative: 5.2 ± 4.4 vs. 2.7 ± 0.9 ; $p = 0.04$; postoperative: 4.0 ± 1.6 vs. 2.7 ± 0.9 ; $p < 0.005$). Elastic properties of the descending aorta did not differ either pre- or postoperatively compared to normals.

Conclusion: Our data suggest that elastic properties of the aorta in the prestenotic region of patients with coarctation are primarily impaired, even in neonates and seem to be unchanged early after successful operation. Surgical correction does not resolve inborn pathology of the prestenotic aortic vascular bed.

Session 11: Basic Science and Genetics

O11-1

Metformin, a possible approach to metabolic modulation of heart failure in children? Increase in mRNA expression of genes involved in fatty acid metabolism upon treatment with Metformin

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Introduction: Modulation of cardiac energy metabolism appears to be a means to improve cardiac function after ischemia/reperfusion damage. Children with congenital heart disease often suffer from acute cardiac failure after corrective operation involving extra-corporal circulation. The antidiabetic drug Metformin has been shown to reduce ischemia/reperfusion damage by myocardial infarction and increase survival in adult overweight type II diabetes patients. The actual mechanism by which Metformin influences cardiac metabolism is still an enigma. The aim of this study was to investigate the effects of Metformin on cardiac energy metabolism to gain further insight into the drug's mechanism of action.

Methods: Neonatal rat cardiomyocytes were cultured in medium containing 1% serum. After two days Metformin (5 mM), WY-14,643 (10 μ M), a specific activator of the transcription factor peroxisome proliferator activated receptor (PPAR α), or a combination of both were added for 48 h. mRNA expression of genes involved in cardiac energy metabolism (PPAR α , retinoid x receptor γ (RXR γ), acyl-CoA synthase (ACS), long chain acyl-CoA dehydrogenase (LCAD), 5'-AMP activated protein kinase (AMPK)) was determined by real time PCR and normalized for 18S rRNA. **Results:** Addition of Metformin significantly up regulated mRNA expression of PPAR α ($+323 \pm 30\%$; $p = 0.009$) and ACS ($+243 \pm 14\%$; $p = 0.002$). Treatment with PPAR activator WY-14,643 alone resulted in a significantly increased expression only of PPAR target genes ACS ($+478 \pm 21\%$; $p = 0.008$) and LCAD ($+96\% \pm 14\%$; $p = 0.004$). Upon addition of Metformin to WY-14,643 treated cultures, mRNA expression of ACS ($+767\% \pm 6\%$, $p = 0.02$) and LCAD ($+73\% \pm 13\%$, $p = 0.05$) increased even further. The expression of the PPAR co-factor RXR γ and putative PPAR modulator AMPK $\alpha 1$ and $\alpha 2$ was not changed significantly by Metformin, WY-14,643 or a combination of both. **Conclusion:** Our study demonstrates for the first time a specific effect of Metformin on the mRNA expression of the transcription factor PPAR α . We propose that this effect of Metformin may be responsible for the observed increment in mRNA expression of PPAR target genes (ACS, LCAD). Our data suggests that Metformin can modulate cardiac energy metabolism by increasing cardiac fatty acid oxidation through the PPAR pathway.

O11-2**Pretreatment of dexamethasone before cardiopulmonary bypass (CPB) upregulates intrahepatic synthesis of interleukin-10 via the transcription factors Sp1 and Sp3 and CCAAT/enhancer-binding protein**Q. Ma¹, M. Wöltje², K. Schumacher¹, M. Sokalska¹, J. Vázquez-Jimenez³, M.-C. Seghaye¹¹Pediatric Cardiology; ²Interdisciplinary Center for Clinical Research BIOMAT; ³Pediatric Cardiac Surgery; Aachen University of Technology, Aachen, Germany

Background and Aim: Interleukin-10 (IL-10) is an anti-inflammatory cytokine produced by a variety of cell types including Kupffer cells and hepatocytes. Recent study showed that IL-10 gene expression induced by endotoxin (LPS) in mouse macrophages is controlled by the cooperation of the promoter-selective transcription factors (SP) 1 and -3 as well as by CCAAT/enhancer-binding protein β (C/EBP β). Dexamethasone (Dex) has been recommended during cardiac surgery since it increases blood IL-10 levels during CPB reduces the release of proinflammatory mediators including TNF- α . In an experimental model of cardiac surgery, it reduces the production of iNOS and COX-2. This study was designed to identify the signaling pathways involved in intrahepatic overexpression of IL-10 induced by pretreatment by Dex before CPB.

Methods: Animals were treated with Dex (1 mg/kg) (n = 9) or with saline (n = 6) given intervenously before normothermic CPB. Samples of liver tissue were taken before and 6 hrs after CPB. IL-10 mRNA was assessed by competitive RT-PCR. Protein levels of IL-10, iNOS and COX-2 were assessed by Western blot. Phosphorylation of extracellular regulating kinase (ERK1/2) and of the inhibitory protein of nuclear factor-kB (IkB) as well as nuclear protein levels of C/EBP β were also detected by Western blot. Activation of Sp1 and Sp3, C/EBP β , NF-kB, and AP-1 were assessed by electrophoretic mobility shift assay with supershift. Liver tissue damage score was assessed by standard histology.

Results: Pigs treated with Dex showed significantly higher intrahepatic concentration of IL-10 and lower concentrations of iNOS and COX-2 than the others. The former also showed lower tissue damage score. This upregulation of IL-10 and downregulation of iNOS and COX-2 observed in the treated group was associated with a higher activation of Sp1 and Sp3 as well as C/EBP β . Moreover, levels of phospho-ERK1/2 and of C/EBP β in nuclear extract were significantly higher 6 h after CPB in pigs treated with Dex than in the others.

Conclusion: Our results show for the first time that Dex administration prior to CPB up-regulates IL-10 via Sp1 and Sp3 as well as throughout C/EBP β activation. This leads to attenuation of expression of iNOS and COX-2 and to hepatic protection.

O11-3**Hypertrophic cardiomyopathy in children; outcome of genetic screening**O. Havndrup¹, P.S. Andersen², M. Christiansen², J.R. Jacobsen³, L. Køber¹, H. Bundgaard¹¹Department of Cardiology, Rigshospitalet, Copenhagen, Denmark; ²Department of Clinical Chemistry, Statens Serum Institut, Copenhagen, Denmark; ³Department of Paediatric Cardiology, Rigshospitalet, Copenhagen, Denmark

Introduction: Familial hypertrophic cardiomyopathy (FHC) is caused by mutations in genes encoding cardiac sarcomere proteins. In the present study we evaluated the outcome of clinical vs. genetic screening of family members with specific focus on children with FHC and children (<18 years of age) identified as mutation carriers.

Methods: A consecutive cohort of 91 FHC probands from the departments of paediatric and adult cardiology and their families (460 persons) of Danish origin was evaluated including patient- and family histories, physical examinations, electrocardiogram and echocardiography. Mutation screening was performed by a combination of single strand conformation/heteroduplex analysis and direct sequencing.

Results: Four of the 91 probands were children or adolescents (5, 8, 14, 17 years of age). A total of 58 children were included from families with adult probands.

Two of the child probands (aged 8 and 14) had sarcomere gene mutations located to the cardiac myosin binding protein C (MYBPC3 – Asp230Asn and g2430delG). MYBPC3 mutations have previously primarily been associated with late onset FHC. No sarcomere gene mutations were identified in the remaining two child probands.

Among relatives 12 (21%) additional children carried a total of 13 mutations (5MYBPC3, 7MYH7 (5 β -myosin + 2 β -myosin rod domain), and 1MYL2 (regulatory light chain)). None of these children were symptomatic and none fulfilled major diagnostic criteria for FHC.

Based on the genetic analyses 26 (45%) children from families with a disease causing mutation could be reassured on their non carrier status. In the remaining 20 (35%) children no sarcomere gene mutations were identified in the probands of their families.

Conclusions: Only a minority of probands in a consecutively included cohort of FHC patients are children. Among child probands 50% were found to carry a sarcomere gene mutation (MYBPC3). Children identified as sarcomere gene mutation carriers by family screening were not identifiable by clinical screening. Genetic screening identifies the ~50% of children in whom the risk for developing FHC can be excluded. Thus, the extension of FHC family screening to include genetic analyses offers a marked diagnostic advantage as compared to clinical screening only.

O11-4**Fibronectin-binding proteins play a major role in the pathogenesis of S. aureus infections****such as endocarditis**R. Heying^{1,3}, J. van de Gevel³, Y.A. Que², P. Moreillon², H. Beekhuizen³¹Department of Pediatric Cardiology, Childrens University Hospital, Düsseldorf, Germany; ²Laboratory of Infectious Diseases, University Hospital of Lausanne, Lausanne, Switzerland; ³Department of Infectious Diseases, LUMC, Leiden, The Netherlands

Staphylococcus aureus is among the most important bacterial pathogens responsible for endocarditis. Essential for the infection process is the high propensity of S. aureus to colonize endovascular tissues. Our recent studies emphasize the significant contribution of vascular endothelial cells (EC) in the pathogenesis of endovascular S. aureus infections and demonstrate that interactions between S. aureus and human ECs induce a variety of proinflammatory and procoagulant endothelial responses.

In the present study we used our in vitro model for endocarditis to compare the individual roles of adhesion molecules expressed by S. aureus in these interactions and further to examine whether bacterial adherence mediated by these adhesions is sufficient to induce proinflammatory and procoagulant endothelial phenotype as well as monocyte adhesion.

Fibronectin-binding protein A (FnBPA) and B (FnBPB) as well as clumping factor A (ClfA) of S. aureus were constitutively expressed in the non-invasive gram-positive organism Lactococcus lactis by means of gene transfer. L. lactis piL253, carrying the empty

expression plasmid, was taken as a control showing no adherence to cultured human venous ECs and was therefore incapable of inducing changes in EC function.

Both FnBPA and FnBPB-expressing *L. lactis* transfectants adhered to cultured ECs (92% and 71% infected ECs after 1 h) and adhesion coincided with significant increases in surface expression of ICAM-1 and VCAM-1, which in turn supported monocyte adhesion. ECs produced IL-8 and expressed tissue factor (TF) and showed TF-mediated procoagulant activity. Prolonged (>24 h) incubation with these transfectants caused severe EC damage.

Slightly increased levels of adhesion were seen with the ClfA-expression transfectants (20% infected ECs after 1 h).

We conclude that *S. aureus* FnBPA and to a lesser degree also FnBPB, but not ClfA, adhesions confer invasiveness and pathogenicity to non-pathogenic *L. lactis* organisms and that bacterial-EC interactions mediated by FnBPA or FnBPB adhesions are dominant pathways to evoke inflammation, tissue damage and fibrin deposition at infected endovascular sites.

O11-5

P22phox subunit of NAD(P)H oxidase gene polymorphism C242T and erythrocyte antioxidant enzymes in Tetralogy of Fallot

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The aim of the present study was to evaluate the possible influence of P22phox C242T gene polymorphism on blood pressure and some markers of oxidative stress in children with tetralogy of Fallot (TOF). **Materials and Methods:** After TOF repair in late infancy or early childhood, 40 children (age 11.7 ± 3.3 years) were included in the study. A group of healthy children ($n = 28$) matched for age (11.6 ± 0.98 years) was also included for control. Protein-tyrosine-phosphatase of low-molecular-weight (PTP-LMW) and methemoglobin reductase (MHbRed) were measured by spectrophotometric methods. P22phox C242T gene polymorphism was determined by PCR-RFLP from DNA.

Results: Although without statistical difference, allele T frequency was lower in TOF group (20%) compared to control group (35.7%) ($p = 0.08$). The TOF group showed significantly lower values of protein-tyrosine-phosphatase of low-molecular-weight, particularly in carriers of the P22phox C242T CC genotype (148.3 ± 53.5 mmol/gHb/min) compared to controls (355.9 ± 134.6) ($p < 0.01$). Similar results were found for methemoglobin reductase, with carriers of the P22phox C242T CC genotype in the TOF group showing lower values (8.0 ± 3.8 mmol/g Hb/h) than controls (33.5 ± 9.1) ($p < 0.001$). No differences were found between groups concerning systolic blood pressure adjusted for age and according to genotypes. However, diastolic blood pressure was significantly lower in P22phox C242T allele T carriers in the TOF group ($78.2 \pm 11.5\%$ to 50th percentile) compared to controls ($93.1 \pm 14.9\%$ to 50th percentile).

Conclusions: It is possible that sustained oxidative stress in early life in TOF patients could condition activities of enzyme redox systems. TOF patients have significantly lower PTP-LMW and MHbRed activities compared to controls, with the lowest values observed in homozygous for the C allele compared to T allele carriers (CT + TT). These results suggest that TOF individuals with P22phox C242T CC genotype may be at a higher oxidative stress status than T allele carriers, which could have prognostic implications. However, long term follow-up of these patients seems to be necessary before definite conclusions can be drawn.

O11-6

Moderate hypothermia during cardiopulmonary bypass reduces intramyocardial expression of TNF-alpha via inhibition of AP-1

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Background and Aim: Moderate hypothermia during CPB inhibits intramyocardial TNF-alpha synthesis. Since the expression of TNF-alpha and other inflammatory mediators such as COX-2 and iNOS is regulated by the NF-kB and activator protein (AP)-1 pathways, this study was intended to analyze the effect of moderate hypothermia during CPB on these signaling pathways in the myocardium.

Methods: Twelve young pigs were randomly mounted on standardized CPB in moderate hypothermia or normothermia (temperature 28°C or 37°C, respectively, $n = 6$ each group). Myocardial probes were sampled from the right ventricle before, during and 6 hours after CPB. Messenger RNA encoding for TNF-alpha was assessed by competitive reverse transcriptase-polymerase chain reaction. Protein levels of TNF-alpha, inducible nitric oxide synthase (iNOS), and cyclooxygenase-2 (COX-2) were assessed by Western blot. Activation of NF-kB and phosphorylation of its inhibitory protein Ikb alpha, activation of AP-1 and phosphorylation of its complex c-Jun as well as of mitogen-activated protein kinase (MAPK) p38 were assessed by electrophoretic mobility shift assay with supershift and/or Western blot, respectively.

Results: Both TNF-alpha-mRNA and -protein were detected as soon as 30 minutes after initiation of bypass in both groups. At that time, expression of TNF-alpha-mRNA and protein levels tended to be lower in pigs operated on under moderate hypothermia than those operated on under normothermia ($p < 0.1$, respectively). Moreover, pigs operated on under moderate hypothermia showed lower expression of TNF-alpha-mRNA and protein levels than the others 6 hours after CPB ($p < 0.05$, respectively). The course of the expression of COX-2 but not that of iNOS during and after CPB paralleled that of TNF-alpha. The activation of p38 MAP kinase and of its downstream effector AP-1 was lower in animals operated on in hypothermia than in the others ($p < 0.05$, respectively). In contrast, phosphorylation of Ikb alpha and nuclear factor-kB activity were similar in both groups.

Conclusion: This study shows that the inhibition of the intramyocardial expression of TNF-alpha and of its secondary mediator COX-2 related to moderate hypothermia during CPB is associated with the inhibition of p38 MAP kinase-AP-1 but not of the NF-kB pathway.

Session 12: General Paediatric Cardiology II

O12-1

Pulmonary atresia with intact ventricular septum. Determinants for subsequent biventricular repair

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Management strategy of pulmonary atresia with intact ventricular septum (PAIVS) is usually determined by morphology of the right ventricle (RV) and coronary circulation. The purpose of this work is to report one centre experience and to assess factors for subsequent biventricular repair.

From January 1990 to September 2003, 35 consecutive patients were referred for PAIVS. Diagnosis was confirmed on echocardiography showing a tripartite RV ($n = 27$), a bipartite RV ($n = 6$) and unipartite RV ($n = 2$). Coronary artery fistulas were suspected in 13 patients. Interventional perforation of the pulmonary valve was attempted in 21 patients. Procedure was successful in 10 pts and failed in 11. These children underwent neonatal surgery: pulmonary valvotomy ($n = 9$) and creation of a Blalock-Taussig anastomosis ($n = 2$). Fourteen other patients were operated as a primary procedure: surgical valvotomy ($n = 3$) and Blalock anastomosis alone ($n = 11$). Four patients died in neonatal period (1 after successful interventional perforation, 3 after creation of a shunt). Five other patients with a shunt died suddenly during follow-up. At latest follow-up, 16 patients evolved to a biventricular repair with 7 of them requiring complementary procedures after initial valvotomy; 10 other patients evolved to a cavo-pulmonary connection, including 4 patients who had undergone initially a strategy of biventricular repair. The only predictive factors noticed at birth in favour of subsequent biventricular repair were: larger diameter of the tricuspid annulus on echocardiography ($10,9 \pm 2,25$ mm versus $6,34 \pm 1,74$ mm, $p = 0,0007$) or on angiography ($10,07 \pm 2,09$ mm versus $8,04 \pm 2,42$ mm, $p = 0,039$), and the morphology of the right ventricle ($p = 0,0011$) with more tripartite, less bipartite and no unipartite right ventricle in the biventricular group.

To conclude, biventricular repair could be achieved in about half of patients presenting with PAIVS. For the remaining patients, Fontan circulation is mandatory.

O12-2

Transcatheter device versus surgical closure of ventricular septal defects: a clinical decision analysis

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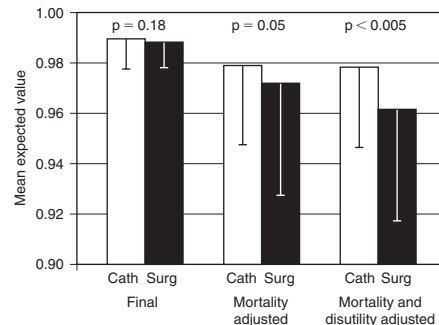
Introduction: Device closure of ventricular septal defects (VSDs) is gaining popularity versus surgical closure, despite the absence of randomized trials. Evidence-based medicine seeks to integrate the best research evidence with clinical expertise and patient values in the context of clinical decision-making. We sought to compare device versus surgical closure of VSDs using a clinical decision analysis.

Methods: A decision model representing plausible outcomes was constructed for surgery and device closure. Probabilities of outcomes were derived from Medline search from published reports regarding 342 device and 605 surgical closures. Relative values or preferences for outcomes were obtained through standard gamble interviews of pediatric cardiology physicians, trainees and surgeons, as well as some lay persons. Probabilities were multiplied by values and summed across the different outcomes to give final (probability weighted) values (ranging from 0 or certain death to 1 or perfect procedure). Final values were further adjusted for procedural disutility (magnitude of preference for a specific procedure type) and perceived procedural mortality. Sensitivity analyses were performed to determine threshold values that would alter the preferred decision.

Results: The initial preference before analysis was for device for 39 respondents (89%) and surgery for 5 (11%). The inherent difference in value between a perfect surgery versus perfect device (disutility of surgery) was equivalent to a mean risk of death of $+1.2 \pm 2.2\%$. The final values from decision analysis were initially equivalent, with a mean final score of 0.990 ± 0.012 for device versus 0.988 ± 0.009 for surgery ($p = 0.18$). Values adjusted for estimated mortality tended to favor device, with a mean of 0.979 ± 0.032 versus 0.971 ± 0.032 for surgery ($p = 0.052$).

When the values were further adjusted for disutilities, device was significantly preferred, with a mean value of 0.978 ± 0.032 versus 0.961 ± 0.044 for surgery ($p < 0.005$). Surgery would be preferred if the probability of major complications decreased below 5% or minor complications below 6%.

Conclusion: We conclude that when outcomes and their values are taken into account in a systematic manner as defined by the goals of evidence-based medicine, transcatheter device closure of VSDs is favored over surgical repair.



O12-3

Longterm neurodevelopmental outcome and exercise capacity after corrective surgery for tetralogy of Fallot (TOF) or ventricular septal defect (VSD) in infancy

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Objectives: The purpose of this prospective study was to assess neurodevelopmental status and exercise capacity of children between 5 and 11 years of age after corrective surgery for TOF or VSD in infancy, respectively.

Methods: 40 unselected children, 20 with TOF and hypoxemia and 20 with VSD and cardiac insufficiency, operated with combined deep hypothermic circulatory arrest (DHCA) and low flow cardiopulmonary bypass (CPB) at mean age 0.7 ± 0.3 (m \pm STD) years, underwent, at mean age 7.4 ± 1.6 years, standardized evaluation of neurological status, gross motor function, intelligence, academic achievement, language and exercise capacity. Results were compared between the groups and related to pre-, peri- and post-operative status and management.

Results: Neurological status, exercise capacity, NYHA classification and socioeconomic status were not different compared to normal children and between the groups. Compared to the normal population, gross motor function, formal intelligence, academic achievement, expressive and receptive language were significantly reduced ($p < 0.01$ to 0.001) in the whole group as well as in the subgroups. Gross motor function was significantly reduced in the TOF compared to the VSD group ($p < 0.01$) and correlated with neurological dysfunction, lower intelligence and reduced expressive language ($p < 0.05$ each). Reduced socioeconomic status significantly influenced dysfunction in formal intelligence ($p < 0.01$) and academic achievement ($p = 0.01$). Preoperative risk factors (prenatal hypoxia, perinatal asphyxia, preterm birth), perioperative management (durations of CPB and DHCA, lowest esophageal temperature, age at surgery) and postoperative course (postoperative cardiocirculatory insufficiency, duration of mechanical ventilation) were not different between the groups and had no influence on outcome parameters. Degree of hypoxemia in TOF and of cardiac insufficiency in VSD patients did not influence the outcome within the subgroups.

Conclusions: Corrective surgery for TOF or VSD in infancy with combined DHCA and low flow CPB is found associated with reduced neurodevelopmental outcome, compared to normal children, but not with reduced exercise capacity in childhood. The risk of longterm neurodevelopmental impairment must be related to deleterious effects of the global perioperative management. Reduced socioeconomic status is associated with cognitive and academic dysfunction as based on formal testing. Children with preoperative hypoxemia in infancy are at higher risk for gross motor dysfunction than those with cardiac insufficiency.

O12-4

Cardiac troponin-I liberation caused by transcatheter atrial septal defect closure depends on occluder size

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Objectives: The Amplatzer septal occluder (ASO) allows easy and effective transcatheter closure of secundum atrial septal defect (ASD). It is not clear whether the procedure leads to more myocardial injury in children than in adults.

Methods: In a prospective study with children and adults cardiac troponin I serum (cTnI) levels were determined by immunoassay (AxSYM, Abbott Laboratories) before, during and up to 20 months after surgical or transcatheter ASD closure.

Patients: Transcatheter ASD closure (group1: 22 children, age range: 3.26–14.7 yrs; group2: 22 adults, 18.0–67.3 yrs). Surgical ASD closure (group3: 18 children, 3.12–13.5 yrs). Diagnostic catheterization (group4: 12 children, 2.68–15.0 yrs).

Results: cTnI values were significantly increased after ASO implantation with higher serum levels in children than in adults (immediately after implantation: group1 = $3.2 \pm 4.4 \mu\text{g/L}$, group2 = $1.1 \pm 4.2 \mu\text{g/L}$, 4 h after implantation: group1 = $4.8 \pm 5.0 \mu\text{g/L}$, group2 = $1.7 \pm 2.3 \mu\text{g/L}$ (both $p < 0.01$, group1 vs. 2); 1d after implantation: group1 = $3.0 \pm 5.7 \mu\text{g/L}$, group2 = $2.2 \pm 5.2 \mu\text{g/L}$), but were less than 20% of those following surgical ASD closure (group3) ($p < 0.001$) where the highest cTnI concentration was found ($37.1 \pm 26.3 \mu\text{g/L}$). Diagnostic catheterization (group4) was not associated with detectable cTnI increase. From the cTnI concentrations the total amount of liberated cTnI following ASO closure was estimated for each patient. This was dependent on the size of ASO ($p < 0.05$) but not on the patient's age or procedure duration.

Conclusions: In regard to interventional ASD closure our data do not provide evidence for the higher vulnerability of the child's myocardium. Transcatheter ASD closure induces minor myocardial lesion. Its extent depends on the size of the Amplatzer septal occluder but is irrespective of the patients age.

O12-5

Plasma levels of brain natriuretic peptide can reflect pulmonary vascular resistance in patients of ventricular septal defect with pulmonary hypertension

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Introduction: Plasma levels of Brain natriuretic peptide (BNP) reflects volume loads to the left ventricle (LV) and pulmonary hypertension (PH) in patients with ventricular septal defect (VSD). However, in case of elevated pulmonary vascular resistance (PVR), there is little information available BNP.

Objectives: To examine relationships between PVR and BNP in patients with VSD/PH.

Methods: We examined 22 subjects with VSD/PH aged from 2 months to 27 years (median 4 months). Four patients showed Eisenmenger's physiology. Pulmonary to systemic pressure ratio (Pp/Ps), pulmonary to systemic flow ratio (Qp/Qs), and pulmonary to systemic resistance ratio (Rp/Rs) were determined by cardiac catheterization using Fick's method.

Results: Pp/Ps, Qp/Qs, and Rp/Rs ranged from 0.5 to 1.0 (median 0.8), from 0.6 to 3.1 (median 2.0), and from 0.1 to 1.9 (median 0.4), respectively. BNP was significantly lower in patients with Eisenmenger's physiology compared with others ($p < 0.0001$), and all patients with Eisenmenger's physiology showed BNP of $< 10 \text{ pg/ml}$. There was a positive correlation between BNP and Qp/Qs ($r = 0.50$, $p < 0.05$), and a negative correlation between BNP and Rp/Rs ($r = -0.51$, $p < 0.05$). However, no relationship was identified between BNP and Pp/Ps. BNP of $< 25 \text{ pg/ml}$ identified patients with Rp/Rs of < 0.35 with a sensitivity of 91% and specificity of 70%.

Conclusions: Plasma BNP reflects Rp/Rs in patients with VSD/PH. Our data suggest that PVR should be determined in patients with BNP of $< 25 \text{ pg/ml}$.

O12-6

Overall mortality in pediatric cardiology

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Introduction: For most congenital heart defects, large series have been published. These series largely consist of surgically or interventionally treated patients, and usually exclude patients for whom no efficient therapy is as yet available. Therefore, they give no insight in overall mortality from cardiovascular diseases in the pediatric age group.

Methods: Retrospective review of all patients that died before the age of 18 years during a 7-year period from February 1996 until March 2003, while followed in a tertiary referral center. All patients below the age of 18 years with a main cardiac diagnosis were included. Age at death, underlying disorder, and therapeutic procedures as well as location of death were identified.

Results: The overall population during the 7-year period consisted of 5600 patients being followed. During this 7-year period 189 patients died. The main diagnosis among these patients was hypoplastic left heart syndrome ($N = 40$), other monoventricular cardiac anomalies ($N = 30$), cardiomyopathies ($N = 28$), and a large group of different biventricular cardiac anomalies ($N = 83$). Median age at death was 4 months (range 1 day to 17 years). During the 7-year period a total of 1470 cardiac operations were performed. Ninety-nine of the 189 patients that died had been operated. Median time of death after operation was 44 days (range 1 day to 11 years). Forty-eight patients died within 30 days of cardiac surgery (3.2%). Ninety patients never underwent any operation. In the group of 48 patients that died within 30 days of surgery hypoplastic left heart syndrome ($N = 15$) and other monoventricular anomalies ($N = 12$) were most prominent. Most patients of the total group of 189 died within the hospital ($N = 151$; 80%), only a small proportion died at home ($N = 23$, 12%). Sudden unexpected death was relatively infrequent in the total group ($N = 25$; 13%).

Conclusions: The largest single causes of mortality in the pediatric age group in our institution are hypoplastic left heart syndrome and cardiomyopathies. Excluding patients for whom no effective therapy is as yet available largely underestimates the effect of cardiac diseases on overall mortality in children. Sudden death is relatively infrequent in children with known cardiac diseases.

Session 13: Fetal Cardiology

O13-1

Predictors of right ventricular growth and selection for fetal pulmonary valvuloplasty in pulmonary atresia with intact septum

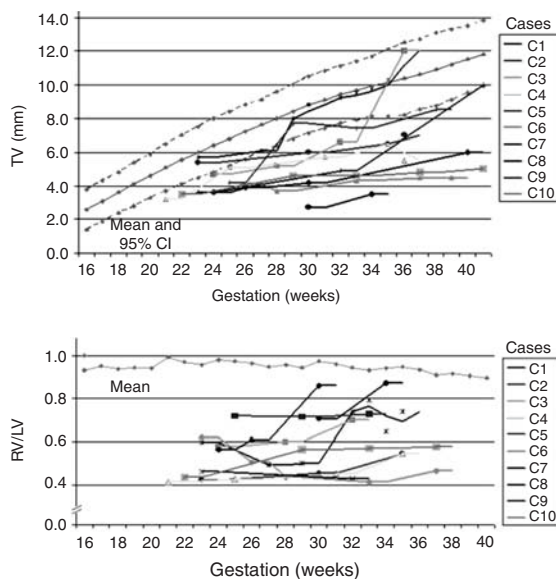
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Background: Early continuity between right ventricle (RV) and pulmonary trunk in pulmonary atresia with intact ventricular septum (PAIVS) is thought advantageous to RV growth. However, childhood data suggests RV growth is poor, even following neonatal pulmonary valvuloplasty.

Aims: To explore the determinants of right-sided growth in the fetus with PAIVS.

Methods: Monthly fetal echocardiography of 14 consecutive fetuses diagnosed with PAIVS in a fetal medicine centre (1999–2003). Assessment of morphology, right and left sided valvular and ventricular growth, Doppler across valves and in arterial and venous ducts (DV). DV waveforms were classified as “abnormal” if absent or reversed end diastolic flow (AREDF), signifying high right atrial pressure (RAP). Postnatal echocardiography confirmed morphology, Doppler & oval foramen restriction. Fetal pulmonary valvuloplasty (x3) performed percutaneously under ultrasound guidance at 21–30 weeks.



Results: Three pregnancies with PAIVS terminated (multiple congenital abnormalities, recipient of twin–twin transfusion syndrome, maternal choice). Six of the remaining 11 survived infancy, four with biventricular circulation. Fetal pulmonary valvuloplasty was offered in selected cases. Morphology was unsuitable in three: Cases 6 (miniature RV), 7 (tricuspid atresia) & 10 (tricuspid stenosis & VSD). Two further monozygotic diamniotic twin pregnancies with good anatomy were excluded (Cases 2 & 4), leaving three suitable for valvuloplasty: Cases 1, 8

(2 procedures) & 11. Valvuloplasty was successful in Cases 1 & 8 but placental bleeding and bradycardia precipitated emergency delivery before valvuloplasty in Case 11.

Two had coronary fistulae (Cases 6 & 8) contributing to eventual uni- & 1.5 ventricle repair.

Eleven had high RAP (tricuspid regurgitation) with AREDF (9) and hydrops in Case 1. The three with low RAP (cases 7, 8 & 10) had the worst TV and PV growth velocities. Figure shows serial evaluation of Cases 1–10, demonstrating impaired TV and RV/LV growth velocities. At birth, median (95% CI) TV annulus Z score was -4.29 (-6.57 to -1.71). TV growth was significantly better in those with high RAP (-4.29 vs. -6.00 , $p = 0.02$) and oval foramen restriction.

Conclusions: Fetuses with high RAP show the best RV growth, but may develop hydrops. Fetal valvuloplasty may be most effective in those with high RAP.

O13-2

Determinants of outcome in pulmonary atresia with intact ventricular septum prenatally detected

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Objectives: To identify fetal echocardiographic features useful to predict the outcome in pulmonary atresia with intact ventricular septum (PAIVS) when prenatally detected.

Method: Among 342 cases of fetal CHD referred to our unit in a 6 years period (01/1999–12/2004) we retrospectively identified all consecutive cases of PAIVS. Fetal and postnatal echocardiograms were reviewed for right ventricle (RV) morphology, ventriculocoronary connections (VCC), and tricuspid regurgitation (TR) in particular.

Results: Our fetal series included 18 cases of PAIVS (5.2%), 2 were associated with Ebstein’s anomaly of the tricuspid valve. The mean gestational age (GA) at diagnosis was 27 wks. Six out of 9 cases (66%) with early diagnosis underwent interruption, one case died spontaneously in utero at 32 wks. All these cases had a unipartite RV with VCC and absent TR. Among the 11 continuing pregnancies, the mean GA at delivery was 38.9 wks, with cesarean section in only one case. The mean birth weight was 3198 g. Four patients underwent percutaneous radiofrequency valvulotomy while other 2 had percutaneous valvuloplasty because of minimal forward flow through the valve, recognizable only at angiography. Seven patients received a modified BT shunt as an isolated or associated procedure. Four patients, who received a BT palliation, died suddenly within the first 4 months of life. Two of them had VCC, a uni- or bi-partite ventricle and absent TR on prenatal echo. Two had Ebstein’s anomaly of the tricuspid valve.

Seven patients are alive and well at a mean follow-up of 10.2 months, 5 of them had definitive biventricular repair and 2 had one and a half ventricle repair. All survivors had a bi- or tri-partite RV, mild or moderate TR and no VCC on prenatal examination. Fetal echocardiography correctly identified VCC in 9 cases, with only one false positive.

Conclusions: Uni- or bi-partite RV, presence of VCC, Ebstein’s anomaly of the tricuspid valve, and absence of TR on prenatal examination are negative predictors of survival. The worst spectrum of PAIVS is detected at an earlier stage with higher probability to undergo termination. Fetal echocardiography can identify VCC with a high sensibility.

O13-3**Ventricular septal defects: prenatal diagnosis and associations in 253 cases**

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Objectives: To document the echocardiographic features, extracardiac associations (ECA) and outcome of fetuses with a ventricular septal defect (VSD) with no other congenital heart disease (CHD). **Methods:** Retrospective analysis of all fetuses with a definite prenatal diagnosis of a VSD with no associated CHD seen between January 1990 and December 2003 in a tertiary fetal cardiology centre. 253 such cases were identified from our database and form the study group.

Results: The most common type of VSD was muscular in 131 (51.8%) cases, followed by perimembranous in 78 (30.8%) and malalignment with aortic override in 44 (17.4%). An ECA was present in 93 (36.8%) and 69 of 126 (54.8%) cases with known karyotype (27.3% of total) had a chromosomal abnormality. The relative frequency of karyotype and extracardiac abnormalities for each type of VSD is shown in the table.

Type of VSD	ECA	Karyotype					
		T21	T18	T13	Other	Normal	NK
Muscular (n = 131)	24 (18.3%)	1 (0.8%)	1 (0.8%)	–	2 (1.5%)	28 (21.3%)	99 (75.6%)
Pm (n = 78)	41 (52.6%)	17 (21.8%)	8 (10.3%)	4 (5.1%)	4 (5.1%)	19 (24.4%)	26 (33.3%)
Malalignment (n = 44)	28 (63.6%)	2 (4.5%)	24 (54.5%)	2 (4.5%)	4 (9.1%)	10 (22.7%)	2 (4.5%)

In 44/253 (17.4%) babies, a VSD was not confirmed after birth, but only 24/44 had a postnatal echocardiogram. In 5 of these cases bidirectional shunting had clearly been documented on the prenatal scan, suggesting closure of the VSD.

Outcome: Fifty pregnancies ended in termination (20%); 20 in spontaneous intrauterine death (8%); 15 babies died postnatally (5.9%) and 161 (63.6%) are still surviving; 6 babies are lost to follow-up (2.4%).

Conclusions: There is a high risk of extracardiac and chromosomal anomalies associated with isolated VSD in the fetus. This risk is related to the type of defect and is particularly high for perimembranous and malalignment type of defects and low for muscular defects. This is important for counselling parents and deciding on which cases should be karyotyped. Spontaneous closure of muscular defects may occur in some cases.

O13-4**Venous Doppler in fetal right heart disease**

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Fetal venous blood velocities have been shown to correlate with right atrial filling pressures. Increased reversal of flow during atrial systole in the inferior vena cava (IVC) is used as a sign of congestive

heart failure (CHF) but has also been reported in certain cases of right heart disease (RHD) without other signs of CHF.

Purpose: to assess which forms of fetal RHD affect venous Doppler blood velocities.

Patients and Methods: Between 2000 and 2004 venous Doppler velocities (IVC, hepatic vein, ductus venosus, umbilical vein) from a group of 51 fetuses with RHD were studied. CHF was diagnosed if additionally increased heart size, more than trivial tricuspid regurgitation, impaired ventricular function or hydrops were present. Fetuses with IUGR were excluded. Mean gestational age was 27,2 ± 5,6 weeks. Fetuses were grouped into tricuspid atresia (N = 8), pulmonary atresia intact septum (N = 7), DORV (N = 8), TOF (N = 19), pulmonary stenosis (N = 5) and Ebstein's anomaly (N = 4). Venous Doppler was considered as abnormal, if reversal exceeded 7% of forward flow in the IVC or hepatic vein, if there was enddiastolic zero or reversed flow in the ductus venosus or enddiastolic umbilical venous pulsations.

Results: abnormal venous Doppler velocities were found in 4/8 fetuses with tricuspid atresia (all without other signs of CHF), 1/19 with TOF (a case of absent pulmonary valve syndrome with hydrops), 1/5 with pulmonary stenosis (with a gradient of 50 mmHg at 27 weeks, no other signs of CHF), 6/7 with pulmonary atresia intact septum (2 of them with and 4 without other signs of CHF), 2/4 with Ebstein (both with other signs of heart failure) and 0/8 of DORV.

Conclusions: Abnormal fetal venous blood velocities in the absence of other signs of CHF may occur in fetuses with RHD, where the whole or almost the whole systemic venous return has to pass the foramen ovale (tricuspid atresia, pulmonary atresia intact septum, critical pulmonary stenosis). Other forms of RHD seem to have normal systemic venous Doppler tracings, unless in CHF. This may be important in the assessment and monitoring of cardiovascular compromise of fetuses with RHD and may have significant implications for further management.

O13-5**Transhepatic ultrasound-guided puncture of the infra-diaphragmatic inferior vena cava in the fetal lamb: a new approach for transcatheter cardiac interventions**

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Objectives: Percutaneous transventricular and fetoscopic umbilical catheterization have been applied to animal and human fetuses. These methods have a high rate of failure and complications. Here, we propose an alternative route for anterograde echo-guided cardiac catheterization through a transhepatic approach of the intra-abdominal vessels in the fetal lamb.

Methods and Results: After exteriorization of the uterus in 12 pregnant ewes between 118–122 days' gestation, a 4Fr sheath mounted over a 1.2-mm trocar was placed into the intra-abdominal portion of the umbilical vein (n = 2) and into the sub-diaphragmatic portion of the inferior vena cava using transhepatic approach (n = 10) under ultrasound guidance. In the first 2 animals using a trans-umbilical approach, it was impossible to reach the heart through the ductus venosus. In the next 10 animals, using a conventional technique, echo-guided catheterization of the four chambers was performed in the all fetuses, atrial or ventricular pacing in 6 fetuses and ballooning of the pulmonary valve in 9/10. Among the 10

fetuses catheterized through the transhepatic approach, 2 were sacrificed immediately after the procedure to evaluate intraperitoneal bleeding (23 and 29 ml respectively) and 3 died after the procedure (one major bleeding and 2 related to balloon catheter manipulation). Finally, 5 were delivered vaginally after an uneventful pregnancy and autopsy at day 5 did not show significant liver, vascular or cardiac injury.

Conclusion: Echo-guided fetal cardiac catheterization through a trans-hepatic approach is feasible. It provides interesting approach for experimental studies, creation of congenital heart diseases and human fetal cardiac interventions.

O13-6

Prenatal ultrasound screening of congenital heart disease in unselected setting: an 18-year experience

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Introduction: Although fetal echocardiography is used more frequently in prenatal diagnosis of congenital cardiac diseases (CHD), the assessment of quality and effectiveness of ultrasound screening (US) is rather difficult due to lack of organization, often misdiagnosed lesions and uncontrolled follow up. The aim of retrospective observational study was to evaluate effectiveness of US in well-defined population.

Methods: Nation-wide US (government guaranteed) introduced in 1986, midtrimester ultrasound scan (four-chamber + outflow tracts) performed in 97% of resident pregnancies. Data of all 1,162 fetuses with prenatally revealed and proved CHD (33.4% associated with extracardiac anomaly) were enrolled in central register. All fetuses who died or those early terminated as well as all children who died postnatally were autopsied, all prenatally diagnosed babies born alive with CHD (prenatally known or unknown) were re-examined. To assess the effectiveness of US, the data were compared to children expected to be born with CHD between 1986 and 2003 using previously published epidemiological data.

Results: During the period, out of 1,960,338 live-born children 11,060 children were estimated as born with CHD, 3,904 with critical lesion. The overall prenatal detection rate was 10.5% of all CHD and 28.9% of critical forms, with gradual increase over the years (0.8% and 2.3% in 1986 compared to 28.5% of all and 80.7% in 2003). Most frequently prenatally diagnosed were double-outlet right ventricle (72.6%) and hypoplastic left heart (45.6%), transposition was prenatally diagnosed only in 9% (but in 26% in 2003).

693 (59.6%) from families expecting baby with complex CHD or/with chromosomal aberration opted for early termination, out of 467 continuing pregnancies, intrauterine death occurred in 53 (11.3%). Only 282 (64.8%) out of 416 children born alive remained alive later, however, while before 1990 the survival rate was 30%, during the last years reached 80%.

Conclusions: Since introduction of prenatal ultrasound screening program, the prenatal detection of CHD has gradually increased. Complex CHD (1/3 associated with non-cardiac lesions) were frequent in fetuses positively scanned at midtrimester. Although the survival rate improved over the years, the long-term prognosis of children with prenatally diagnosed anomalies remains less optimistic than expected.

Session 18: Surgery and Intensive Care for Congenital Heart Disease

O18-1

Cardiac output monitoring by transpulmonary thermodilution and pulse contour analysis after congenital heart surgery – a feasible method

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Objective: In patients with congenital heart disease conventional methods of cardiac output monitoring using pulmonary arterial catheters may not be feasible because of patients' small size or aberrant anatomy. The PiCCO[®] device uses pulse contour analysis to measure continuous cardiac output. The equilibration of the pulse contour analysis is performed by a aortic transpulmonary thermodilution technique. In this prospective clinical study we assessed the accuracy of this device in 24 children in the first 24 hours after congenital heart surgery.

Methods: In 24 patients (mechanically ventilated, mean age 4.6 yr (SD 2.8), mean weight 16.1 kg (SD 6.5), mean height 102 cm (SD 20.7)) 168 data points were obtained in the first 24 h after intensive care unit admission. We evaluated the difference between cardiac index (CI) derived from aortic transpulmonary thermodilution (TDCI) and CI derived from pulse contour analysis (PCCI). In each patient 1, 4, 8, 12, 16, 20, 24 h after admission a set three thermodilution were performed and their mean was calculated by the PiCCO system. Simultaneously the PCCI was documented.

Intracardial shunts were excluded by transesophageal or transthoracic echocardiography postoperatively.

Results: The mean TDCI was 3.64 l/min m² (SD 1.27, range 1.89 and 6.87).

The mean bias and limits of agreement between TDCI and PCCI over all data points were 0.04 ± 0.66 l/min m² (95% Confidence interval 0.11 to -0.03).

Coefficient of correlation r between TDCI and PCCI was 0.90.

The correlation equation was PCCI = 0.90 TDCI + 0.33.

Conclusion: PCCI is a feasible method to monitor CI after congenital heart surgery. It allows an online monitoring of CI. Relevant bias between TDCI and PCCI was observed especially after relevant changes of vasoactive drugs and volumetherapy.

Therefore the PiCCO[®] device had to be equilibrated regularly and if substantial changes of therapy were performed.

O18-2

Bovine jugular vein for right ventricle to pulmonary artery valved conduits: a valid alternative to homografts

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In the continuous search for alternatives to homografts, the medium-term outcome of the bovine jugular vein valved conduit (Contegra[®], Medtronic, Minneapolis, MN) was evaluated in a multi-centre prospective study.

From April 1999 to September 2004, 171 patients, mean age 11.1 ± 16.0 years (3 days to 55 years), mean weight 33.6 ± 25.1 kg (2.4 to 125 kg) were discharged after implantation of a Contegra[®]

conduit. The diagnosis was: pulmonary valve replacement during Ross operation (n = 65), pulmonary valve regurgitation (n = 9), tetralogy of Fallot (n = 16), pulmonary atresia with ventricular septal defect (n = 24), double outlet right ventricle (n = 11), truncus arteriosus (n = 14), Taussig-Bing (n = 3), obstructed conduit (n = 21), transposition with ventricular septal defect and pulmonary stenosis (n = 5), double discordance (n = 1) and other in 2. Conduit size used was 12 mm in 11, 14 mm in 7, 16 mm in 32, 18 mm in 28, 20 mm in 15, and 22 mm in 78 patients. All patients were evaluated with post-operative echocardiography, 41/171 (24%) with cardiac catheterization, and 23/171 (13%) with electrocardiograph-gated multi-slice computer tomography.

In a mean follow-up of 30 months (1 to 65 months) there were three late deaths (3/171 patients = 1.8% mortality), two non conduit-related, one because of conduit obstruction. Twelve patients required interventional cardiology procedures, 9/12 non conduit-related and 3/12 to stent a twisted and/or stenotic conduit. Ten patients underwent re-operations, 7/10 non conduit-related and 3/10 for conduit replacement: one to replace a twisted conduit, one to replace the conduit because of pulmonary confluence stenosis and one to relieve infundibular stenosis. The transconduit pressure gradient remained stable during follow-up, with a mean peak pressure gradient of 16.6 ± 10 mmHg. Internal diameters corresponded to $110 \pm 20\%$ of the diameter at implantation at level of proximal anastomosis, $112 \pm 18\%$ at valve level, and $110 \pm 14\%$ at distal anastomosis. Calcifications were not found, with the exception of a minimal (2.3 mm) parietal calcification.

Contegra[®] valved conduits are a suitable and reliable alternative to conventional homografts, because their constant availability in size from 12 to 22 mm, and the excellent medium-term hemodynamic results with minimal incidence of calcifications.

O18-3

The presence of a VSD does not influence aortic arch development after neonatal subclavian angioplasty

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Objective: We hypothesized that the presence of a VSD could influence the growth of the aortic arch after neonatal coarctation repair.

Methods: Arch development was retrospectively analysed in patients who underwent subclavian flap angioplasty at neonatal age (<90 days). 127 Patients (mean weight 3.6 ± 0.8 kg), operated between 1979 and 2003, were included. Concomitant pathology was prevalent (65%) and 23% of the patients underwent additional surgical procedures. In 43% of the patients, a VSD was still present after coarctation repair.

Arch stenosis was defined as any echocardiographic peak gradient >20 mmHg at the level of the aortic arch. The mean follow-up was 7.6 years. Demographic and echocardiographic variables were analysed for correlation with arch stenosis (Cox regression).

Results: Thirteen patients (10%) died during follow-up due to associated diagnoses. Nineteen patients (15%) developed arch stenosis. Kaplan-Meier freedom of arch stenosis was $95 \pm 1.8\%$ at 1 year, $92 \pm 2.6\%$ at 5 years and $81 \pm 4\%$ at 10 years.

Factors associated with arch stenosis by univariable Cox regression included the presence of a bicuspid aortic valve ($p = 0.04$), the ascending aorta diameter ($p = 0.03$), the transverse arch diameter ($p = 0.0003$), the isthmus diameter (0.004) and not the presence

of a VSD ($p = 0.30$). Smaller transverse arch ($p = 0.001$) and the presence of a bicuspid aortic valve ($p = 0.027$) were the independent predictors of recoarctation by multivariable Cox analysis. An absolute transverse arch diameter <3.5 mm correlates significantly with recoarctation.

Conclusion: The transverse arch diameter and a bicuspid aortic valve are independent risk factors for arch stenosis after subclavian angioplasty in neonates. The presence of a VSD does not influence the growth of the aortic arch. In the presence of a small transverse arch (<3.5 mm), the coarctation repair should include the distal arch.

O18-4

Transatrial repair of tetralogy of Fallot under 3 months of age as routine approach

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Objectives: Surgical repair of tetralogy of Fallot (TOF) is a well established procedure which is currently performed in infancy. Aim is to evaluate surgical results of early correction before 3 months of age.

Methods: From January 1991 to December 2003, 48 consecutive patients (25 males, 23 females) with a mean age 53 days (range 13–90) underwent repair of TOF. All patients had transatrial VSD closure and transpulmonary/transatrial RVOT miotomy/miectomy. In addition, RVOT enlargement was performed by means of transannular patch in 44 patients (91%), using pulmonary homograft monocusp patch in 31, autologous pericardial patch in 13. No patch was used in remaining 4 patients (9%). Associated surgical procedures were: LPA patch augmentation in 5, LPA reimplantation from descending aorta in 1, subaortic stenosis resection in 1. **Results:** There was one hospital death (2%). Major postoperative complications included: LOS treated with inotropes for more than 48 hrs in 2 and ECMO support for 48 days in 1. Forty-seven patients were discharged home in good hemodynamic conditions. At a mean follow up of 6.1 years (range 4 months–12 years) 46 patients are in good hemodynamic conditions and asymptomatic. There was 1 late death. Six patients (12.7%) required late reoperations, 2 for RVOT obstruction, 4 for LPA stenosis. Late reinterventions included LPA percutaneous balloon dilatation in 7 (14.8%).

Conclusions: Transatrial approach can be performed safely routinely in early infancy with low operative risk, good early hemodynamic result and low incidence of reoperation.

O18-5

Normal pulmonary arterial development following transplantation in patients with hypoplastic left heart syndrome who were palliated with internal pulmonary artery bands

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Neonates with hypoplastic left heart syndrome (HLHS) are at risk for developing pulmonary hypertension and subsequent early graft failure if waiting time to transplantation is prolonged. Interventional

palliation consisting of ductus arteriosus stenting, atrial septal angioplasty for left atrial decompression and placement of internal pulmonary artery bands to restrict pulmonary blood flow has been a successful bridge to transplantation in infants with HLHS. We evaluated the anatomy of the pulmonary arteries following transplantation in infants with HLHS who had undergone this palliative approach. From 5/02 through 10/03, 11 infants with HLHS underwent interventional palliation and subsequent transplantation at our institution. Mean age at placement of the internal pulmonary artery bands was 87 ± 45 days (range 47–187 days), with a mean age at transplant of 137 ± 43 days (range 74–203 days). The bands were in place for an average of 50 days with a range of 6–152 days. The bands were easily removed at the time of transplantation without any need for reconstruction of the pulmonary arteries. On echocardiographic evaluation all patients had normal Doppler examination of their branch pulmonary arteries. Routine surveillance catheterization at one year post-transplantation (380 ± 36 days from transplant) has been performed on 10 of these patients. Mean pulmonary artery pressure was 17.8 ± 3.5 mmHg. Pulmonary angiograms demonstrated no distortion of pulmonary artery anatomy in any of the patients. There was significant growth of the pulmonary arteries when comparing angiographically measured diameters at the time of placement of the bands 6.5 ± 0.9 mm for the left and 7.3 ± 1.3 mm for the right vs. the diameters at one year post-transplant of 8.6 ± 1.7 mm for the left and 9 ± 1.7 mm for the right (p value <0.01). Interventional palliation of neonates with HLHS results in successful transplantation with 100% early transplant survival. At one year post-transplant, pulmonary artery angiograms demonstrate no stenosis or distortion of the pulmonary arteries. Internal pulmonary artery banding may be the preferred method of palliation in neonates with HLHS awaiting transplantation as 1. a surgical procedure is avoided, 2. there is maintenance of normal pulmonary artery architecture following removal of the bands and 3. the ability for growth of the pulmonary arteries is preserved.

O18-6

Re-Coarctation after Norwood-Operation in Children with Hypoplastic-left-heart-syndrome

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Background: Re-Coarctation (Re-Coa) is a critical condition in children after Norwood-Operation. We review our experience with Re-Coa in infants with Hypoplastic-left-heart-syndrome (HLHS).

Methods: Between 1997 and 2003, 60 consecutive newborns with HLHS underwent Norwood-procedure in our institution. Reconstruction of the aortic-arch was carried out with homograft material from the ascending aorta to the isthmus. Resection of the isthmus was not performed. Analyzed parameters were prevalence, time interval between surgery and diagnosis, treatment and outcome. Re-Coa was defined by blood-pressure-difference more than 20 mmHg between right arm and legs or by clinical and echocardiographic findings.

Results: 9/60 patients (15%) developed Re-Coa. Time-interval from Norwood-Operation was 2–8 months (median 4.5). 2 children were before and 7 after Glenn-Operation. 3/9 (33%) had signs of congestive-heart-failure (CHF). RR-difference ranged from 15–55 mmHg. All had moderate to severe tricuspid-insufficiency.

Body-weight at cardiac-catheterization was 3.2–6.4 kg (median 4.8). Peak-to-peak gradient was 10–55 mmHg (median 30) and

was lower in the CHF group. In all patients the site of obstruction was the most distal part of the aortic-arch. Descending aorta was 6–9 mm and defined the maximum balloon-diameter. Angioplasty was performed retrograde in 7 and antegrade in 2 patients. In all cases a 20 mm Tyshak®-Ballon over a 0.014 inch floppy-guide-wire was used. Residual gradients ranged from 0–18 mmHg (median 7.5). Complications were transient femoral-artery-occlusion in one case; 3 patients required repeat angioplasty within 3–6 months and a stent was implanted in one case. Six patients are free from Re-Coa in follow-up of 14–80 months (median 34). CHF disappeared in all patients except one child with spongy-myocardium. There were two late-deaths. One patient with spongy-myocardium died 9 months and one patient with severe pulmonary AV-malformations died 12 months after angioplasty, both without aortic reobstructions.

Conclusion: Re-Coa of the reconstructed aortic arch after Norwood-Operation was a frequent complication (15%). It developed early after surgery and frequently with severe signs of CHF. Angioplasty of Re-Coa was safe and effective even in the CHF-group. However re-obstruction can occur and might be due to residual ductal-tissue in the aortic-arch. Complete resection of ductal-tissue and the isthmus in Norwood-Operation may be beneficial.

Session 20: Imaging II

O20-1

Evidence of atrial dysfunction in patients after Fontan operations: evaluation by tissue

Doppler echocardiography

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Introduction: Assessment of ventricular diastolic and atrial function in children and adult with morphologically and functionally univentricular heart using conventional echocardiographic method is difficult.

This study aimed to determine ventricular diastolic function and atrial performance following Fontan operation using tissue Doppler imaging.

Patients and Methods: Forty-six patients at mean 15 years (range 2 to 43 years) after Fontan procedure were studied prospectively. Twenty-one patients had primary diagnosis of tricuspid valve atresia and 25 patients double inlet left ventricle. Median age at Fontan operation was 7.7 years (range 1 to 37 years). Data obtained were compared to those of 30 age-matched healthy control subjects.

All patients underwent conventional Doppler and tissue-Doppler echocardiography (TDE) with simultaneous ECG. Measurements of isovolumic relaxation time to ejection fraction ratio (IVRT:ET) and Tei-index from TDE-derived velocity curve were applied as parameters for the assessment of global univentricular performance. For the global atrial function common atrial maximal area (A_1), area at onset of atrial kick (A_2), minimal area (A_3), and common atrium active emptying area fraction [AEAF = $(A_2 - A_3)/A_2 \star 100\%$] were evaluated. TDE-derived strain rate (SR) late diastolic peak (RA_{sr} - and LA_{sr} -waves) was measured in

the middle of left and right lateral walls as a parameter for regional atrial wall contractile function.

Results: The Tei-index and IVRT/ET: in all Fontan-patients were significantly higher ($p < 0.001$) indicating altered global univentricular function. The AEF as a parameter of the global, and the A_{sr} as a parameter of regional atrial function were significantly lower ($p < 0.001$) in Fontan patients than in normal controls.

Patients operated on at an early age (< 7.7 years) have significantly better global ventricular function with more favorable Tei-Index ($p = 0.02$) and IVRT:ET ratio ($p = 0.05$) and higher RA_{sr} - and LA_{sr} -waves ($p = 0.01$) than patients operated on later (> 7.7 years).

Conclusion: Ventricular diastolic and atrial function in patient with univentricular heart can be evaluated with tissue Doppler echocardiography, which provides reproducible information on their altered atrial contractile function. Ventricular diastolic and regional atrial function in Fontan-patients depends on age at operation.

O20-2

Functional response to percutaneous pulmonary valve implantation assessed by magnetic resonance imaging and metabolic exercise testing

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Background: Pulmonary stenosis/incompetence is a common late sequelae of surgical repair to the right ventricular (RV) outflow tract. Percutaneous pulmonary valve implantation (PPVI) is a recently developed method for treating this clinical scenario. In this study, we present the changes in ventricular indices and great vessel blood flow measured by magnetic resonance (MR) imaging, and exercise capacity soon after PPVI.

Methods and Results: 28 subjects with pulmonary stenosis/incompetence (age 19 ± 8 years) underwent MR imaging at 1.5 T prior to (median 6 days) and soon after (median 6 days) PPVI. All subjects had NYHA assessment of symptoms, and a subset of 16 consecutive subjects underwent metabolic exercise testing on the same day as MR imaging. There were significant reductions in the gradient across the pulmonary trunk (39 ± 18 vs. 25 ± 15 mmHg, $p < 0.001$), pulmonary regurgitant fraction (21 ± 13 vs. $3 \pm 4\%$, $p < 0.001$), and RV end-diastolic volume (EDV) (94 ± 28 vs. 82 ± 24 mL/beat/m², $p < 0.001$), and significant increases in left ventricular EDV (64 ± 12 vs. 71 ± 13 mL/beat/m², $p < 0.01$) and effective stroke volume (37 ± 7 vs. 41 ± 9 mL/beat/m², $p < 0.05$) after PPVI. There were significant improvements in subjective patient symptoms, NYHA classification 2 vs. 1 ($p < 0.001$), and metabolic exercise capacity (VO_2 max, 26 ± 7 vs. 29 ± 6 mL/kg/min, $p < 0.001$), after PPVI. In 12 patients, an increase in VO_2 max corresponded to reduction in RVEDV, and in 2 patients, a decrease in VO_2 max corresponded to increase in RVEDV.

Conclusion: PPVI leads to a quantifiable improvement in MR defined ventricular parameters and pulmonary incompetence, which is associated with both a subjective and objective improvement in exercise capacity.

O20-3

Normal LV function and decreased right ventricular compliance 10 years after arterial switch operation

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Introduction: Relatively few data are available about ventricular function long-term after arterial switch operation (ASO). Diastolic function changes may precede systolic abnormalities. We sought to determine if differences from normals could be found by using conventional and advanced echocardiography 10 years after ASO. **Methods:** We studied 33 patients 10.2 ± 1.5 years after ASO. Detailed echocardiography was performed (Philips® Sonos 5500). Mitral and tricuspid inflow parameters as well as hepatic venous and pulmonary venous inflow parameters and tissue Doppler indices of the basal part of the left ventricle and septum were obtained. Results were compared to normal values (Cardiol Young 2003;13:143–151, and J Am Soc Echocardiogr 2004;17:212–221). **Results:** All patients were in NYHA class I. Left and right ventricular systolic function were normal. Signs of increased RV pressure were absent (no tricuspid regurgitation, and normal septal movements). However, the transposition patients had a larger tricuspid E wave velocity and a decreased systolic hepatic venous inflow. All other values did not differ from normal.

Conclusions: At 10 ± 1.5 years after ASO we found, besides a completely normal LV function, an increased tricuspid E wave velocity and a decreased systolic hepatic venous inflow, which may, in the absence of increased RV pressure, indicate a decrease in right ventricular compliance.

	Present study	Normal values
MV E	1.06 ± 0.23	0.95 ± 0.16
MV A	0.45 ± 0.10	0.49 ± 0.14
TV E	0.75 ± 0.17	$0.60 \pm 0.11^*$
TV A	0.44 ± 0.12	0.39 ± 0.11
TV Dec Time	0.19 ± 0.05	0.14 ± 0.02
PV S	0.44 ± 0.15	0.49 ± 0.11
PV D	0.72 ± 0.12	0.58 ± 0.12
Hep V S	0.42 ± 0.13	$0.76 \pm 0.23^*$
Hep V D	0.55 ± 0.21	0.63 ± 0.23
TDI LV S	0.14 ± 0.21	0.11 ± 0.03
TDI LV E	0.16 ± 0.05	0.20 ± 0.03
TDI LV A	0.05 ± 0.02	0.06 ± 0.02
TDI Septum S	0.05 ± 0.01	0.08 ± 0.01
TDI Septum E	0.11 ± 0.03	0.15 ± 0.03
TDI Septum A	0.05 ± 0.01	0.06 ± 0.02

O20-4

Correlation of stored 3D volumes of echocardiographic images to 2D and operative findings

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Correlation of stored 3D volumes of echocardiographic images to 2D and operative findings.

Objective: To study the feasibility of independent analysis of stored full volume 3D images of atrioventricular septal defects (AVSD)

and correlate the findings to 2D echocardiograms and surgical findings.

Background: Assessment of AVSD for suitability of biventricular repair can be tedious and difficult. Decision-making regarding septability of unbalanced defects depends on assessing the morphology of the AV valve components, its competence, degree of development, AV septum, additional defects, outflow tract obstruction, commitment of the AV valves to underlying ventricles and ventricular size. We evaluated the role of 3D echocardiography in delineating these specific aspects from stored images in patients with AVSD referred for 3D echocardiography.

Method: Patients with AVSD confirmed on routine 2D echocardiography referred for 3D echo analysis with stored full volume loop images were studied. Images acquired by different operators using the Philips Sonos 7500 from 10 patients stored in the hard drive were analysed using Qlab software by a single operator. Aspects studied included functional morphology and anatomy of the AV valves, size and position of the AV septal defect, number of leaflets and configuration, degree of extension of the bridging leaflets, degree of valve incompetence, degree of formation of each leaflet, presence of additional abnormalities and septability.

Results: Images were adequate in all patients except one with respiratory artefact which affected image interpretation. Two were found unsuitable for biventricular repair. Two had good morphology and no residual problems envisaged. One had unbalanced AVSD with double outlet right ventricle. It was felt that biventricular repair is possible with significant risk of residual problem. Four had malformed bridging leaflets (3 inferior left and 1 inferior right) and predicted to have residual AV valve regurgitation. Information from 3D image analysis corresponded to 2D and operative findings. The information derived from 3D analysis was more detailed gave predictable surgical results.

Conclusion: Independent analysis of stored 3D full volume loops can provide detailed anatomical information of Atrio-ventricular septal defects and insight in to surgical outcome. This form of image acquisition and analysis may be applicable in telemedicine.

O20-5

Magnetic resonance assessment of aortic flow dynamics and aortic arch geometry in patients with successful repair of coarctation of the aorta

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Introduction: Anomalies of the aortic arch geometries have been associated with resting hypertension after coarctation repair but the mechanisms for this association remain unknown.

Objective: We sought to investigate by magnetic resonance imaging (MRI) the influence of the post-operative aortic arch geometry on the flow dynamics in the thoracic aorta in patients with successful repair of coarctation and to detect differences between these patients and matched control subjects.

Materials and Methods: Thirty patients (mean age 15.3 ± 5.7 years, follow-up after surgery 13.9 ± 6.1 years) with successful repair of coarctation and 15 matched control subjects underwent MRI of the thoracic aorta with flow mapping acquisitions. Three categories of aortic arch shape were defined based on the global geometry of the aortic arch: gothic, crenel and normal. Flow wave velocity (FWV) along the aortic arch was calculated by analytic method. We also visualized three-dimensional blood flow in the

thoracic aorta and quantified the regurgitation volume during systolic phase in the ascending aorta.

Results: Compared with the control subjects, patients with successful repair of coarctation had higher FWV along the aortic arch (6.7 ± 2.9 versus 3.8 ± 0.4 m/sec, $P = 0.001$). FWV was also higher in patients with gothic arch (8.6 ± 3.4 m/sec) compared to those with crenel form (4.5 ± 1.6 m/sec) and normal form (3.7 ± 0.5 m/sec) ($P < 0.0001$). Systolic regurgitation was recorded early at the protosystolic period in only gothic and crenel arches. Systolic regurgitation was significantly higher in gothic arch (14.4 ± 5.3 ml/beat) compared to the crenel form (7.9 ± 1.3 ml/beat) and the normal form (5.3 ± 1.9 ml/beat) ($P < 0.001$).

Conclusion: Despite successful repair, patients with CoA had increased aortic stiffness compared to control subjects. In addition, gothic arch appeared to be inadequate to flow dynamics since this geometry was associated with increased stiffness and abnormal flow dynamics in the ascending aorta compared to the two others geometries.

O20-6

Pulmonary and caval blood flow patterns in patients with intracardiac and extracardiac Fontan: a magnetic resonance study

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Introduction: Pulmonary and caval blood flow and pulsatility after different types of Fontan operation were compared using magnetic resonance imaging.

Methods: We studied 37 consecutive patients, 6 with classic total cavopulmonary connection (TCPC), 18 with intra-atrial lateral tunnel (LTFO) and 13 with extracardiac Fontan (ECFO). Median age at examination was 19 years (range, 8 to 32 years) in the classic TCPC group, 11 years (range, 6 to 44 years) in the LTFO group and 9 years (range, 4 to 35 years) in the ECFO group. Using magnetic resonance phase-contrast velocity mapping, we measured the blood flow in the superior vena cava, inferior vena cava (IVC), left (LPA) and right pulmonary artery (RPA) and calculated the pulsatility index for each vessel defined as (maximum flow – minimum flow)/mean flow.

Results: Blood flow distribution between superior and inferior vena cava was normal for all modifications. Only patients with a classic TCPC had a backward flow in the inferior vena cava with a median regurgitation fraction of 36% (range, 30% to 56%) and a massively dilated right atrium. Blood flow distribution between the left and right pulmonary artery was equal for the LTFO (1.4 ± 0.6 and 1.5 ± 0.6 L/min \cdot m²) and ECFO groups (1.7 ± 0.6 and 1.7 ± 0.5 L/min \cdot m²). The ECFO group had lower pulsatility indices than the LTFO group in the LPA and RPA (0.8 ± 0.4 vs 1.2 ± 0.9 ; NS and 0.7 ± 0.4 vs 1.1 ± 0.6 ; $p < 0.04$).

Conclusions: Patients with the classic TCPC have an abnormal backward flow in the IVC which is most likely caused by atrial contraction and the dilated right atrium. Patients after lateral tunnel and extracardiac Fontan operation have equal pulmonary blood flow distribution with lower pulsatility in patients with ECFO. The

presence or absence of pulsatility in the Fontan circulation deserves further observation in regard to long-term outcome.

Session 25: Morphology and Coronary Arteries

O25-1

An investigation for determining normal dimensions of aorta in infants

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Introduction: For surgical strategy, knowing normal dimensions of aorta in congenital heart disease complicated with hypoplastic aorta is very important. However, only few reports on normal aortic dimensions in infants have been made so far.

Objectives:

1. To calculate normal predictive values of aortic dimensions in infants from their body surface area (BSA).
2. To compare these normal values with ventricular septal defect (VSD) patients' values.

Methods: We performed a retrospective analysis of cineangiograms of 47 patients under 2 years old who underwent left-ventriculograms or aortograms, whose diagnosis was Kawasaki disease or mild pulmonary valve stenosis without aortic disease (Normal group). The median BSA was 0.42 m², with a range from 0.22 to 0.52. Systolic aortic dimensions were measured at the level of ST junction (D1), the proximal portion of brachiocephalic artery (D2), the distal portion of left subclavian artery (D3), the narrowest portion of aortic isthmus (D4), and the level of diaphragm (D5). A simple regression analysis was used to determine association between aortic dimensions and BSA. We also made the same measurement in 43 infants with VSD (VSD group), whose median BSA was 0.35 m², with a range from 0.17 to 0.50. The D2/D1, D3/D1, D4/D1, and D5/D1 ratio of all patients were calculated, and compared those values of VSD group with those of Normal group.

Results: Normal predictive values of aortic dimensions were as follows: D1 = 20.7 × BSA ± 3.2 mm (p < 0.001, R₂ = 0.69); D2 = 15.1 × BSA + 4.6 mm (p < 0.001, R₂ = 0.48); D3 = 15.3 × BSA + 2.6 mm (p < 0.001, R₂ = 0.67); D4 = 17.8 × BSA + 1.1 mm (p < 0.001, R₂ = 0.70); D5 = 16.1 × BSA + 1.3 mm (p < 0.001, R₂ = 0.74). The D3/D1, D4/D1, and D5/D1 ratio of the patients in VSD group was significantly smaller than that in Normal group (p < 0.05).

Conclusions: Normal predictive values of aortic dimensions in infants were calculated from BSA. We could evaluate a degree of hypoplasia of aorta by means of these normal predictive values, and these might be helpful to decide surgical strategy. The distal portions of aorta in infants with VSD were smaller than those in normal infants. These results might indicate that a change of the distribution of systemic blood flow has occurred in VSD infants to maintain cerebral blood flow that is the most important for infants.

O25-2

Tissue Doppler derived strain rather than wall velocities detect microvascular disease in paediatric heart transplant recipients

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Introduction: Coronary allograft vasculopathy (CAV) remains the main cause of graft failure and limiting long term survival after heart transplantation. The novel tissue Doppler imaging (TDI) has the potential to provide information on the longitudinal ventricular function.

The aim was to determine whether the tissue derived parameters can detect CAV after heart transplantation in children.

Method: Out of total transplanted 132 paediatric heart transplants recipients in the German Heart Centre Berlin 30 paediatric patients with a median age of 13 years and median period of 5.98 years after heart transplantation, received selective coronary angiography and myocardial biopsy to determine the degree of coronary artery disease. Tissue Doppler Imaging (TDI) was done one day before cardiac catheterization and systolic and diastolic myocardial wall motions were analysed in 4 chamber view and short axis. The TDI spectra over 3 heart cycles were analysed for velocities, isovolumetric contraction and relaxation time intervals, and strain. The left ventricular (LV) Tei-index (summation of the isovolumetric contraction and relaxation divided by the ejection time) was calculated from the TDI-spectral.

Results: Isovolumetric contraction time rather than relaxation time was significantly lower in the patients with CAV indicating altered systolic function. End-diastolic pressure, cardiac output and cardiac index did not revealed any significant differences between the patients with and without histologically detected CAV. TDI-derived Strain values rather than the wall velocities were found significantly lower in those patients with CAV in the left ventricular rather than the right ventricular walls. The area under the curve of receiver characteristic curve (ROC curve) for different values was the highest (0.84) for the strain ratio of the left to the right ventricle.

Conclusion: The TDI derived strain is reliable non-invasive methods for early screening of microvascular disease in paediatric heart transplant recipients. Early screening of paediatric patients using TDI may help to identify those patients at increased risk who may benefit from therapeutic and diagnostic intervention and thereby from modification of immunosuppressive therapy.

O25-3

Residual adverse changes in arterial endothelial function and LDL oxidation after a slight systemic inflammation

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Background: Several studies have pointed out that acute systemic inflammation in humans is associated with impairment of endothelial vasodilation. We investigated whether arterial endothelial dysfunction could persist beyond the inflammatory state, and whether amplified oxidative modification of LDL accompanies this vascular disturbance.

Methods and Subjects: Flow-mediated and glyceryl trinitrate (GTN)-induced dilatory responses of the brachial artery and carotid intima-media thickness of the carotid artery were assessed by ultrasound in 10 healthy male volunteers (age 17–30 yr) before, 2 and 14 days after subcutaneous administration of influenza vaccine. Plasma levels

of high-sensitivity C-reactive protein (CRP), fibrinogen, nitrate, von Willebrand, intercellular adhesion molecule (ICAM)-1, and antibodies against oxidized LDL were measured at each time-point. Data are means \pm SE.

Results: Influenza vaccination caused a slight elevation in CRP (from 0.8 at baseline, to 1.6 ± 0.3 mg/l, $p < 0.05$) and fibrinogen (from 2.4 ± 0.2 to 2.9 ± 0.2 g/l, $p < 0.05$) at 2 days, which completely resolved at 14 days (CRP: 0.7 ± 0.4 mg/l, $p = 0.9$, and fibrinogen: 2.4 ± 0.1 g/l, $p = 0.9$ vs. baseline). Ox-LDL antibody levels rose significantly at 2 days (from 1 ± 0.09 at baseline to 2 ± 0.4 , $p < 0.05$), and remained elevated at 14 days (1.7 ± 0.3 , $p = 0.1$ vs. baseline). FMD of the brachial artery decreased at 2 days (from 8.3 ± 1.2 at baseline, to $5.3 \pm 1\%$, $p = 0.05$) with a further decrease at 14 days ($4.9 \pm 0.8\%$, $p = 0.03$ vs. baseline). A similar trend, yet statistically nonsignificant, was noted with regard to plasma ICAM-1 (from 176 ± 10 at baseline, to 197 ± 17 at 2 weeks, $p = 0.2$). The dilatory responses to GTN remained unchanged throughout the study period ($p > 0.8$).

Conclusion: A slight and transitory increase in inflammatory markers leads to augmented modification of LDL oxidation and arterial endothelial dysfunction. These changes may persist for at least 2 weeks after the resolution of systemic inflammation.

O25-4

Multislice computed tomography in long-term follow up after arterial switch operation for transposition of the great arteries

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Background: Coronary artery obstructions are one the late complication after the arterial switch for transposition of the great arteries (TGA). Precise anatomical assessment of the fate of the coronary artery is currently performed using selective coronary artery angiogram. While this technique allows precise diagnosis, it is invasive and may have its own complications.

Objective: Investigate the clinical usefulness of MSCT angiography as a follow-up exam for children operated for transposition of the great arteries (TGA) by arterial switch operation (ASO).

Methods and Results: Thirty-eight children (age 12 ± 5 years) operated for TGA underwent selective coronary artery angiography and MSCT angiography. Analysis of MSCT images was performed blinded of the angiography results. In comparison to coronary angiography in patients with normal coronary arteries, MSCT could measure all ostia and proximal segments of coronary arteries. 15 of the 18 (83.3%) significant stenoses (>50% diameter reduction) could be precisely described by MSCT. In the remaining 3 cases (one right coronary artery and 2 left ostium), the stenosis was not accurately described. Sensitivity (%) calculated on 258 coronary artery segments was 87.5% and specificity 99.6%. In patients with normal coronary artery distribution (Yacoub's type A), sensitivity and specificity were at 100%. In other coronary artery patterns, MSCT remains insufficiently sensitive to eliminate coronary artery stenosis.

Conclusion: MSCT angiography may be the only necessary anatomical control for patients with normal coronary distribution after the arterial switch. Technical limitations have to be overcome to use this methods safely in patients with other coronary artery patterns.

O25-5

Indomethacin treatment decreases coronary average peak flow velocity in newborn lambs

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Background: Indomethacin (IND) is widely used as a pharmacological treatment for closing a symptomatic patent ductus arteriosus (PDA) in premature infants. The hemodynamic side-effects such as diastolic dysfunction and a reduction of blood flow to brain, intestinal organs and kidney are well known. The effects that IND on coronary flow with clinically used doses is poorly documented.

Methods: We studied 9 near-term lambs of mixed breed and gender during the first day of life. Their gestational age varied between 132 and 134 days (term 145 days) and weight between 3–4.7 kg, mean 3.7 kg.

Coronary flow velocities were measured with an Intra coronary Doppler Guide Wire (IDGW) in the proximal left anterior descending coronary artery (LAD). Continuous flow profiles with simultaneous ECG were recorded on videocassette. Maximal flow velocity and average peak flow velocity (APV) were measured before and after Indomethacin delivery of 0.2 mg per kilogram of body weight.

Results: IND decreased APV in all lambs ($p = 0.03$). The maximal fall in coronary velocity appeared after 1–7 minutes and was regained in 21 (3–53) minutes after the delivery. The maximal reduction of coronary flow was 53%, mean 30%. Regression analysis showed a linear correlation of per cent lowering APV and recovery time ($R = 0.91$, R squared 0.84, P -value 0.002).

Conclusions: Coronary flow can decrease very significantly with ordinary doses of indomethacin used for closing open ductus arteriosus. This can be deleterious for sick newborn babies.

O25-6

Effects of neonatal hypoxia on coronary arteriolar morphology in adult rats

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Introduction: We have previously shown that neonatal hypoxia in the rat has long-lasting effects on adult cardiac function. We have asked whether neonatal hypoxia (NH) in the rat has long-lasting effects on intramural coronary arteriolar (ICA) morphology.

Methods: Fourteen adult, 90 day old, Sprague-Dawley rats were studied. Seven animals were neonatally hypoxic (NH) ($FiO_2 = 0.12$, days 1–10 of life) while 7 others were not (Control (C)). After anesthesia (pentobarbital 40 mg/kg i.p.) and echocardiography (Acuson 128XP, 7.5 MHz probe), their hearts were arrested in diastole by i.p. injection of KCL and fixed in 10% formalin. Five micron transverse sections, taken midway between cardiac apex and base, were stained with H&E or Mason's trichrome. ICA of the right ventricular free wall (RVFW), interventricular septum (IVS), and left ventricular free wall (LVFW) with the same external diameter ($0.17 \pm 0.05 \mu\text{m}$ (SEM)) were examined. Features noted were; arteriolar area (Aa), luminal area

(La) and diameter (Ld), wall thickness (Wt), wall area (Wa), and perivascular collagen area (Ca).

Results: Wt, Wa, and Ca were significantly increased in NH vs. C (0.015 ± 0.005 vs. 0.006 ± 0.001 mm, 0.006 ± 0.003 vs. 0.003 ± 0.001 mm² and 0.006 ± 0.002 vs. 0.002 ± 0.002 mm²; $P < 0.0001$). La/Aa in NH was lower than C (0.50 ± 0.16 vs. 0.70 ± 0.16 ; $P < 0.0001$) while Wa/La, Wa/Aa and Ca/Aa were higher (1.12 ± 1.2 vs. 0.35 ± 0.2 , 0.44 ± 0.16 vs. 0.23 ± 0.06 and 0.50 ± 0.20 vs. 0.17 ± 0.1 ; $P < 0.0001$). The intima appeared normal in both groups. The medial thickening in NH was the result of smooth muscle hyperplasia and increased intercellular collagen. There were no differences in these measures between the three regions in either the NH or C hearts. While IVS thickness was similar in the both groups (1.70 ± 0.02 mm) RVFW as well as LVPW were thicker in NH than C (0.9 ± 0.16 vs. 0.53 ± 0.06 and 2.01 ± 0.05 vs. 1.7 ± 0.08 mm; $P < 0.0001$). Echocardiography also showed a higher pulmonary artery pressure (PAP) in NH than C (35 ± 6 vs. 11 ± 2 mmHg; $P < 0.0001$).

Conclusions: Our findings indicate that neonatal hypoxia in the rat, which results in mildly elevated PAP, has long-lasting effects on ICA morphology independent of ventricular pressure and wall thickness. The increased medial thickness and decreased luminal area suggest the possibility of increased coronary vasoreactivity and decreased vasodilatory reserve in adults following NH.

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Session 26: Interventions and New Technologies

O26-1

Interventional ASD-closure – safe, effective and harmless?

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Introduction: Percutaneous transluminal device closure of atrial septum secundum defects developed to be the treatment of choice during the last decade. The intervention is said to be safe and effective. Aim of this study was to investigate failure rate and complications.

Methods: Prospective observational study. Included were all patients entering the cath lab for device closure of interatrial defects. Major end point was the need of subsequent surgery due to failure of the procedure, device embolization or significant residual shunt. Other end points were procedure or device related complications.

Patients: 385 patients were included from 01/1998 to 12/2004. Age 0.21 to 78, median 24 years. Weight 4 to 123, median 59 kg. Height 54 to 192, median 160 cm.

Results: Surgical defect closure was necessary in 36 patients (9.4%): Interventional defect closure had not been attempted in 12 (3.1%) and had failed in 18 (4.7%) of them. Device embolization occurred early in 3 (0.8%) and delayed in 1 (0.2%) patients, device removal was surgical in 3 and interventional in 1. Significant residual shunt was the reason for surgery in 2 patients (0.5%), in one due to overlooked partial anomalous pulmonary venous drainage, due to a underestimated multiperforated cribriforme septum in the other.

No patient died. Four patients (1%) had significant other complications: Two patients developed pericardial effusion requiring pericardial drainage in one and prolonged hospital stay in both. Neurological complications were cerebral infarction due to air embolism in one and plexus brachialis paresis due to wrong arm position during anesthesia in another patient. There were no complications of the access vessels. No patient required blood transfusion or developed arrhythmia, atrial thrombi or infection during follow up.

Conclusion: Percutaneous transluminal device closure is righteously the treatment of choice for atrial septum secundum defects. However, the rates of failure or severe complication are not negligible and require careful patient selection, meticulous interventional techniques and attentive postinterventional follow up.

O26-2

Stenting of residual hypoplastic aortic segments late after coarctectomy

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Objective: Residual hypoplasia of the aortic cross and/or isthmus may persist despite adequate coarctectomy; such hypoplasia creates a gradient, hypertension and long term morbidity. This study was set to assess the feasibility, efficacy and safety of stent expansion of residual hypoplastic segments.

Methods: 21 consecutive patients (age 19.2 ± 10.0 years, median 15.0 years, range 11.2–45.8 years) with residual hypoplasia of the aortic cross or the isthmus and hypertension, were treated with stent expansion of the hypoplastic segment 15.6 ± 8.8 (median 13.5) years after coarctectomy. The procedure was delayed until the stent could be deployed up to a (near) adult size. All procedures were done under general anaesthesia; stent delivery occurred through an 11 F Mullins sheath on a BIB balloon (Numed, NY, USA); post procedure haemostasis of the femoral artery was obtained with local compression or Prostar XL (Biomedicon, India). No chronic medication (anticoagulation nor anti-aggregation) were given excepted antihypertensives when indicated.

Results: 23 stents were implanted: 9 stents in the cross, 14 stents in the isthmus (stents: CP or 2 covered CP (Numed, USA), Genesis (J & J, USA), Intrastent (EV3, USA)). The stents were dilated up to 17.2 ± 2.2 (median 17.0) mm. The left subclavian artery was electively crossed with the stent in 3 patients, without any complications in early or medium term follow-up. The gradient across the aortic arch decreased from 18.6 ± 9.6 (median 18.5) mmHg to 3.5 ± 6.2 (median 0.0) mmHg. Some gradient did persist just distal of left carotid artery, due to residual orificial narrowing or due to acute angulation. Arterial hypertension resolved during early follow-up in 16 pts, 5 required residual medication at significantly lower dosage. No complications occurred but 2 groin haematoma prior to use of transpuncture closing device.

Conclusions: Pressure loss due to residual hypoplastic aortic segments can effectively and safely be treated with stent implantation. Our limited data confirm the larger “radiologic” experience that the origin of the subclavian artery can be crossed with a stent. Some patients remain mildly hypertensive, especially during exercise, and will require additional medical treatment.

O26-3

Safety and efficacy of the Amplatzer Duct Occluder in patients under 6 kg using femoral or jugular access

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In order to determine safety and efficacy of the Amplatzer Duct Occluder in an un-selected population of small patients with large

patent ductus arteriosus (PDA), we reviewed our experience in all consecutive patients weighing 2.5–6.0 kg. No patient was referred for surgery or deferred. Thus, device occlusion was attempted in 11 patients, aged 2–7 months (median 3.7 months), weighing 3.8–5.8 kg (median 4.9 kg) and accomplished in all. All patients had high output congestive failure, failure to thrive and at least mild pulmonary artery hypertension. Pulmonary artery pressure was 34–100% systemic (median 64% systemic). Left ventricular end diastolic pressure was elevated in most patients, ranging from 5 to 25 mmHg (mean 13.4 mmHg). The smallest ductus diameter was 2.5–4.9 mm (median 4.1 mm). We used 4/5 mm, 4/6 mm and 6/8 mm occluders. Access was from the right internal jugular vein in 2 patients. Procedure time was 42–153 min with a median fluoroscopy time of 14.0 min (8.5–27.4 min). There were no device embolizations or other major complications. One patient required intubation for laryngospasm from ketamine. The initial post-procedural echocardiogram showed a significant decrease in shortening fraction that normalized during subsequent follow-up. There was no protrusion into the pulmonary artery but 5 patients had trivial to mild protrusion into the aorta with Doppler gradients of 0–10 mmHg. Complete occlusion of the ductus was achieved in 5/11 patients (45%) after 10 min, in 7/11 (64%) after 4–12 hours, in 8/9 patients (89%) after 6 months. There were no late complications. We conclude that PDA occlusion using the Amplatzer Duct Occluder is safe and effective from the femoral or jugular approach in infants under 6 kg.

O26-4

Tissue engineering of autologous human heart valves

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Objective: Tissue engineering of autologous heart valves with the potential to grow and to remodel represents a promising concept in pediatric cardiovascular surgery. Currently we are exploring the impact of cryopreserved human umbilical cord cells (CHUCCs) for the fabrication of tissue engineered heart valves for patients diagnosed prenatally with congenital heart lesions.

Methods: Human umbilical cord cells were isolated from vascular segments of umbilical cords and cryopreserved in a cell bank. After 12 weeks the cryopreserved cells were again expanded in culture and characterized by histology, immunohistochemistry and proliferation assays. Trileaflet heart valve scaffolds were fabricated from a porous polymer and sequentially seeded with CHUCCs (n = 10). Five of the heart valve constructs were grown for 7 days in a pulse duplicator and, as a control, five constructs were grown under static cell culture conditions for 7 days. Analysis of all tissue engineered heart valves included histology, immunohistochemistry, electron microscopy, functional analysis, and biomechanical and biochemical examination.

Results: We found that CHUCCs remained viable after 12 weeks of cryopreservation and showed a myofibroblast-like morphology. Histology of the tissue engineered heart valves showed layered tissue formation including connective tissue between the inside and the outside of the porous scaffold. Immunohistochemistry was positive for collagen (type I, III and IV), desmin, Laminin, α -actin and a

fibroblastspecific marker. Electron microscopy showed that the cells had grown into the pores and formed a confluent tissue layer during maturation in the pulsatile flow system. Biochemical examination showed an increase of extracellular matrix formation in constructs after pulsatile flow exposure compared to the static control group. Functional analysis demonstrated a physiological increase of the intracellular Ca^{2+} concentration of the recultivated cells and the conditioned constructs after stimulation with histamine.

Conclusion: This study demonstrates in vitro generation of viable and functional human heart valves based on CHUCCs and biometric flow culture systems. The CHUCCs demonstrated excellent growth potential and abilities of in-vitro tissue formation. These findings suggest the potential benefit of establishing autologous human cell banks for pediatric patients diagnosed intrauterinely with congenital defects that will potentially require heart valve replacement in the early years of life.

O26-5

Telemetric adjustable pulmonary artery banding with FloWatch. Initial UK experience

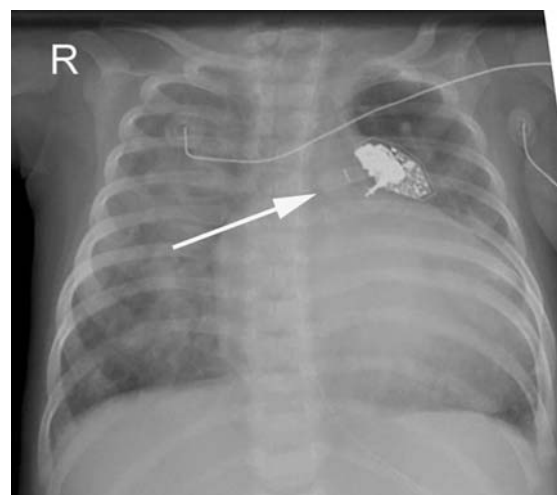
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Introduction: Patients with complex congenital heart defects may require pulmonary artery banding (PAB) to control the pulmonary blood flow or to re-train the left ventricle. Following conventional PAB, re-operations are often required for further adjustments of pulmonary blood flow and intensive care stays can be prolonged. The telemetrically adjustable PAB (FloWatch™) has been successfully introduced to clinical practice after experimental research.

We report the first experience using the telemetrically adjustable PAB (FloWatch™) in the United Kingdom.

Methods: The battery-free FloWatch™ is implanted around the pulmonary artery (Image). A remote control box delivers energy to the device and allows the adjustment of the percentage occlusion of the pulmonary artery.



Results: Nine children (median age 3 months; range 7 days to 6 months; mean weight 4.0 ± 0.6 kg) underwent implantation of the FloWatch™ through median sternotomy in 8 and left

thoracotomy in 1. The diagnosis was ventricular septal defect (VSD) with elevated pulmonary vascular resistance in 5, multiple VSDs with complex anatomy in 3, and complex transposition of the great arteries in 1. Four patients had a previous cardiac operation (two previous coarctation repairs; one previous conventional PAB; and one previous coarctation and multiple VSDs repair with residual VSD). Cardiopulmonary bypass was used in a single case with simultaneous repair of hypoplastic aortic arch. Neither death nor device-related complication occurred during a mean follow-up of 23 weeks (range 5 to 58 weeks). All patients had distal systolic pulmonary artery pressure within normal range at last follow-up. One patient has had a successful removal of the device and an arterial switch operation. The other eight are awaiting correction.

Conclusions: The device appears to be safe and to allow optimal adjustment of the pulmonary artery flow. The use of this technology may obviate the need for re-operations and appears to be a valuable surgical option for the management of selected infants. The initial result of the use of this device in the UK appears promising.

O26-6

Can 3D models of the right ventricular outflow tract and pulmonary artery improve patient selection for percutaneous pulmonary valve implantation?

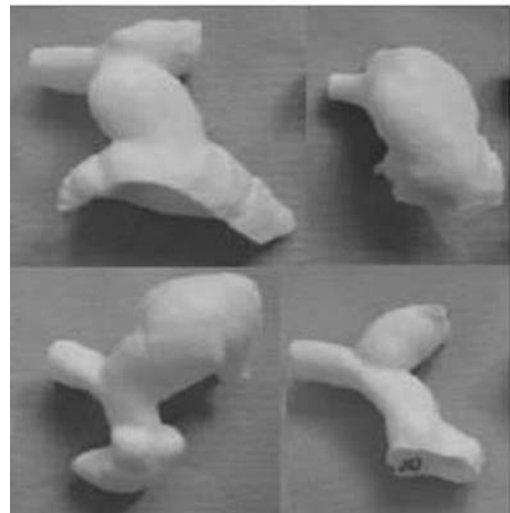
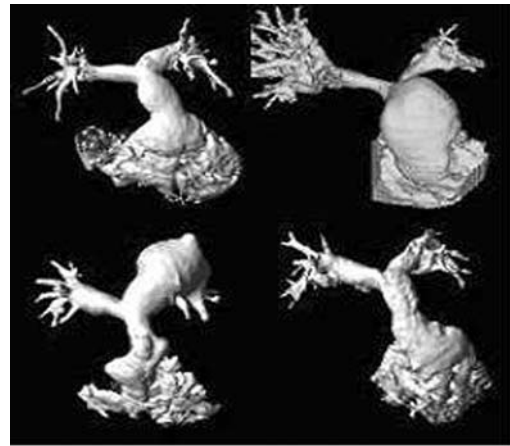
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Background: Significant pulmonary valvular heart disease can now sometimes be treated with percutaneous pulmonary valve implantation (PPVI). The selection of patients for PPVI is dependent on the 3D anatomy and size of the right ventricular outflow tract and pulmonary trunk/conduit (PA). A diameter between 14 and 22mm is most suitable for successful PPVI. Currently, this information is acquired using a combination of echocardiography and 2D and 3D MR images; however, interpretation of these data can still be difficult.

Purpose: To create detailed, 3D models of the pulmonary anatomy from MR data using Computer Aided Design (CAD) and Rapid Prototyping (RP), and compare the clinical usefulness of these models to the 3D MR reconstructions.

Methods: 12 patients with borderline anatomy for PPVI were clinically treated, with or without success of PPVI. We set out to retrospectively reassess this group of patients using 2 expert interventional cardiologists who were blinded to the outcome of the procedures. For all patients we created a 3D rigid, nylon model from the raw DICOM MR data, imported in a software for image elaboration and reconstruction of 3D volumes. The model was then printed by a RP system, a technology used to fabricate physical objects directly from CAD data sources (some examples in Figure). On the basis of conventional MR assessment the cardiologists expressed judgement over feasibility of the procedure (Figure). Then, they were given the 3D model of the same patient group and they adjusted their previous judgement.



Results: The cardiologists made the correct decision, based on the known clinical outcome, respectively in 66% and 50% of the cases using conventional MR assessment and improved to 75% and 75%, with the availability of the 3D models.

Conclusions: 3D rapid prototyping is a novel, inexpensive method of model building that allows for complete appreciation of 3D anatomy. This study indicates that such models can be used to select patients for PPVI more accurately than 3D MR images.

Session 33: Heart Failure, Transplantation and Pulmonary Hypertension

O33-1

Outcome of acute fulminant myocarditis in children

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Introduction: Acute fulminant myocarditis (AFM) is characterized by critical illness at presentation but excellent long-term survival in the adult population. We sought to highlight clinical features and outcome of AFM in children.

Methods: Diagnostic criteria of AFM were: 1) presence of a severe and acute heart failure 2) left ventricular (LV) dysfunction on echocardiography 3) recent history of viral illness without personal or familial history of cardiomyopathy.

Results: Eleven children with AFM were included between 1998 and 2003. Median age at presentation was 1 year (0–9 years) and initial left ventricular ejection fraction ranged from 10 to 40% (mean: 22%). Endomyocardial biopsy was performed in 3 patients. A viral agent was identified in 5 cases: Human Parvovirus B19 (n = 2), Epstein Barr Virus (n = 1), Varicella Zoster Virus (n = 1) and Coxsackie (n = 1). All the patients were managed in the intensive care unit for a median duration of 13 days. Intravenous inotropic support was required in 9 patients and 8 were mechanically ventilated. All patients received corticosteroids therapy, associated with intravenous immunoglobulin in 7 cases. Five patients experienced cardio-circulatory arrest that was successfully resuscitated in 4 cases.

At a median follow-up of 47.7 months, the 10 survivors have no cardiovascular or neurological sequelae, with normalized left ventricular parameters by echocardiography.

Conclusions: Despite a severe presentation, the subsequent outcome of AFM is favorable in the majority of the cases. Aggressive symptomatic management is warranted and heart transplantation should be considered only when no improvement is observed under maximal supportive therapy.

O33-2

Mortality and mode of death in pediatric patients with congenital heart disease

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Introduction: Prenatal diagnosis of congenital heart disease (CHD), newer imaging modalities, medical, catheter interventional, surgical therapies, and structured patient follow-up may improve survival in patients with CHD. While the rate of death due to heart failure and cardiac surgery may be reduced by newer medical and surgical therapies, the effect on sudden cardiac death remains uncertain. **Methods:** In a retrospective cross-sectional study, data of 3789 consecutive patients under 18 years of age with CHD, who were evaluated between 1994 and 2003, were analyzed. Mortality, mode of death, extra-cardiac co-morbidity potentially contributing to mortality, interventional cardiac catheterizations, cardiac surgery and autopsy findings were reviewed. The principal anatomy was defined by echocardiography.

Results: Overall mortality was 5.7% (n = 216). Age at death was <1 month in 165 (76.4%) and <1 year in 200 (92.6%). Death occurred in 98 (45%) cases peri-operatively, in 78 (36%) due to congestive heart failure, and sudden in 6 (2.7%) patients. Other cardiovascular events accounted for 9 deaths (4.2%) and non-cardiac events for 25 (11.6%) casualties. Despite higher surgical complexity, operative mortality decreased from 4.7% in 1994/1995 to 2.8% in 2002/2003. Severe extra-cardiac co-morbidity were found in 116 (54%) of the 216 deceased patients and required comfort care in 28 children. Previously undetected anatomic information was found in 18 of the 69 performed autopsies.

Conclusions: Children with CHD have a low mortality, with most deaths occurring in the first year of life. Although surgical mortality is less than 3% nowadays, the majority of deaths are peri-operative or due to heart failure. Sudden cardiac death is a rare event.

Extra-cardiac co-morbidity is frequent in children with CHD who expire. Autopsies still present a valuable source of anatomical information in children with CHD.

O33-3

Ability of plasma levels of natriuretic peptides type B and A to detect heart failure and haemodynamically significant volume or pressure load in children with heart disease

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Objective: To evaluate the ability of natriuretic peptide types B and A (BNP and ANP) to differentiate heart failure from volume or pressure load in children with congenital or acquired heart disease. **Methods:** Plasma levels of BNP and ANP were determined in 137 children with various types of congenital or acquired heart disease and 23 control (C) children. Haemodynamically, heart diseases were classified as resulting in heart failure, volume or pressure load or to be haemodynamically insignificant (I). Receiver operating curves (ROC) were constructed to evaluate the ability to differentiate the different haemodynamic consequences of heart disease.

Results: ROC areas for heart failure compared with all other children were 0.88 for BNP and 0.85 for ANP. Using a BNP cutoff level of 100 pg/ml, sensitivity was 92% and specificity 91%. For ANP, a cutoff level of 150 pg/ml resulted in sensitivity and specificity of 73% and 86% respectively. ROC area for volume load compared with I and C children combined was 0.84 for BNP. Using a BNP cutoff at 10 pg/ml sensitivity was 93% and specificity 75%, while a cutoff at 20 pg/ml resulted in sensitivity of 61% and specificity of 94%. Similarly, the ROC area for pressure load compared with I and C was 0.76. Using a BNP cutoff at 10 mg/ml sensitivity was 72% and specificity 75%, while a cutoff at 20 pg/ml resulted in a sensitivity of 48% and specificity of 93%. ANP was inefficient in detecting pressure and volume loads with ROC areas <0.6.

Conclusions: Plasma levels of BNP >100 pg/ml and ANP >150 pg/ml are both efficient in differentiating heart failure from other types of heart disease. Moreover, BNP levels are helpful in detecting significant haemodynamic load in asymptomatic patients and this ability seems more efficient to detect volume load than pressure load. For both volume and pressure load, a BNP >20 pg/ml strongly suggests a haemodynamically significant load, while children with significant volume load very rarely have BNP <10 pg/ml.

O33-4

Is midregion proANP a prognostic marker in children with heart transplantation?

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Objective: Natriuretic peptides are accepted markers for heart failure. The main lifelong health hazards after heart transplantation (HTx) are rejections and infections. Additional biomarkers are needed that allow discrimination between the two, individual risk appraisal and early diagnosis and treatment. Midregion proANP (mpANP) is a newly studied natriuretic peptide with the

advantage of long stability in vitro. This study aims to determine mpANP concentrations in correlation to post-transplant time and their prognostic value for clinical episodes of rejection and infection.

Methods: In a prospective observational study we analyzed 228 mpANP serum levels in 64 heart-transplanted patients (26 male, 38 female; median age 12.6 years, range 171 days–27.6 years; body weight 36.9 kg, range 5.8–95.2 kg; time since HTx 697 days, range 1 day–13.0 years). In addition 23 mpANP concentrations at time of endomyocardial biopsy were determined. mpANP levels were analyzed using a new sandwich immunoassay (B.R.A.H.M.S. SERISTRA[®]).

Results: Regarding gender, age and post-transplant time we found no significant differences in mpANP serum levels. Children in terminal heart failure listed for HTx showed high levels of mpANP which decreased under unloading of the myocardium by mechanical assist device for bridge-to-HTx (n = 9); when no mechanical support was necessary, mpANP remained elevated and declined only after HTx.

Median plasma mpANP concentration during rejection episodes was also highly elevated (432, range 4–3140 pg/ml) compared to routine measurements made without signs of infection or rejection (median 245, range 43–2690 pg/ml; p = 0.003).

In 4 children with biopsy-proven rejection (ISHLT 3A) median mpANP was 589 (range 355–2030) pg/ml, compared to 241 (range 4–1710) pg/ml in 19 children with mild or no rejection (p = 0.067).

Conclusion: Our results suggest that mpANP plasma concentrations are highly elevated in children with terminal heart failure before HTx. mpANP appears to be a promising tool for individual risk estimation for rejection in transplanted children and for stratification of therapy options. Studies of more patients and events are necessary to show whether mpANP is able to discriminate between rejection and infection.

O33-5

Cardiac graft growth after heart transplantation in children

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Objective: The aim of this study was to assess anatomic changes of cardiac allograft and compare them to linear growth in pediatric heart-transplant patients.

Methods: From 1987, 53 pediatric heart transplantations (HT) were performed in a single center. The study group included 17 recipients (8 males and 9 females) who were less than 13 years old at the time of HT (2 days to 13 years, mean = 5.7 years, median = 5 years) and whose follow-up was more than 18 months post-transplant (18 months to 12 years, mean = 6.1 years, median = 5.8 years). The donor age varied from 7 days to 13 years (mean = 5.9 years, median = 3 years); the weight ration donor/recipient varied from 0.91 to 4.5 (mean = 1.63, median = 1.39). Measurements were collected every month during the first post-transplant year, every 2 months after one year, and included: linear growth parameters (weight, height) and echocardiographic parameters (end-diastolic left ventricle (LV) diameter, end-systolic LV diameter, interventricular diastolic thickness, left posterior wall diastolic thickness). Body surface area (BSA), LV mass (g) and LV mass index (g/m²) were calculated.

Results: Mean BSA increased from 0.68 m² to 0.94 m² during follow-up. Thirteen patients had normal and 4 had moderate-impaired linear growth. Maximum linear growth was observed in infants less than 5 years old (18.2% every year).

Diastolic LV diameters, systolic LV diameters and LV mass increased linearly with BSA in all the cases. LV mass index increased in the first post-transplant month (mean = 168.2 g/m²) and decreased later to reach normal range within the first six months post-transplant. LV echographic measurements ranged within normal value for age beyond the sixth postoperative month.

Conclusion: In our experience, cardiac graft grows linearly with BSA in children and mid-term and long-term graft measurements range within normal value for age.

O33-6

Mortality after pediatric heart transplant. Two decades of single centre experience

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Twenty years after the first successful pediatric heart transplantation (HTx), the long term outcome of this young population still remains unknown. Aim of the study is to analyse late mortality in our pediatric HTx population.

Since 1985, we performed 605 HTx. 43(7%) were children <18 yrs old. 6 patients were <1 yr old.

Twenty Seven (56%) patients were male. Age at operation was 9.7 ± 6.3 (38 days–18).

Mean weight at surgery was 29 ± 18 Kg (2.7–70). Indications to HTx were: cardiomyopathy in 33 patients (76%), CHD in 9 (21%), cardiac tumor in 1 (3%). We performed orthotopic HTx in 40 pts, while 3 patients underwent heterotopic HTx. Immunosuppressive regimen was Cyclosporine A and Azathioprine-based in all. Steroids were used only in selected cases. Fifty percent of all patients are immunosuppressed with only Cyclosporine A, at last follow-up. Induction therapy was used in 20 (46%). Under 10 yrs of age, rejection was diagnosed on clinical and echocardiographic grounds and biopsies were performed in unclear cases. Vasculopathy was detected with coronarography.

Overall survival at Kaplan Meyer analysis (confidence interval 95%) was 83% at 1 yr post-HTx, 75% at 5 yrs and 69% at 10 yrs. 60% at 15 yrs. We had 13 deaths (30%): 7 occurred within the first yrs after HTx, 6 occurred later. Early causes of death were: graft failure in 3 (42%), acute rejection in 3 (42%) and non Hodgkin lymphoma in 1 (16%). Late causes of death (1 yr after HTx) were: neoplasms in 3 (50%), 2 PTLTD, infections in 2 (33%) (fatal viral myocarditis in 2 pts both transplanted with a pre-HTx diagnosis of post-viral dilated cardiomyopathy), severe vasculopathy in 1 case (17%).

Conclusions: Early mortality (first year post HTx) was higher than late mortality. In the subset of survivors after 1 yr post HTx, cumulative survival was 87% at 10 years (15 pts), and 80% at 15 yrs (10 pts). In our experience, the main cause of late mortality was neoplasms, lack of risk-factors for atherosclerosis in children might explain our low incidence of vasculopathy. Among infections, only recurrences of pre-HTx myocarditis had a fatal outcome.

O33-7**Incidence of Epstein-Barr virus infection in pediatric heart transplant patients – a prospective clinical study**

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Background: Epstein-Barr virus (EBV) infection has been reported to be associated with posttransplant lymphoproliferative disorders (PTLD) in adult and children after organ transplantation. The aim of this prospective study was to analyze the incidence and characteristics of EBV infection or persistence in pediatric heart transplant (HTX) patients.

Methods: During 2002 to 2004 molecular analysis of Epstein-Barr virus activity (EBV load) was performed by real-time PCR (TaqMan) in 65 pediatric de-novo heart patients. Data are expressed as copies/ μ g Namalwa DNA. The incidence of PTLD was also analyzed in regard to EBV infection.

Results: EBV load was significantly increased in 23% (15/65) of the patients, median 3475 copies/ μ g DNA (range 1032–72000 copies/ μ g DNA). Mildly increased (100–1000 copies/ μ g DNA) EBV activity was detected in 46% (30/65 patients) and 31% (20/65 patients) of the patients studied were negative for EBV DNA in the peripheral blood.

The incidence of PTLD was 5.3% (7/127) of all pediatric heart transplant patients in our pediatric transplantation program during 1988–2003. PTLD was dominantly of B-lymphoma type and associated with EBV in 75% (5/7) of cases. Two patients have ocular manifestation of PTLD; thus tissue biopsy was not performed.

PTLD occurred 3.3 (range 0.5–4.6) years after HTX. Immunosuppressive medication consisted of cyclosporine (6/7) and FK506 (1/7), azathioprine (Imurek) in 6/7 patients, and mycophenolate in 1/7 patients. Complete remission was achieved in 4/7 patients. Two patients relapsed after initially successful surgical and antitumor treatment, with lethal outcome in one. Reduction of immunosuppression was performed in all patients with elevated viral load, followed by tight monitoring of EBV activity.

Conclusions: EBV infection is associated with increased risk of PTLD in pediatric heart transplant patients. Early screening of EBV load may identify those patients with an increased risk of PTLD and may allow accurately timed preemptive interventions, including reduction of immunosuppression, antiviral therapy or adoptive immunotherapy.

O33-8**Oral therapy with the endothelin antagonist bosentan improves the clinical, exercise and haemodynamic status of patients with pulmonary arterial hypertension related to congenital heart disease**

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Introduction: The purpose of this prospective nonrandomised open clinical study was to evaluate the clinical, exercise and haemodynamic effect of chronic oral administration of the nonselective endothelin receptor antagonist bosentan on patients with

pulmonary arterial hypertension (PAH) related to congenital heart disease (CHD).

Methods: Twenty-one patients with chronic PAH related to CHD (15 with Eisenmenger syndrome) aged 22 ± 3 years underwent clinical, exercise and haemodynamic evaluation at baseline and after 16 weeks of treatment with bosentan. Patients were in World Health Organisation (WHO) Class II–IV and had oxygen saturation $87 \pm 2\%$.

Results: Bosentan therapy improved ($p < 0.01$) peak oxygen consumption from 16.8 ± 1.4 to 18.3 ± 1.4 $\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and exercise duration from 9.0 ± 0.8 to 10.7 ± 0.6 min at treadmill test, walking distance from 416 ± 23 to 459 ± 22 m and Borg dyspnoea index from 2.8 ± 0.2 to 2.0 ± 0.1 at 6 min walk test. Bosentan treatment improved ($p < 0.05$) WHO Class, mean pulmonary artery pressure from 87 ± 4 to 81 ± 14 mmHg, pulmonary blood flow index from 3.2 ± 0.4 to 3.7 ± 0.5 $\text{L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$, pulmonary to systemic blood flow ratio from 1.2 ± 0.2 to 1.4 ± 0.2 , and pulmonary vascular resistance index from 2232 ± 283 to 1768 ± 248 $\text{dyne} \cdot \text{s} \cdot \text{cm}^{-5}$. Two, presumably arrhythmic, deaths occurred in baseline WHO Class IV patients who had improved during treatment.

Conclusions: Bosentan induces short and mid-term clinical, exercise and haemodynamic improvement in patients with PAH related to CHD. Larger studies with long-term endothelin receptor antagonism are needed to assess safety and possible therapeutic role of bosentan in this population.

O33-9**Long-term safety profile of bosentan in paediatric patients with pulmonary arterial hypertension: results from the TRAX database**

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Introduction: Pulmonary arterial hypertension (PAH) is a progressive orphan disease associated with a poor prognosis in adults, as well as in children. The oral dual endothelin ETA/ETB receptor antagonist bosentan (Tracleer) is approved in Europe since 2002 for the treatment of PAH. There is evidence from a randomised controlled study (BREATHE-3) and open-label studies confirming the favourable profile of bosentan in paediatric patients.

Methods: Confirmatory data is available from the TRAX database, which is a European non-interventional, prospective surveillance system initiated by the manufacturer in agreement with the European Agency for the Evaluation of Medicinal Products (EMA). TRAX has been set up as a web-based database, which provides treatment and drug monitoring algorithms. Information entered by the prescribers is directly transferred on a secure internet connection to a central database, and is reviewed regularly by the manufacturer's global safety department to determine whether safety signals have been detected. Notifications are automatically provided in real-time to the person entering information. Safety signals include adverse events, elevations of liver function tests (ALT/AST), other abnormal lab values, death, and hospitalization.

Results: Until 19 November 2004, a total of 146 children aged 2–11 years (36.3% 2–5 yrs, 63.7% 6–11 yrs) were included in the database. 51.4% were males, 40.4% had idiopathic PAH, 45.2% PAH associated with congenital systemic-to-pulmonary shunts.

Most children were in NYHA class II (28.1%) or III (50.7%). Concomitant medications at baseline included prostanoids (19.2%; epoprostenol 6.8%, inhaled iloprost 8.2%, beraprost 4.8%) and anti-coagulants (45.2%). Mean exposure to bosentan was 36.2 (\pm 30.1) weeks (adults: 38.8 weeks). 37 (25.3%) patients were treated with bosentan for at least 1 year. Safety signals were recorded in 33.6%, which is lower than in patients \geq 12 years/adults (40.4%). Elevated ALT and/or AST values were recorded in 2.1% (adults: 7.4%). Discontinuation rates were low (14.4%).

Conclusions: The TRAX data provide supportive evidence on the long-term safety of bosentan in children with PAH under real life conditions. Bosentan was safe and well tolerated, and the liver signal rates in children aged 2–11 years compared to older children/adults were lower.

Session 22: Oral Poster Session I

OP22-1

Electrocardiographic changes predicting sudden death following long-term high-dose propofol sedation

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Introduction: An association between long-term high-dose propofol infusion in head-injured patients and the occurrence of metabolic acidosis, rhabdomyolysis and hyperkalemia is referred to as Propofol Infusion Syndrome (PRIS). PRIS is associated with sudden death, presumed of cardiac origin. Following a case of PRIS, we explored the ECG abnormalities associated with PRIS to identify possible pathophysiological mechanisms.

Methods and Results: ECG changes characterized by downsloping ST segment elevation in the precordial leads V1 to V3 (Brugada-like ECG pattern), which reversed after the discontinuation of propofol, were observed in our index-patient. To assess the relation between propofol infusion, the ECG pattern and development of arrhythmias and sudden death, we reanalyzed a previously described cohort of 67 head-injured patients, of whom 7 had been identified to have PRIS. The presence of the electrocardiographic pattern of ST segment elevation in leads V1 to V3 was the first alteration recorded in the patients. Six of the 7 PRIS patients developed the Brugada-like ECG pattern and subsequently died of malignant arrhythmias within 10 ± 12 hours, whereas all unaffected patients with available ECG exhibited a normal pattern and developed no ventricular arrhythmias.

Conclusions: Our findings indicate that in patients with PRIS, the development of Brugada-like ECG pattern can forewarn of impending cardiac electrical instability and ventricular arrhythmias. We recommend periodic monitoring of 12-lead ECG in patients during long-term high-dose propofol infusion.

OP22-2

Buying time before conversion or transplantation in failing atrio-pulmonary Fontan hearts by dual chamber epicardial pacing

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Objectives: The atrio-pulmonary Fontan circulation frequently leads to uncontrollable arrhythmias, heart failure, or protein-losing enteropathy (PLE). Conversion to total cavo-pulmonary anastomosis (TCPC) or transplantation may represent the only solutions to these problems. In hesitant patients/families, we sought to evaluate the effect of dual chamber epicardial pacing, as an intermediate time-buying measure.

Methods: Between 1997–2004, 9 decompensated patients (aged 6–18 years) with an atrio-pulmonary Fontan circulation and sinus node dysfunction received dual chamber epicardial pacing systems (left thoracotomy; n = 8, and sternotomy; n = 1). Indications included refractory arrhythmias (n = 5), PLE (n = 2), intractable heart failure with effusions (n = 1), and severe exercise intolerance (n = 2). Patient and lead data (mean \pm standard deviation) were compared between hospital discharge after pacemaker implantation, and last follow-up (mean 3.3 ± 1.0 years).

Results: There was no mortality or morbidity, and good lead values were obtainable at each implantation, despite heavily scarred epicardium in a redo surgery setting. Lead survival was 100%. At follow-up, both atrial (impedance = 683 ± 40 Ohm; threshold = 0.8 ± 0.1 V at 0.5 ms; sensing P waves = 3.3 ± 0.8 mV) and ventricular (impedance = 630 ± 68 Ohm; threshold = 1.3 ± 0.3 V at 0.5 ms; sensing R waves = 8.7 ± 2.5 mV) leads retained satisfactory pacing characteristics, similar to those at discharge. More remarkably from a clinical standpoint, arrhythmias subsided in all instances and no longer required medication in 3 patients, PLE improved temporarily in one and disappeared in another patient, exercise intolerance diminished, and heart failure was controlled.

Conclusions: Although the unfavorable hemodynamics and electrophysiology of an atrio-pulmonary Fontan circulation will eventually need a TCPC with arrhythmia surgery or transplantation, some patients and/or their families may want to delay or refuse these more extensive options. Severely sick patients may be temporarily helped by dual chamber pacing, intuitively through improved single ventricle hemodynamics, although our data is purely clinical and qualitative. In a multiple-redo surgery setting remote from initial surgery, a left lateral thoracotomy provides safe access, and allows for quantitatively reliable and durable epicardial pacing.

OP22-3

KLF13, a novel GATA4 cofactor, is required in Xenopus heart formation

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Candidate genes causative for congenital heart disease are increasingly identified through a variety of approaches. Comparative analysis of the rat B-type natriuretic peptide (rBNP) promoter identified an evolutionarily conserved CACCC box, flanked by GATA elements, which can be bound by members of the Krüppel-like family (KLF) of zinc finger proteins. This CACCC box was found to be important for rBNP activity in primary cardiomyocyte cultures, as its mutation decreased promoter activity by 5 fold. KLF13, the major family member expressed in the heart, bound this element and activated the rBNP promoter. We used biochemical and genetic approaches in mouse, rat and Xenopus to investigate the function of KLF13 in heart development. Cotransfection of a rat-BNP reporter into P19 murine embryonic carcinoma cells with KLF13, GATA4 and both resulted in 3.5, 12 and 160 fold activation, respectively. Co-immunoprecipitation showed direct physical association between KLF13 and GATA4. Immunohistochemical analysis shows preferential expression in the developing

myocardium and valves. We cloned the *Xenopus* KLF13 homolog and found high conservation across species, with >90% homology in the DNA binding domain. Morpholino knockdown in *Xenopus* leads to severe cardiac morphogenetic defects including ventricular hypoplasia and hypotrabeulation, with ensuing pericardial edema. Molecular analysis of the knockdown model shows severe disturbance of the temporal orchestration of transcription factor cascades. Salient features include decreased initiation and maintenance of NKX2.5, GATA5/6, TBX5, ANF and *aMLC*. The severe phenotype may be explained (1) by the finding that KLF13 and GATA4 physically and functionally interact (2) by the dysregulation in temporal and dosage coordination of important cardiac regulators. Taken together, these results identify KLF13 as a novel important modulator of GATA4 activity and an essential regulator in heart formation. We speculate that mutations in KLF13 may be causative in congenital heart disease.

OP22-4

Effect of BRPP on neonatal rat cardiomyocyte culture during in vitro norepinephrine and isoproterenol stimulation

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Introduction: Myocardial sympathetic activity is increased in heart failure, and norepinephrine (NE) stimulate apoptosis of cardiomyocytes through alpha- and beta-adrenergic pathway. Isoproterenol (ISO), as well as NE, induces apoptosis in neonatal rat cardiomyocyte cell (NRC) culture. BRPP (brain-pig polypeptide) has shown positive effect on growth in several cell-lines (CHO-K1, BHK) as well as some primary cell cultures. Our goal was to test influence of BRPP on NRC culture during adrenergic pathway stimulation.

Material and Methods: Primary ventricular cardiac myocytes were prepared from 6–8 days old Fisher rats hearts were removed, ventricles pooled and ventricular cells isolated with Worthington Neonatal Cardiomyocytes Isolation Kit. Isolated cells were plated to 24-well culture plates (Falcon) at density of 1.25×10^5 cells/cm² in DMEM with 10% FBS. NRC were maintained at 37°C in humidified air with 5% CO₂. After 24 hours, cells were treated with NE (1 or 10 mcmmol/L), ISO (1 or 10 mcmmol/L) and with or without BRPP 0.1 mcgr/cm², as well as with NE (1 or 10 mcmmol/L) + BRPP and ISO (1 or 10 mcmmol/L) + BRPP. 48 hours after treatment cells were harvested and counted. BRPP is isolated from fresh young pig brain tissue by own procedure.

Results: NRC treated with BRPP has shown significantly ($p = 0.002$) higher cell number vs. control. Addition of BRPP to any other selected NRC group have shown significant increase vs. without BRPP as follows: with NE 1 mcmmol ($p = 0.001$), NE 10 mcmmol ($p = 0.003$), ISO 1 mcmmol ($p = 0.002$) and ISO 10 mcmmol ($p = 0.002$). NRC groups + NE 1 mcmmol treatment with BRPP had significantly higher cell numbers vs. sample without BRPP ($p = 0.001$) while with NE 10 mcmmol significant difference was not observed. NRC groups with ISO and BRPP have shown significant increase vs. without BRPP for ISO 1 mcmmol and ISO 10 mcmmol.

Conclusion: BRPP has shown its potential stimulation NRC in vitro alone or with different proapoptotic agents and in different

amounts. Its relevance in neonatal cardiac pathology remains to be elucidated.

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OP22-5

Reproducibility of free-breathing magnetic resonance coronary angiography

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Introduction: Magnetic resonance coronary angiography (MRCA) has been successfully used for visualizing coronary arteries without radiation or contrast agents. However, the reproducibility of coronary artery dimensions imaged by MRCA has not been ascertained. The aim of this study was to determine the reproducibility of luminal dimensions of right coronary (RCA), left anterior descending (LAD) and left circumflex (LCX) coronary arteries using free-breathing steady-state free precession (SSFP) MRCA.

Methods: Twenty two healthy volunteers (mean age 32 ± 7 years, 12 males) without known coronary artery disease were imaged at 2 centers (Tuebingen, Germany and Baltimore, USA) using navigator-gated and corrected 3D SSFP MRCA on a commercial whole body 1.5 T System (Philips Medical Systems, Best, NL). Repeat images of RCA ($n = 21$), LAD ($n = 14$) and LCX ($n = 14$) were obtained in separate sessions using identical imaging parameters. True visible vessel length, signal to noise, contrast to noise ratios (SNR and CNR) and the average luminal diameter over the first 4 cm of the vessel were measured using a semi-automatic tool. Intra-, inter-observer and inter-scan reproducibility of coronary artery diameters were determined using linear regression (LR) and intraclass coefficients (ICC).

Results: The mean length of the RCA (12.5 ± 2 cm vs. 12.4 ± 2 cm), LAD (8 ± 2 cm vs. 8 ± 1 cm) and LCX (4.8 ± 2 cm vs. 4.6 ± 2 cm) imaged for original and repeat scans were not significantly different (all $p > 0.30$). Mean SNR and CNR were similar between original and repeat scans for right ($p = 0.28$) and left ($p = 0.98$) coronary systems. For RCA, LAD and LCX luminal diameters, there was a highly significant intra-, inter-observer and interscan correlation (Table 1). High to excellent ICC's were calculated for intra-, inter-observer and interscan measurements of the RCA, LAD and LCX diameters (Table 1).

Table 1.

	RCA		LAD		LCX	
	LR (r)*	ICC (r)	LR (r)*	ICC (r)	LR (r)*	ICC (r)
Intra-observer reproducibility	0.99	0.98	0.90	0.89	0.85	0.95
Inter-observer reproducibility	0.98	0.98	0.90	0.89	0.88	0.94
Interscan reproducibility	0.84	0.86	0.81	0.63	0.81	0.79

* = $p < 0.001$

Conclusions: Free-breathing SSFP MRCA is a non-invasive technique which can repeatedly visualize long segments of coronary

arteries with high reproducibility. MRCA could potentially have a role in following of progression of coronary artery disease and in longitudinal therapeutic studies involving coronary arteries.

OP22-6

FETCH-Study: prospective fetal cardiology study in Switzerland

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Introduction: Switzerland has a population of 7 million with 70–75 000 live births per year. Assuming an incidence of congenital heart disease (CHD) of 0.7–0.8%, 490–600 affected newborns would be expected per year, of which 230–260 with haemodynamically significant and prenatally detectable CHD. Obstetricians should detect CHD with ultrasound screening and refer them to a tertiary fetal cardiology centre for confirmation and further treatment. The aim of this prospective study was to analyse prenatally detected CHD and compare them with the postnatally diagnosed cohort.

Methods: Prospective study of all fetal examinations done in 7 tertiary fetal cardiology centres in Switzerland during a period of 2 years time (1.7.01–30.6.03) and prospective assessment of all haemodynamically relevant and prenatally detectable CHD of children born during the same period of time in these centres.

Results: A total of 433 fetal examinations were done, of which only 35% before 24 weeks of gestation. 272 (62%) were normal, 94 (22%) showed major CHD, 21 (5%) mild CHD and 46 (11%) arrhythmias. The sensitivity of fetal diagnosis for CHD was 99% and the specificity 87%. Postnatal diagnosed major CHD were 306. This means that only 23% of all 400 major CHD were diagnosed in utero. The spectrum of in utero diagnosed CHD was: single ventricle malformation 22 (23%), Conotruncal malformation 30 (33%), septal defects 28 (30%), valvar abnormalities 7 (7%), others 7 (7%). Referring to the fetal and postnatal cohort 50% of the single ventricle malformations, 22% of the conotruncal malformation, 17% of the septal defects, 12% of valvar abnormalities and 20% of other malformations were diagnosed in utero.

Conclusions: Although it could be demonstrated that not only major CHD detectable in a four-chamber view were diagnosed in utero, only 23% of major CHD were detected prenatally. This means that more emphasis should be given to prenatal screening.

OP22-7

Outcome in utero and after birth of fetuses with isolated complete atrioventricular block.

Efficacy of the maternal-fetal therapy

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Background: Complete atrioventricular block (AVB) can occur in presence of maternal connective tissue disease or antibodies anti SSA/Ro, anti SSB/La, in structurally normal heart, at times with myocarditis/endocarditis. Maternal-fetal treatment (MFT) with steroids was suggested in the last decade with the aim to regress the conduction disorder and/or to improve the fetal compensation.

Objectives: To analyse retrospectively the data of 3 centers regarding fetal cases with isolated AVB and the efficacy of MFT.

Material: Between 1990–2004, 29 pregnant women with antibodies anti. Ro/La (10 with autoimmune disease) were studied by fetal echocardiography. Complete AVB was diagnosed in 27 singleton pregnancies, in one twin of a twin pregnancy and in one twin of a triplet pregnancy that presented initially signs of myocarditis. 21 cases (c.) – group (gr.) 1 were compensated, 8 c. – gr. 2 showed heart failure (HF) – 3 at presentation. 23 c. underwent MFT with steroids (20 dexamethasone, 2 with associated salbutamol) and 1 with isoproterenol.

Results: Age at presentation was not significantly different in groups: mean in gr. 1 – 23.7 w.g. (19–30), gr. 2 – 25.4 w.g. (20–32), $p = 0.38$. Fetuses of gr. 2 had a lower mean heart rate (HR) at presentation. 48.5 ± 9.26 (32–60), versus 61.38 beats/min. ± 10.12 (50–90), $p = 0.004$ and mean neonatal HR: 42.6 ± 5.1 (38–50) versus 57.6 ± 14.8 beats/min. (29–110), $p = 0.015$. HR reduced throughout pregnancy in both groups (at pair T-test $p = 0.084$ versus 0.08).

Outcome: Total mortality was 2/21 c. of gr. 1 (9.5%) and 3/8 c. (37.5%) in gr. 2 (2 died in utero, one at presentation): Cases of gr. 1 were delivered at higher gestational age -35.5 w.g. ± 2.04 (34–38) versus 31.7 w.g. ± 10.8 (28–38), $p = 0.002$. Pacemaker was implanted in 25/28 survivors at 1day–5 yrs (2 neonates of gr. 2 dying after). Another twin of the triplet pregnancy showed after birth the 1st–2nd degree AVB.

Conclusions: Outcome of our cases was dependent on the heart rate at presentation and presence of HF. Steroid treatment did not regress the conduction disorder, however improved the heart compensation. Close follow-up allowed to anticipate the delivery in cases with HF in order to perform an early pacemaker implant.

OP22-8

Behavior of the foramen ovale flow in fetuses of diabetic mothers with myocardial hypertrophy

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Introduction: The foramen ovale (FO) is an extremely important structure in fetal circulation, as it is the natural passage for the highly oxygenated blood coming from the placenta directly to the left atrium. Frequently, fetuses of diabetic mothers (FDM) display myocardial hypertrophy (MH), with disturbed left ventricular diastolic function, which could cause FO flow changes, with consequent changes in its pulsatility index.

Objective: To test the hypothesis that FDM with MH have higher pulsatility index of the FO flow than fetuses with no MH of either diabetic or non-diabetic mothers.

Methods: This is a controlled cross-sectional study comparing FDM with MH to FDM with no hypertrophy and normal control fetuses.

Subjects: 16 FDM with MH (group I), 36 FDM with no MH (group II) and 39 normal control fetuses (group III). Doppler fetal echocardiography was performed and the foramen ovale pulsatility index (FOPI) was obtained as the ratio [maximal velocity (systolic or diastolic) – pre-systolic velocity/mean velocity]. ANOVA and

the test of least significant differences were used, with a critical alpha of 0.05.

Results: Mean FOPI was 4.07 ± 1.32 in group I, 2.28 ± 0.65 in group II and 2.39 ± 0.35 in group III ($p < 0.001$). Group I was different from group II ($p < 0.001$) and from group III ($p < 0.001$). Group II was not different from group III ($p = 0.487$).

Conclusion: Fetuses of diabetic mothers with myocardial hypertrophy show a higher foramen ovale pulsatility index than fetuses with no myocardial hypertrophy and normal control fetuses. It is suggested that this difference is due to the lower left ventricle compliance secondary to interventricular septum hypertrophy.

OP22-9

Chronic inflammation with and without Fontan palliation in univentricular heart patients

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Objectives: Protein-losing enteropathy (PLE) is a late complication of patients with Fontan circulation characterised by massive enteric protein loss in the absence of chronic enteric infections. The pathogenesis of PLE is not fully understood but hemodynamic alterations and immunological participation is presumed. Characteristic laboratory findings of patients who develop PLE are signs of inflammation. The present study aimed to examine whether there are cellular and humoral signs of inflammation in patients with univentricular heart who do not suffer from PLE.

Methods: Ten patients with univentricular heart were analysed before and after the Fontan operation. Results were compared to a group of age-matched healthy control persons ($n = 25$). Cellular parameters (cell count and activation parameters), major serum proteins, complement components, electrolytes as well as soluble serum (s) components: sIL-2R, IL-6, IL-8, IL-10, TNF- α , sE-, sL-, sP-selectins, sPSGL, sICAM-1, sPECAM-1, sHistamine, sNeopterin were measured. Detailed explorative statistical analysis was performed.

Results: Many parameters indicating increased inflammation were found which differ to control group both before as well as after surgery. Moreover, parameters were determined differing to healthy control persons only before surgery or only after surgery. Our data suggest a relation between some laboratory parameters and vena cava superior or inferior blood pressure.

Conclusions: The results show that these changes in the immune system do not only appear because of the new circulation. Some of them appear even earlier and are in part strengthened after or even by the operation.

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OP22-10

Prospective, systematic long-term follow-up after arterial switch operation for transposition of the great arteries

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Background: Despite numerous reports on the results of the arterial switch operation (ASO) few studies have systematically and prospectively evaluated long-term results. Purpose of this study was to assess clinical outcome in patients who underwent ASO for transposition of the great arteries in our institution from 1990–1995.

Methods: A chart-review was performed. Patients alive, living in Holland, traceable and speaking Dutch, received an invitation for prospective assessment, including echocardiography and exercise testing.

Results: There were 54 survivors of ASO. Follow-up was lacking for 5 patients, who moved abroad immediately postoperatively. Of 49 remaining patients mean duration of follow-up was $10,0 \pm 2,0$ years. **Residual Lesions** were pulmonary stenosis (mild to moderate): 8; VSD: 1; aortic regurgitation (none severe): 4. Re-interventions were performed for valvular and supra-valvular pulmonary stenosis (1 balloon valvuloplasty, 1 transannular patch and 1 stent implantation). One patient was re-operated for newly developed subvalvular aortic stenosis. One patient had poor LV-function, following myocardial infarction directly postoperatively. This was the only patient using cardiac medication.

For prospective assessment of the 54 survivors, 10 couldn't be traced, 3 didn't speak Dutch, 8 refused, leaving 33. Of these 33 patients mean duration of follow-up was $10,5 \pm 1,5$ years (n.s. versus entire cohort). The percentage residual lesions did not differ from the entire cohort. All patients reported their health as good/very good. Exercise capacity: $86 \pm 20\%$ of the predicted. Mean VO_2 -max: 42 ± 8 ml/min/kg (n.s. versus normal). Seventy-two % of the patients had aortic root enlargement (Z-score: mean: $1,23 \pm 1,65$, range $-2,65$ to $+5,03$). Thirty-four % of the patients had mild and 7% moderate aortic regurgitation. LV dimensions and systolic function were normal. No arrhythmias were detected. No ischemic changes were noted on the exercise-ECCG.

Conclusions: The number of re-interventions after ASO is limited. At long-term after the ASO, there are no arrhythmias. Subjective health assessment is excellent, as is the maximal work performance. Despite enlargement of the aortic root in 72% of the patients, significant aortic regurgitation or dilated LV are absent at 10 year follow-up. Aortic root enlargement needs careful follow-up.

OP22-11

Tissue Doppler imaging combined with pulsed Doppler echocardiography estimates mean left atrial pressure in patients with left-to-right shunt

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Introduction: Pulmonary vascular resistance (PVR) is an important variable in deciding the surgical indication and outcome of patients with congenital heart disease. PVR is calculated using the equation: $PVR = (\text{mean pulmonary pressure} - \text{mean left atrial pressure}) / \text{pulmonary blood flow}$. Although pulmonary systolic pressure and pulmonary blood flow are determined by echocardiography, noninvasive assessment of mean left atrial pressure (LAP) that is needed for PVR measurement is unavailable in patients with congenital heart disease. Brain natriuretic peptide (BNP) and early diastolic transmitral velocity/tissue Doppler mitral annular velocity (E/Ea) are both indicators of mean LAP. Those techniques may be applied in patients with left-to-right shunt disease.

Methods: We studied 48 patients (9 ± 6 months) with ventricular septal defect. Plasma levels of BNP were measured using standardized

assays. Pulmonary-to-systemic flow ratio (Qp/Qs) and mean LAP were calculated with routine cardiac catheterization. LV myocardial wall motion velocities during early (Ea) and LV inflow velocity during early diastole (E) were measured. The ratio of E/Ea was calculated. E/Ea in the patients were compared to 30 age-matched normal children.

Results: Qp/Qs and mean LAP were 1.1 to 3.4 (1.9 ± 0.5) and 5 to 13 (9 ± 2) mmHg, respectively. Peak E correlated with mean LAP and Qp/Qs ($r = 0.47, p = 0.001$ and $r = 0.53, p = 0.0002$, respectively). Peak Ea showed negative relationships with mean LAP and Qp/Qs ($r = -0.49, p = 0.0003$ and $r = -0.35, p = 0.02$, respectively). Although BNP did not correlate with mean LAP, E/Ea correlated well with mean LAP and Qp/Qs ($r = 0.81$ and $0.65, p < 0.0001$, respectively). In addition, E/Ea of >10 identified patients with mean LAP ≥ 10 mmHg with a sensitivity of 88% and specificity of 97%, respectively.

Conclusions: Tissue Doppler imaging combined with pulsed Doppler echocardiography (E/Ea) predicts mean LAP. Furthermore, this ratio has a good diagnostic accuracy for detecting mean LAP ≥ 10 mmHg in patients with left-to-right shunt.

OP22-12

Histological changes in the liver late after the Fontan operation

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Introduction: Although the Fontan circulation has provided excellent long-term palliation for individuals with single ventricle physiology, late hemodynamic decompensation is common. Such hemodynamic changes may cause venous hypertension, hypoxia, and venous hepatic reflux, leaving the liver vulnerable to chronic injury. We sought to delineate histopathological changes late after the Fontan operation and correlated these with hemodynamic characteristics.

Methods: Retrospective hospital record based review of all patients evaluated for total cavopulmonary conversion. All patients had undergone cardiac catheterization and endovascular liver biopsy.

Results: Of 11 patients (3 female) identified, mean age was 24.9 years (range 16.5–42.9) and mean body surface area 1.65 (range 1.2–1.9). Mean duration of Fontan circulation was 15 years (range 7–27). Five of 10 patients had established cirrhosis (sinusoidal fibrosis predominantly) with the remainder having various degrees of fibrosis. Their comparative hemodynamic characteristics are presented in the table. Intrahepatic large veno-venous collaterals were present in 3 patients. Four patients had protein-losing enteropathy (PLE), 2 with cirrhosis. One patient who did not have Fontan conversion because of severe cirrhosis and PLE, died 27 years after his Fontan due to liver related complications. There was significant positive correlation between transpulmonary gradient and hepatic wedge pressure ($0.77, p < 0.1$).

Conclusions: Liver injury is evident in all patients late after Fontan operation, with established cirrhosis being present in at least 50%. Cirrhotic patients tend to have had their Fontan for longer duration, and are more likely to have high trans-pulmonary gradient and PLE. Hepatic wedge pressures may be confounded by the presence of intrahepatic veno-venous collaterization. Histological assessment of liver injury provides important information for pre-operative Fontan conversion assessment, late PLE, liver related morbidity and mortality.

	Fibrosis	Established cirrhosis	p-value
Fontan duration	13 (3)	18 (5)	0.1*
NYHA III and IV	1 (20%)	2 (40%)	0.4
Hb	170 (22)	137 (7)	<0.1*
Fontan pressure (mmHg)	14 (5)	16 (7)	NS
Systemic ventricle EDP (mmHg)	9 (3)	9 (8)	NS
Hepatic vein pressure (mmHg)	14 (4)	18 (8)	NS
Hepatic vein saturation (%)	55 (2)	47 (25)	NS
Hepatic wedge pressure (mmHg)	14 (4)	18 (8)	NS
Hepatic wedge saturation (%)	65 (10)	56 (13)	NS
Transpulmonary gradient (mmHg)	5 (3)	9 (4)	0.2*

Session 23: Oral Poster Session II

OP23-1

Physical activity in adults with congenital heart disease: are they active enough?

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Introduction: Regular physical activity (PA) has been associated with a wide range of health benefits, but the level of PA in adults with congenital heart disease (CHD) is not known.

Methods: 61 adults with CHD [36 male; age 18–63 years, mean 31.7 ± 10.9 yrs] were recruited from the unit database and divided into 3 groups according to NYHA class. Group I (NYHA I), Group II (NYHA II), Group III (NYHA III & IV). Median body mass index was 25.6; 14 patients being overweight (BMI 25–29.9) and 7 obese (BMI > 30). All patients undertook a Physical Activity Questionnaire [PAQ] designed to assess attitude to exercise. Scores above 60 indicated favourable attitude towards exercise.

PA was measured using an accelerometer (Actigraph Model 7164; MT Inc, USA) programmed to record data each minute. PA volume was calculated as mean accelerometer counts per minute. Moderate to vigorous intensity physical activity (MVPA) was estimated using established cut off point (>2010 counts/minute equivalent to 3 METS).

Results:

Table 1.

	Number	Example
Group I	N = 26, 14M	Atrial septal defect, small ventricular septal defect, mild aortic or pulmonary stenosis etc.
Group II	N = 18, 10M	Tetralogy of Fallot's post correction with pulmonary regurgitation, mitral valve stenosis with pulmonary HT
Group III	N = 17, 12M	Eisenmenger syndrome, complex pulmonary atresia etc.

Patients in Group II were 22% less active, whilst those in Group III were half (50%) as active than those in Group I. At least 3/4 of patients in Groups I and II, and all of the patients in Group III failed to achieve UK national health guidelines for PA [accumulating 30 minutes or more of MVPA on at least 5 days of the week]. Although, the mean PAQ score for patients in Group I was higher than those in Group II or III but it was still less than 60, indicating uncertain attitude towards exercise. In Group III [mean score 43] most patients were indifferent towards exercise.

Table 2.

	Total	Group I (n = 26)	Group II (n = 18)	Group III (n = 17)
Mean physical activity (counts per minute)	328.5 ± 213.6	392.4 ± 255.0	308.3 ± 143.2	198.7 ± 79.1
% achieving guideline (30 mins MVPA ≥5 days/week)	17.4	20.8	25.7	0
PAQ Score (Mean)	49	51	46	43

Conclusions: Objective measurement of physical activity showed that adults with CHD have a range of physical activity levels between normal and severely limited, relating to their NYHA classification. Subjective assessment showed indifferent or uncertain attitude to exercise in majority. Although low levels of PA may reflect the underlying cardiac disorder, regular exercise has been shown to be of physical and psychological benefit in patients with cardiac disease. Intervention to increase PA levels may be a low risk, low cost treatment strategy.

OP23-2

Long-term cardiopulmonary exercise capacity after modified Fontan operation: relationship to hemodynamic parameters

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Introduction: After successful Fontan operation in strictly selected patients the postoperative physical capacity mostly improves. Furthermore it is postulated that early separation of the blood circuit preserves ventricular function. Therefore we analyzed our data regarding the long-term postoperative cardiopulmonary exercise capacity in children and adults.

Methods: Thirty-seven patients with a median age of 14 (range 7–43) years underwent testing by spiroergometry at a median of 3, 5 and 7 years after the Fontan operation. Twelve patients were operated on under 4 years of age, 13 as older children and 12 as adults (16–37 years). The physical exercise (EC) and oxygen consumption capacity (OC) was quantitatively determined. Twenty-nine of these patients underwent postoperative heart catheterization and 19 patients were analyzed by MRI.

Results: The invasively measured data showed stable hemodynamic parameters with low pulmonary artery pressure (PAP; median 10 mmHg) and low transpulmonary gradient (TPG; median 5.5 mmHg). There was no statistical relationship between increased PAP (>12 mmHg) or TPG (>6 mmHg) or high ventricular end diastolic pressure (>10 mmHg) and reduced cardiopulmonary exercise capacity. The decreased ejection fraction of 49% in median, measured by MRI at median 7 years after surgery revealed no statistical relationship to cardiopulmonary exercise capacity. The mean OC in children compared to adults was slightly better early postoperatively (median 29.2 + 1.5 vs. 25.1 + 1.7 ml/min/kg; p = 0.08, n.s.) and significantly better later (32.7 + 2.1 ml/min/kg [73% of the norm] vs. 16.9 + 1.5 ml/min/kg [39% of the norm], p = 0.012). EC showed no differences between children and adults during the early postoperative testing but was significantly better in children late after surgery (2.4 + 0.6 w/kg vs. 1.1 + 0.5 w/kg). All patients, both children and adults, showed a significant reduction of

OC between the early and later postoperative testing (27.8 + 6.7 vs. 23.8 + 9.31/ml/min/kg; p < 0.01).

Conclusions: Fontan operation in early childhood provides better cardiopulmonary capacity during long-term follow up. Nevertheless, exercise and oxygen consumption capacity decrease continuously in all age groups. Regular surveillance of the physical capacity by spiroergometry is indispensable for the supervision and medical support of Fontan hemodynamics and accurately timed decision-making for heart transplantation.

OP23-3

Impact of myocardial strain imaging by trans-esophageal echocardiography on detecting of optimal pacing site for cardiac resynchronization therapy in infants with congestive heart failure

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Background: The pacing site is an essential key to decide the outcome of cardiac resynchronization therapy (CRT) for congestive heart failure (CHF) even in infants, however, no measure to set optimal pacing site has been reported. The purpose of this study is to clarify how to set optimal pacing site by using myocardial strain imaging of trans-esophageal echocardiography (TEE) during the surgery. **Subject and Method:** The three infants with intractable CHF (NYHA class IV), one with dilated cardiomyopathy and two with complete atrioventricular block, ranging 3 months to 3 years, were enrolled to this study. All underwent pacemaker implantation (PMI) with epicardial leads.

During the PMI, myocardial strain imaging of TEE was obtained each at epicardial pacing site by Vivid 7 (GE medical Inc.) and 7 mm diameter TEE probe, and recorded on hard disc for further analysis. Systolic dyssynchrony index (SDI) (standard deviation of R wave to peak systolic strain interval of 6 segments of LV) at each pacing site was calculated from myocardial strain profile and compared.

Result: SDI at RV pacing was higher than that at LV pacing (54 ± 20 ms vs 18 ± 9 ms, p < 0.001). One with CRT showed shorter SDI at RV outflow (42 ms) than RV apex (67 ms) and RV inflow (58 ms). Optimal pacing sites of all set at shortest SDI had favourable long term outcome as improvement in NYHA class up to less than II and fractional shortening of LV from 0.19 to 0.27.

Conclusion: Intra-operative evaluation of myocardial strain using TEE to assess optimal epicardial pacing site for CRT is feasible and beneficial to obtain long-term myocardial synchronicity in infants.

OP23-4

Reliability of echocardiographic non-invasive monitoring for detection of acute rejection after heart transplantation in children

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Invasive monitoring for detection of acute rejection (AR) is recommended for heart transplant pediatric recipients.

Aim: To assess non-invasive echodoppler value to detect AR and guide endomyocardial biopsy (EMB).

Methods: All biopsy-proven AR episodes were reviewed in pediatric heart transplant recipients (n = 53 from 1987). Mean age at HT was 12.5 years. Immunosuppression was achieved by induction prophylaxis and ciclosporine-based triple therapy. Non-invasive monitoring included clinical, ECG and echocardiographic and Doppler parameters, collected monthly during the first post-transplant year, every 2 months thereafter. Routine EMB (R-EMB) were performed at 1st, 3rd, 6th and 12th months and then yearly; additional non-routine EMB (NR-EMB) were performed whenever AR was suspected. AR episodes were reviewed to assess: indication for EMB (R-EMB or NR-EMB), histological grading (ISHLT classification), treatment and outcome.

Results: Seventy-five AR episodes occurred during follow-up: 47 early AR (<3rd month = 37, from 6th to 12th month = 10) and 28 late AR (>1st year). Thirty-eight were low-grade (<grade III: 29 early and 9 late AR) and 37 were high-grade (\geq grade III: 18 early and 19 late AR) episodes. All low-grade AR were treated with steroids and resolved; 26 grade IIIa AR received steroids and/anti-thymocyte globulins and resolved. Eleven grade IIIb AR received anti-thymocyte globulins: 5 resolved, 3 led to graft function impairment, 1 to retransplantation and 2 to death.

Fourteen episodes were diagnosed on R-EMB (19%): 13 early AR (all <3rd month: 10 low-grade and 3 grade IIIa) and only 1 late AR (low-grade). Sixty-one episodes were detected by NR-EMB (81%): 34 early (16 high-grade) and 27 late AR (19 high-grade).

R-EMB detected 13 of 47 early AR (28%) and only 1 of 37 late AR (3%), 11 of 38 low-grade (29%) and only 3 of 37 high-grade AR (0.08%). NR-EMB detected 62% of early and 97% of late AR, and higher histological grading AR (57% grade III versus 21%, $p < 0.05$).

Conclusion: Routine EMB helps to detect AR in the first 3 post-operative months; non-invasive monitoring based on clinical, ECG and echoDoppler parameters should be preferred beyond the third month post-transplant.

OP23-5

Monocrotaline-induced myocardial and coronary arteriolar lesions

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Introduction: Pulmonary hypertension (PH) represents a serious clinical situation that can affect heart function. Several animal investigations have examined cardiac function following induction of pulmonary hypertension with the toxin monocrotaline (MCT). It has been assumed that MCT has no direct effect on the heart. We have examined the effects of MCT treatment in the rat on intramural coronary arteriolar (ICA) and myocardial histology of the right ventricular free wall (RVFW), interventricular septum (IVS) and left ventricular free wall (LVFW).

Methods: Twenty adult, 340 ± 10 g, Sprague–Dawley male rats received MCT (50 mg/kg; s.c.) (MCT group). Twenty-one days following MCT injection the animals were anesthetized (pentobarbital 40 mg/kg i.p.) and underwent echocardiography (Acuson 128XP, 7.5 MHz probe). Their hearts were arrested in diastole by i.p. injection of KCL and fixed in 10% formalin. 5 μ m transverse sections, taken midway between cardiac apex and base, were stained with H&E and Mason's trichrome. Nine adult male rats,

340 ± 10 g, that did not receive MCT were investigated in the same fashion as controls (C group).

Results: Pulmonary artery pressure (PAP) by echocardiography in the C group was 11 ± 2 mmHg. In the MCT group PAP was <20 mmHg in 35%, 20–60 mmHg in 25% and >60 mmHg in 45%. RVFW and LVFW but not IVS thickness was increased proportionally to PAP ($r = 0.82$). Myocardial histology in the MCT group showed in all foci of myocyte degeneration, coagulative necrosis, and diffuse mononuclear infiltration. ICA's in the MCT group exhibited concentric arteriolar wall thickening and luminal narrowing. The intima was thickened with enlarged and bizarre endothelial cell shapes. The media was thickened due to hypertrophy, disarray and disorganization of the smooth muscle cells along with dense intercellular collagen deposition, detachment of the outermost medial layer and perivascular mononuclear infiltration. There were no differences in these myocardial or coronary artery features between LVFW, RVFW, IVS or with the degree of PH. The C group showed none of these histological changes.

Conclusions: These findings indicate that MCT has significant direct toxic effects on the myocardium and ICA. The investigation of the cardiac effects of PH using MCT must be called into question.

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OP23-6

New insights in mini-invasive valve replacement: description of a cooperative approach for off-pump replacement of mitral valves

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Objective: The aim of the present study was to evaluate a mini-invasive collaborative approach to replace the mitral valve in animals.

Methods: We firstly replaced surgically under extracorporeal circulation mitral valves of 6 sheep using a Mosaic[®] valve. Prior to its insertion, we added a radio-opaque ring on its base to enhance its visualization under fluoroscopy. A bovine jugular valve mounted into a stent was then inserted off-pump through an opening of the atrial wall. Because of the discrepancy between the diameter of the annulus and the Mosaic valve, we expected to sacrifice all animals after the procedure.

Results: Mitral valves were replaced successfully in all animals. Following the surgical valve insertion, mean left atrium and left ventricular end-diastolic pressures were respectively 38-mmHg (22–42-mmHg) and 18.8-mmHg (13–22-mmHg). Angiography showed perfectly functioning valves, no subaortic valve obstruction and a mild paravalvular leak in one animal. In one animal, we were unable to control the bleeding from the atrial opening. In this case, trans-atrial valvulation was not attempted. The off-pump valvular implantation was successful in all other 5 sheep. Hemodynamic data did not change after the insertion of valved stents. Implanted valves were all competent. The animal with the better hemodynamics was kept alive and is still alive after 3 months of implantation.

Conclusions: The use of a surgically implanted valve frame provides excellent support for off-pump insertion of a valved stent. Further experiments are necessary, in particular with appropriate valve size, before considering this approach in humans.

OP23-7**Transcatheter closure of secundum atrial septal defect in small children, immediate and medium term follow-up**L. Cardenas¹, J. Panzer², C. Baguette¹, M. Gewillig³, D. DeWolf², Th. Sluysmans¹, H. Dessy¹, C. Ovaert¹¹Pediatric Cardiology; Cliniques Universitaires Saint-Luc, UCL, Brussels; ²UZG, Gent; ³Gasthuisberg, KUL, Leuven; ⁴Hôpital Universitaire des Enfants Malades Reine Fabiola, Brussels, Belgium

Objectives: Evaluation of indications, safety and efficacy of percutaneous secundum atrial septal defect (ASD) closure in small children. **Background:** Because percutaneous ASD closure is safe and efficient, indications have been extended to smaller children. Follow-up (FU) remains scarce in this population.

Methods: A multicentric, retrospective study, was performed across the Belgian paediatric interventional cardiology centres. From 4-2000 to 8-2004, the cohort of children <15 kg, in whom percutaneous ASD closure was attempted, was analysed.

Results: 52 patients were enrolled (55.7% females). Median age and weight at procedure were 36 months (7–60) and 13.2 kg (4.7–15). Median FU was 24.5 months (5–56). Associated cardiac anomalies were present in 23%, non cardiac conditions in 32.7%, including 15.4% preterm babies with lung disease, and genetic syndromes in 9.6%. Indication for closure was purely haemodynamic in 53.8%, respiratory symptoms in 36.5%, feeding problems in 5.7%, and cyanosis in 3.8%. All patients <10 kg were symptomatic, but only 33.3% of those >10 kg ($p < 0.01$). Median size of the ASD was 11 mm and median stretched diameter 13 mm. Procedural success rate was 94.2%. Devices implanted were: 49 Amplatzer, 2 Starflex, and 1 Helex. Median size of sheath used was 9F and device 14 mm (Amplatzer). Immediate complete closure was obtained in 69.2%. A mild or trivial residual shunt was present in 24.4%, a moderate in 6.1%. Complication rate was 12.2%, including 2 cases of device embolisation (snare retrieval), 1 air embolism, 2 transient complete AV blocks, and 1 transient repolarisation anomaly. Complications and procedure failure were not related to weight but only to size of the ASD. There was no mortality. At 6 months follow-up, 23/24 (95.8%) of symptomatic patients had clinically improved. Complete closure was obtained in 93.2% (43/46). All patients were in sinus rhythm.

Conclusions: Closure of ASD in small children is often justified by symptoms or by presence of other cardiac and extracardiac lesions. The procedure is efficient and safe. Incidence of procedural complications is slightly higher than in older children. Percutaneous closure of ASD in this subgroup should therefore be reserved to symptomatic children. Asymptomatic children can be treated at a later age.

OP23-8**Systemic-to-pulmonary collaterals in children with single ventricle after hemi-Fontan palliation**A. Rudzinski¹, P. Werynski¹, Z. Kordon¹, W. Krol-Jawien¹, E. Malec²¹Pediatric Cardiology, University Children's Hospital of Cracow, Poland;²Cardiac Surgery, University Children's Hospital of Cracow, Poland

After hemi-Fontan procedure (h-F), some children with functionally single ventricle (SV) develop significant systemic-to-pulmonary collaterals (SPAC) increasing SV volume load.

Aim: To determine the incidence of SPAC in patients (pts) with SV after h-F, and their association with specific postnatal cardiac anatomy and related treatment.

Material and Methods: The prevalence and location of SPAC in 149 SV children were analyzed based on results of cardiac catheterization

performed from 01.01.1996 to 31.12.2004. HLHS pts after initial RV-PA conduit were excluded. The children were divided into 4 groups, depending on the type of postnatal lesions and preliminary surgery: Group 1 included 42 pts with decreased pulmonary blood flow (PBF) after B-T shunt, Group 2 – 38 pts with increased PBF after pulmonary artery banding, Group 3 – 30 HLHS pts after the classic Norwood stage I procedure, and Group 4 – 39 pts with balanced circulation, without preliminary operation. Table 1 present analyzed dates.

Group	No. of patients	Type of and age at preliminary operation (days, mean, SD)	Age at h-F (mo. mean, SD)	Age at cardiac catheterization (mo. mean, SD)	SPAC prevalence
1	42	R-BTS 16.8 ± 13.1	25.3 ± 21.8	49.3 ± 30.0	18 (42.8%)
2	38	PAB 45.3 ± 21.3	18.9 ± 9.2	38.8 ± 23.1	10 (26.3%)
3	30	Norwood stage I. 12.0 ± 8.4	7.3 ± 0.8	24.2 ± 12.2	4 (13.3%)
4	39	–	23.9 ± 22.1	48.6 ± 15.7	8 (20.5%)
Total	149	–	18.8 ± 13.4	38.2 ± 27.7	40 (26.8%)

Results: The average age at h-F was significantly higher in Groups 1 and 4 as compared to Group 3, as well as the age at catheterization ($p < 0.025$) before Fontan completion. SPAC were the most common (42.8%) and significantly more prevalent in Group 1 pts as opposed to Groups 3 and 4 ($p < 0.008$ and $p < 0.03$, respectively). Right-sided SPAC developed in 21 (52.5%) pts, left-sided in 4 (10.0%), while bilateral in 5 (12.5%).

Conclusions: Approximately 1/3 of SV patients after h-F demonstrate SPAC, predominantly to the right lung, which formation facilitate specific postnatal lesion and related surgery.

OP23-9**DeltaStream: a blood pump that reduces hemolysis during pediatric pulsatile perfusion**J. Optenhoefel, S. Tiedge¹, R. Suempelmann², A. Osthaus², D. Boethig¹, T. Breyermann¹¹Department for Anaesthesiology, Hannover Medical School; ²Unit of Pediatric Cardiac Surgery, Department for Thoracic and Vascular Surgery, Hannover Medical School, Hannover, Germany

Introduction or Basis or Objectives: Occlusive roller pumps for extracorporeal circulation are widely distributed, but an elevated grade of hemolysis is inevitable when pulsatile perfusion (PP) is performed. DeltaStream is a newly designed non occlusive low volume pump with diagonal blood stream, combining the advantages of non occlusive perfusion, low priming volume (30 ml), excellent pulsatile properties and reduced hemolysis.

Methods: 5 roller pump (RP) and 5 DeltaStream diagonal pump (DP) mock loops were filled with 250 ml saline suspension of packed erythrocytes, and perfused with 0.6 l/min flow at 90 beats per minute, pulse width 40%. Pressure transducers were placed immediately behind the “aortic” cannula. Free haemoglobin and temperature were determined at 0, 30, 60, 90, 120 minutes, also from a non perfused sham group. Repeated measurement analyses (SPSS 12) was performed to assess significant ($p < 0.05$) differences of the measured parameters.

Results: Peak pressure was 300 mmHg (RP) and 225 mmHg (DP). Negative pressures (29 mmHg) were observed only with RP. Each RP pressure impulse was interrupted 2 or 3 times by short periods of negative pressures, when the rollers exit the pump cage, thus setting the proximal tube section free. In contrast, the pressure curve obtained with the DP was physiologic with no pressure drops below

40 mmHg. Hemolysis was significantly reduced in DP (free haemoglobin mean values were 219, 329, 416, 510, 617 mg/l with RP and 215, 249, 295, 351, 387 mg/l with DP) after the described intervals 30 minutes PP led to 3 times less hemolysis with DP when compared to RP. After 2 hours, this RP advantage factor was still 2.3. Temperature rise was (statistically not significant) less marked in the DP group.

Conclusions: The DeltaStream diagonal pump promises to be an excellent alternative to roller pumps for pulsatile perfusion in pediatric cardiac surgery. It combines low priming volume, permits nearly physiologic pulsatile perfusion and reduces hemolysis markedly when compared to roller pumps. We intend to perform in vivo studies to see whether the DeltaStream keeps this promise.

OP23-10

NTpro-BNP plasma levels in the perioperative period – an applicable marker for individual risk assessment?

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Objectives: Natriuretic peptides are widely accepted markers for heart failure in adults. Studies in children show increased levels also in patients with congenital heart disease (CHD). This study aimed to assess NTpro-BNP plasma levels in children admitted for primary cardiac surgery preoperatively and following cardiopulmonary bypass (CPB) surgery. The focus was on the perioperative course in different heart defects and the possible influence of CPB.

Methods: We measured 164 NTpro-BNP plasma levels in 52 children (median age 134 d; range 2 d–6.9 y) undergoing primary CPB surgery for CHD preoperatively and up to 3 days postoperatively using an automated enzyme immunoassay (Roche) in a prospective clinical trial. Laboratory values were correlated to clinical parameters such as medication/catecholamines, mechanical ventilation, hospital stay etc. All children survived until discharge home.

Results: With the exception of patients with only ASD closure we found highly elevated plasma NTpro-BNP levels preoperatively (median 2267; range 313–55697 pg/ml) and postoperatively. Preoperative values were lowest in children with ASD (262; 55–1262 pg/ml) and highest in patients with univentricular heart (47717; 17477–55697 pg/ml). The postoperative courses of NTpro-BNP plasma levels also differed (fig. 1).

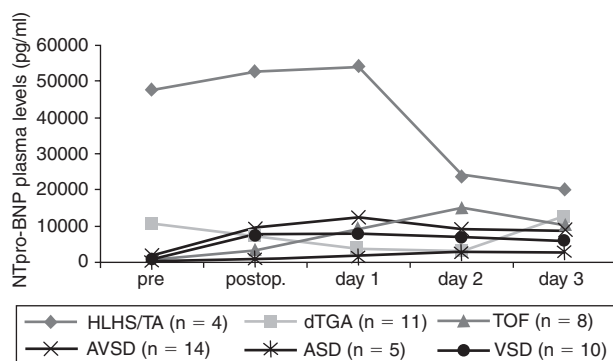


Figure 1. Postoperative course of NTpro-BNP plasma levels in CHD

Nineteen out of 52 patients received high-dose adrenaline (>0.1 µg/kg/min) for >6 hours postoperatively. Compared to

the group with no or low-dose adrenaline there were no significant differences in the baseline values (2417 vs. 1764; p = NS) but significantly higher values up to 6 hours (17323 vs. 4576, p = 0.005) and at day 1 after surgery (28455 vs. 5350; p < 0.001).

There were no differences in NTpro-BNP levels between short-term ventilation (<3d; n = 26) and ventilation for more than 3 days (n = 26).

Conclusions: NTpro-BNP plasma levels are elevated in children with CHD before and within the first days after primary CPB surgery. The preoperatively low levels in ASD patients and the highly elevated levels in children with HLHS/TA appear to reflect not only the physiological age-dependent decrease but also cardiac function prior to surgery. The correlation of NTpro-BNP levels with the need for catecholamines suggests that this marker may be applicable even in the perioperative period, becoming a valuable tool for individual risk stratification of high-risk patients.

OP23-11

Effects of cardiopulmonary by-pass surgery on arterial endothelial function and systemic inflammation

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Background: Previous studies have shown that patients undergoing cardiopulmonary by-pass (CPB) surgery are at significant risk for postoperative vascular-related complications such as hypertensive crisis and myocardial ischemia. Injury to the vascular endothelium secondary to a widespread inflammatory reaction to CPB has been hypothesized as mechanism.

Methods: Flow-mediated (endothelium-dependent) dilatation (FMD) of the brachial artery was assessed by ultrasound in twenty patients (8 children and 12 adults and, mean age: 13.8 ± 2.6 and 52 ± 2.4, respectively) undergoing CPB surgery for either congenital heart disease (in children and in 6 adults) or coronary artery bypass grafting (in the remaining 6 adults). The ultrasound measurements were done before, and 6–10 hours after surgery. High-sensitivity CRP, fibrinogen, and troponin T were analyzed from plasma collected from all patients before, 6–10 hours, and 48 hours after surgery. All data are mean ± SEM. ANOVA was used for statistical analyses.

Results: As compared to baseline (pre-surgery), the post-surgery FMD values were markedly decreased in all patients (p < 0.01), with a more significant drop in adults (from 6.8 ± 1.2 to 1.8 ± 0.5%, p < 0.001) than in children (from 7.1 ± 0.8 to 4.1 ± 1%, p < 0.01). In the adult group, the drop in FMD was more marked in those patients (n = 5) whose postoperative course was later (24–72 hours after surgery) complicated by systemic hypertension (p < 0.1). As compared to baseline, CRP and fibrinogen increased significantly at 48 hours after surgery (CRP: from 2.5 ± 0.5 to 186.1 ± 14.9 mg/l, respectively, and fibrinogen: from 3.3 ± 0.2 to 5.6 ± 0.3 mg/ml, respectively; p < 0.001 for both). CRP and fibrinogen elevations were more prominent in adults than in children (p < 0.001). Significant rise in troponin T, at similar levels in pediatric and adult patients, was observed at both 6–10 hours (from 0.05 ± 0.002 to 1.1 ± 0.2 ng/ml, p < 0.0001) and 48 hours after surgery (0.4 ± 0.1 ng/ml, p < 0.001).

Conclusion: CPB surgery is associated with endothelial dysfunction of peripheral arteries and with intense systemic inflammation. These abnormalities appear to be more pronounced in adult patients than in pediatric patients. Arterial endothelial dysfunction, which is amenable to treatment, could predict the risk for hypertensive crisis during the postoperative period.

OP23-12**Pulmonary artery branch remodeling and systemic to pulmonary artery collaterals formation in children with HLHS after hemi-fontan operation**Z. Kordon¹, A. Rudzinski¹, W. Krol-Jawien¹, P. Werynski, E. Malec²¹University Children's Hospital of Cracow, Pediatric Cardiology, Poland; ²University Children's Hospital of Cracow, Cardiac Surgery, Poland

Aim: To assess the anatomy of pulmonary artery branches and the systemic to pulmonary artery collaterals (SPAC) in HLHS patients (h-F) at the mean time of 18.4, \pm 6.1 mos. following hemi-Fontan (h-F) operation (mean age at h-F -6.7, \pm 1.7 mos.).

Material: In twenty pts (18M, 2F) at the mean age of 25.0 \pm 6.8 mos. prior to Fontan completion, selected from the total of 107 HLHS pts treated by preliminary RV-PA conduit, the size of pulmonary artery branches, the presence and significance of collaterals and their effect on selected hemodynamic parameters were assessed during cardiac catheterization. Based on the ratio of the pulmonary artery branches (LPA/RPA), the patients were divided into 2 groups: Group 1-8 pts (LPA/RPA \geq 0.5), Group 2-12 pts (LPA/RPA < 0.5).

The groups showed no significant differences in the age at h-F and at the cardiac catheterization as well as in body weight and body surface area. Significantly narrower diameter of LPA and lower LPA/RPA index were present in Group 2 than in Group 1 pts (2.8 mm \pm 1.2 vs. 5.0 mm \pm 1.5, $p = 0.002$ and 28.8% \pm 10.4 vs. 60.1% \pm 9.5, $p < 0.001$ respectively). No differences were found for Groups 1 and 2 in: mean Qp (2.23 vs. 2.3/min/m²), Qs (3.3 vs. 3.6 l/min/m²), mLAp (9.0 vs. 8.3 mmHg), mRAp (7.6 vs. 7.3 mmHg), RVedp (8.9 vs. 8.5 mmHg), and mSVCp - mLAp (4.8 vs. 4.8 mmHg). The LPA/RPA index was noted to decrease with age ($r = -0.51$, $p = 0.04$). In 15 (75%) pts, equally commonly in both groups, significant SPAC were seen, showing a preference for the right lung in 12 pts. Azygos vein distention with significant retrograde flow to the venous system below the diaphragm was more common in Group 2 (33.3% vs. 12.5%).

Conclusions: 1. After h-F, HLHS pts with age demonstrate increasing narrowing of the left pulmonary artery branch and tendency towards decreasing the load in the pulmonary circulation by the formation of natural veno-venous collateral (azygos vein). 2. The SPAC formation shows no association with the progression of LPA narrowing and involves mostly the right lung.

Session 27: Oral Poster Session III**OP27-1****Percutaneous pulmonary valve implantation acutely improves global right and left ventricular systolic function in repaired congenital heart disease assessed by tissue Doppler imaging**I. Coats¹, S. Khambadkone¹, M. Burrows², K. Maslin¹, J. Deanfield¹, P. Bonhoeffer¹, D. Pellerin²¹Cardiac Unit, Great Ormond Street Hospital for Children and Institute of Child Health, London, UK; ²The Heart Hospital, London, UK

Introduction: Percutaneous pulmonary valve implantation (PPVI) enables us to study the acute response of the right and left ventricle to alterations in pressure and volume overload without the confounding influence of cardio-pulmonary bypass and surgery.

Methods: We studied 33 consecutive patients (57% male, median age 18 years, range 9-44) with repaired complex congenital heart defects (57% Tetralogy of Fallot) before and at a median of 1 day (range 0-7)

after PPVI. On both occasions, the peak velocity across the right ventricular outflow tract (RVOT) and of the tricuspid regurgitant (TR) jet was recorded from the continuous wave Doppler. Pulmonary regurgitation was graded from 0-4 on colour-flow mapping according to the ratio of the regurgitant jet to the outflow tract width at valve level. The myocardial velocity profile of the tricuspid and mitral annulus was recorded during quiet breathing (Vivid 7, GE). Isovolumic acceleration (IVA) and peak systolic velocity were measured offline from an average of three cardiac cycles as objective measures of right and left ventricular systolic function.

Results: Two patients were excluded due to arrhythmia. Following PPVI, peak RVOT gradient decreased from 68.0 mmHg to 38.5 mmHg ($p < 0.005$) and TR jet velocity decreased from 4.1 m/s to 3.6 m/s ($p < 0.005$). Pulmonary regurgitation fell from a median grade of 3 to 0 ($p < 0.005$). No change was seen in IVA at the tricuspid annulus (pre 0.72 m/s², post 0.73 m/s², $p = 0.794$) or at the mitral annulus (pre 0.91 m/s², post 0.97 m/s², $p = 0.534$). Peak systolic velocity significantly improved from 4.7 cm/s to 5.4 cm/s at the tricuspid annulus ($p < 0.005$) and from 5.0 cm/s to 5.8 cm/s at the mitral annulus ($p = 0.005$).

Conclusion: PPVI reduces RVOT gradient, right ventricular systolic pressure and pulmonary regurgitation. The different effect of PPVI on IVA and systolic velocity suggests that the change in loading conditions results in acute improvement in global systolic function of both ventricles without change in intrinsic myocardial contractility.

OP27-2**Assessment of myocardial function of the systemic right ventricle in patients with D-transposition of the great arteries after atrial switch operation by tissue Doppler echocardiography**A. Rentzsch¹, M.Y. Abd El Rahman¹, W. Hui¹, A. Helweg¹, P. Ewert¹, M. Guterlet², P.E. Lange¹, F. Berger¹, H. Abdul-Khaliq¹¹Department for Congenital Heart Disease and Paediatric Cardiology, Deutsches Herzzentrum Berlin, Germany; ²Department of Radiology and Nuclear Medicine, University Hospital Charité, Humboldt University Berlin, Germany

Introduction: In the long-term follow-up of patients with D-transposition of the great arteries (D-TGA) after atrial switch operation specific problems such as failure of the morphologic right ventricle (RV) in systemic position may occur. Assessment of the myocardial contractility of the subaortic RV by conventional echocardiography is limited. The use of tissue Doppler echocardiography (TDI) with strain and strain rate imaging provides a new approach to quantitative analysis of longitudinal myocardial function. The aim of this study was to assess patterns of wall motion and regional contractile function of the systemic RV in patients after atrial switch operation for D-TGA and to compare them to those of normal subjects.

Methods: Twenty-four patients with D-TGA after atrial switch operation with a mean age of 21.3 years (16.9 years after operation) were examined and compared to 22 age-matched control persons. TDI studies were obtained from apical 4-chamber view to determine regional systolic and diastolic velocities at the basal free wall. The presystolic IVC peak was assessed and the quotient from presystolic peak velocity to isovolumic acceleration time was calculated (IVA index). Strain and peak systolic and diastolic strain rates were assessed on basal, middle and apical segments of the RV free wall. Data obtained from the RV in patients were compared to those derived from the left ventricle (LV) and from the RV in controls.

Results: The RV free wall systolic and diastolic velocities were significantly reduced in patients compared to velocities obtained from the normal RV and LV. On the other hand, the IVA index was only reduced in patients compared to the IVA index in the normal subpulmonary RV. Compared to data obtained from the normal systemic LV, the IVA index in patients was not significantly different. In contrast, strain and strain rate parameters in all analyzed segments were significantly reduced when compared to normal RV and LV data.

Conclusions: TDI is a promising tool for the evaluation of regional myocardial contractile function of the morphologic right systemic ventricle in patients following atrial switch operation for D-TGA. Presystolic, systolic and diastolic regional ventricular function is reduced in systemic RV.

OP27-3

Direct magnetic resonance assessment of aortic biophysical properties in patients with successful repair of coarctation of the aorta

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Introduction: Biophysical properties of the ascending aorta after coarctation repair may contribute to late resting hypertension.

Objective: We sought to investigate by magnetic resonance imaging (MRI) the biophysical properties of the entire pre-coarctation aorta in patients with successful repair of coarctation and to detect differences between these patients and matched control subjects.

Materials and Methods: Thirty-three patients (mean age 16.7 ± 7.7 years, follow-up after surgery 13.7 ± 5.1 years) with successful repair of coarctation and 17 matched control subjects underwent MRI of the thoracic aorta. Three local elasticity indexes including distensibility, compliance and stiffness beta-index were calculated at the ascending aorta. Using an analytic method, we also calculated automatically the flow wave velocity (FWV) along the aortic arch, which is a regional elasticity index at the horizontal aorta.

Results: Compared with the control subjects, patients with successful repair of coarctation had significant impairments of the biophysical properties at the pre-coarctation aorta. They had decreased distensibility (2.2 ± 1.2 versus 4.8 ± 1 , $\text{mmHg}^{-1} \cdot 10^{-3}$, $P = 0.0003$), decreased compliance (1.36 ± 0.53 versus 2.1 ± 0.46 $\text{mm}^2 \cdot \text{mmHg}^{-1}$, $P = 0.006$), increased stiffness β -index (5.08 ± 2.36 versus 2.7 ± 0.7 , $P = 0.005$) at the ascending aorta and increased FWV along the aortic arch (5.7 ± 2.3 versus 3.5 ± 0.4 m/sec, $P = 0.001$). There was no difference between CoA patients and control subjects regarding to distensibility, compliance and stiffness beta-index at the descending aorta.

Conclusion: MRI reveals direct impairments of the biophysical properties of the pre-coarctation aorta, namely the ascending and horizontal aorta, in patients with successfully repaired CoA.

OP27-4

Delineation of functional anatomy in Ebstein anomaly using 3D echocardiography

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Delineation of functional anatomy in Ebstein anomaly using 3D echocardiography.

Ebstein anomaly is a broad spectrum of malformations of the tricuspid valve. The severest form presents with intrauterine death and milder forms survives to late adulthood. The pathognomonic feature is apical displacement of the hingeline of the septal leaflet, but the variabilities in formation of the mural and anterosuperior leaflets add to challenges in assessing the valve's functional integrity. **Methods and Results:** Nine patients were evaluated between May and November 2004 using the Phillips Sonos 7500 Live 3D system and Q Lab software. Full volume loops of each patient were analysed by an independent operator. The anatomical details of each leaflet, degree of displacement, severity of regurgitation, and defect size at the line of coaptation were evaluated. Five were males and the mean age of presentation ranged from 0–50 years. All had previous 2D echocardiographic assessments, 2 underwent TEE and 1 had MRI. All showed displacement of the septal leaflets but failed to demonstrate the morphology of the mural or anterior superior leaflets and were inadequate to define the functional anatomy.

The tricuspid valve morphology was clearly defined on 3D echocardiography in all. Individual leaflets were identified. Their morphology, extent of attachment, degree of mobility, plane of coaptation and degree of displacement could be well delineated. The anterior superior leaflet was redundant and displaced into the right ventricular outflow tract in 1 patient. It was plastered with the mural leaflet without any clearly definable valvar structure in another patient. Regarding the mural leaflet, even severe dysplasia did not contribute to significant functional disturbance if other leaflets were relatively well preserved. The septal leaflet was involved in all with varying severity. Two patients were considered unsuitable for any form of intervention to enable biventricular repair while three patients were judged not to require intervention. Surgical intervention was proposed in 4 patients.

Conclusions: The degree of displacement and development of the septal and anterosuperior leaflets influenced the hemodynamic severity of this condition. 3D imaging defines the functional anatomy of Ebstein's anomaly and is the technique of choice for imaging this condition.

OP27-5

Tricuspid annular motion by tissue Doppler imaging correlates with right ventricular function during dobutamine infusion in corrected tetralogy of Fallot

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Introduction: Reliable echocardiographic assessment of right ventricular function and reserve in corrected tetralogy of Fallot (TOF) is challenging. We evaluated Doppler tissue imaging parameters of the tricuspid annular motion at rest and during increasing dobutamine infusion as potential right ventricular function indices in corrected TOF.

Methods: We assessed 29 patients (age 11 ± 6 years, 18 male) 8 ± 4 years after TOF repair. Peak systolic (Sa), early (Ea) and late diastolic velocity of the tricuspid annulus at the right ventricular free wall, and time from onset of QRS complex to Sa (Q – Sa) were recorded with pulsed Doppler tissue imaging. The ratio Sa/Q – Sa (Sa acceleration) was computed. Right ventricle cardiac index (RVCI) was estimated with pulsed Doppler flow through the pulmonary valve. All parameters were measured at 0, 10, 20, 30 and 40 mcg/kg/min of dobutamine infusion. Data are expressed as mean \pm SD and were analysed with repeated measures analysis of variances and Pearson's correlation coefficient.

Results: Sa, Ea, Sa/Q – Sa and RVCI gradually increased (* $p < 0.01$) with increasing dobutamine rates (see table).

Table

Dobut (mcg/kg/min)	0	20	40
Sa (m/s)	0.11 ± 0.02	0.16 ± 0.06*	0.18 ± 0.05*
Ea (m/s)	0.11 ± 0.03	0.14 ± 0.05*	0.16 ± 0.04*
Sa/Q – Sa	0.68 ± 0.27	1.45 ± 0.99*	1.77 ± 0.89*
RVCI (L/min/m ²)	7.8 ± 4.1	10.2 ± 5.8*	11.9 ± 5.6*

RVCI increase from 0 to 40 mcg/kg/min related to the corresponding increase in Sa ($r = 0.6, p < 0.01$), Ea ($r = 0.5, p < 0.01$), and Sa/Q – Sa ($r = 0.71, p < 0.0001$).

Conclusions: Tricuspid annular motion, evaluated by Doppler tissue imaging during dobutamine infusion in corrected TOF, correlates with RVCI and may help in assessing right ventricular function and reserve.

OP27-6

Real-time transthoracic three-dimensional echocardiographic assessment of left ventricular volume and ejection fraction in congenital heart disease

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Background: The purpose of this study was to assess in patients with congenital heart disease (CHD): 1) the feasibility of real-time 3D echocardiography (RT-3DE) data acquisition, and 2) the volumes and function of the abnormal left ventricle, compared with MRI data.

Methods: 32 patients (59% male) with CHD were evaluated on the same day by MRI and RT-3DE. Six patients were excluded by insufficient image quality of MRI or RT-3DE. The results for LV-EDV, LV-ESV, and LV-EF were obtained from 3D images by manual and automatic border detection. RT-3DE was performed with Hewlett-Packard Sonos 7500 echo-system. LV analysis was done off-line with TomTec[®] 4D LV analysis 1.2 (TomTec, Inc., Munich, Germany).

Results: RT-3DE data sets acquisition was feasible in 29 of the 32 (91%) patients. The time of 3D data acquisition was 4 ± 2 min. LV analysis was 17 ± 5 min for manual and 6 ± 2 min for automatic border tracing per patient. A strong correlation was observed between RT-3DE with manual border detection and MRI for LV-EDV ($r = 0.97$; $y = 0.92x \pm 9.34$; SEE = 9.5 mL), LV-ESV ($r = 0.98$; $y = 0.96x + 3.1$; SEE = 5.0 mL) and LV-EF ($r = 0.94$; $y = 0.98x + 0.3$; SEE = 3.5%). A substantially lower correlation for automatic contour detection was found, compared with MRI data. Intra- and interobserver agreement was good ($r > 0.94$).

Conclusion: This is the first study using the second-generation 3D matrix transducer for the assessment of LV volume and function in congenital heart disease. RT-3DE is feasible for volumetric analysis of the abnormal left ventricles and allows accurate determination of LV volume and EF compared with MRI in patients with congenital heart disease.

POSTER PRESENTATIONS

Arrhythmias (see also OP22-1–2)

P1

Acute effect of resynchronisation therapy (CRT) on left ventricular performance in patients with heart failure and congenital heart disease using tissue Doppler imaging

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Background: Cardiac resynchronisation therapy (CRT) is now an established method for treatment of heart failure in association of LV asynchrony in adults. The experience of CRT in children and adults with congenital heart diseases is limited. The detection of asynchrony and the response of therapy is still challenging. In this study several indices of LV were studied before and after CRT to evaluate the response to CRT using Tissue Doppler imaging and conventional Doppler parameter.

Patients and Methods: Left ventricular asynchrony was detected in 8 patients (age 3–24 years), 5 with existent RV dual pacing, after corrective surgery of congenital heart disease according to QRS width, and evaluation of electromechanical delay using tissue Doppler derived strain.

Resynchronization and LV pacing was performed via coronary sinus in 5 and epimyocardial in 3 patients. Biventricular pacing (BV) was resulted in significant reduction of LV delay in all patients ($p = 0.001$). In contrast to RV pacing, BV and LV pacing was associated with acutely improvement of LV filling time, flow velocity integral in LVOT, Tei-Index ($p = 0.01$) and increased systolic and diastolic wall velocity excursions in the LV lateral wall ($p < 0.01$).

Conclusion: Tissue Doppler imaging in combination with measurement of Doppler derived inflow and outflow indices allow non-invasive assessment of asynchrony and the response to CRT therapy. RV pacing in patients with heart failure seem to deteriorate the LV performance. CRT by biventricular pacing seems to improve left ventricular performance.

P2

Combined congenital heart disease repair and intraoperative radiofrequency ablation of atrial tachyarrhythmias

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Objectives: To evaluate whether combined intraoperative congenital heart disease repair and radiofrequency ablation (RFA) were safe and effective in the cure of drug-refractory and poorly-tolerated atrial tachyarrhythmias.

Methods: 13 patients (mean age at operation 40 years; range 7–68) underwent combined surgical repair and RFA for drug-refractory or failure of catheter ablation of atrial tachyarrhythmias (atrial fibrillation/flutter in 8 pts, atrial tachycardia in 4, reentry tachycardia through accessory pathway in 1 pt). Diagnosis included: atrial septal defect (3 ASD secundum, 1 partial atrio-ventricular septal defect), single ventricle (4 pts), Ebstein's anomaly of tricuspid valve (3 pts), TGA s/p LV retraining and partial pulmonary anomalous venous drainage (1 case each). Preoperative electrophysiologic study (6 pts) and electroanatomic mapping "CARTO" (3 pts) were performed

in a total of 6 pts. Surgical procedures consisted with: ASD pericardial patch closure (5 pts), Fontan conversion (4 pts), tricuspid valve plasty (4 pts), partial AVSD repair (1 pt) PAPVC repair (1 pt), RVOT enlargement (1 pt) and bidirectional Glenn (1 pt). Anatomically-guided endocardial right (9 pts) and biatrial (4 pts) linear lesions were performed using electrosurgical RFA probe with malleable shaft and 7 electrodes.

Results: There were no intraoperative complications related to the technique. There was 1 early postoperative death (Fontan conversion). RFA mean time was 8 ± 2 min. At follow-up (mean 2 years; range 19 months–4.5 years), recurrent episodes of incisional atrial tachycardia occurred in 1 ASD pt; stable sinus rhythm (SR) was present in 8 of the 12 survivors.

Conclusions: Combined intraoperative congenital heart disease repair and RFA is a safe and highly effective treatment to restore SR in pts with drug-refractory atrial tachyarrhythmias.

P3

Initial experience with epicardial and pleural electrode defibrillator systems in pediatric patients

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Introduction: Implantable cardioverter defibrillators (ICD) have proven to be life saving as primary or secondary prevention of sudden death due to ventricular tachy-arrhythmias. Although transvenous ICD systems can be implanted even in infants, electrode insertion may be precluded by unfavorable cardiovascular anatomy, or the risk of lead dislocation in growing children. We report on our initial experience with epicardial and pleural electrode ICD systems.

Methods: Single (n = 1) or dual chamber (n = 3) ICD systems were implanted in 4 children (mean age of 10.2 ± 3.8 years, and mean weight of 28 ± 7.5 kg). Indications for ICD implantation were hypertrophic cardiomyopathy in 3 children, and long QT syndrome in 1 child. Bipolar steroid-eluting epicardial pacing leads were inserted through a left lateral thoracotomy and placed on the left ventricle and, in case of dual chamber systems, additionally on the left atrium. Through the same thoracotomy, a coil electrode was inserted and sutured to the pleura at the posterior thoracic aspect. The ICD was implanted in the right or left rectus muscle sheath, depending on the defibrillation threshold. Lead measurements and defibrillation thresholds were measured at implant using standardized techniques.

Results: All ICD implantations were done without complications, and the systems functioned well during follow-up (range 1–17 months). In 2 patients with familiar hypertrophic cardiomyopathy, ventricular fibrillation could not be induced for defibrillation threshold determination at implant. Lead measurements at implant and last follow-up showed no significant changes except for lead impedance ($p < 0.04$):

Parameter	Implant	Last follow-up
Ventricular lead impedance Ohm	1340 ± 168	666 ± 66
Pleural coil impedance Ohm	73 ± 6	75 ± 11
R wave mV	15.3 ± 6.7	10.6 ± 7.0
Ventricular threshold @ 0.5 ms	1.0 ± 0.6	1.0 ± 0.4

An adequate 30 Joules ICD discharge occurred in a child 1 year after implant, and an inappropriate discharge due to sinus tachycardia occurred in another child 1 month after implant.

Conclusions: Initial experience demonstrates the feasibility and adequate lead and ICD function with epicardial and pleural electrodes.

Further studies are needed to evaluate the long-term performance of epicardial and pleural ICD lead systems to promote this alternative implantation technique.

P4

Progression of the paced QRS width in children with chronic right ventricular pacing: implications for cardiac resynchronization therapy

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Introduction: Current recommendations for cardiac resynchronization therapy (CRT) are based on trials with adult patients. These recommendations cannot be automatically applied for pediatric patients. As right ventricular (RV) pacing creates artificial left ventricular dyssynchrony we used it as a surrogate for left bundle branch block. Our aim was to assess the progression of the QRS width in chronic RV pacing in different pediatric age groups with and without structural heart disease (HD).

Methods and Results: 98 pediatric patients with a previously implanted pacemaker (59 males) were studied retrospectively. 42 patients had pacemaker indication without structural heart disease. 25 out of the remaining 56 patients had isolated and the others complex congenital malformations. Patients were distributed into six age groups (group I: <1 yr, group II: 1–2 yrs, group III: 3–4 yrs, group IV: 5–7 yrs, group V: 8–11 yrs, group VI: 12–15 yrs) and were followed up for an average of 58.69 ± 45.23 months (ranging: 3–188.5 months). QRS width was measured in lead V5 or II on ECG recordings with paper speed of 50 or 25 mm/sec. Paced and non-paced QRS widths showed progressive widening during the follow up period (group I: 109.2 ± 23.3 ms, group II: 126.6 ± 21.5 ms, group III: 133.9 ± 20.7 ms, group IV: 141.6 ± 21.8 ms, group V: 148.1 ± 17.4 ms, group VI: 157.1 ± 22.6). Similar increase in non-paced QRS was observed (group I: 59.7 ± 17.8 ms, group II: 77.6 ± 22.7 ms, group III: 87.7 ± 23.7 ms, group IV: 92.1 ± 27.6 ms, group V: 98.5 ± 28.2 ms, group VI: 94.2 ± 28.9). Patients with complex congenital defects reached the widest paced QRS (group VI: isolated 161.4 ± 27.3 ms, complex 168 ± 10.9 vs. no structural disease: 149 ± 17.2 ms; $p < 0.001$).

Conclusions: 1, Chronic RV pacing in pediatric patients with or without structural heart disease does not cause widening of the QRS complex over 120 ms until the age of 2 yrs. 2, Current adult cut-off value for CRT is not reached until the age of 4 years and cannot be used as parameter for selecting the optimal pediatric patients for CRT. 3, The presence of an either isolated or complex congenital defect results in a significantly wider paced QRS complex.

P5

Exercise induced ventricular arrhythmias in young athletes

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Introduction or Basis or Objectives: Exercise induced (EI) ventricular arrhythmias (VA) are rare, but very dangerous cardiac rhythm disturbances in. VA can be sign of subcellular heart defects on structurally normal heart. Aim of this paper is to reveal incidence and etiology of EIVA in young competitive athletes without structural heart disease. Another goal is to redefine preparticipation screening approach regarding early diagnostic and treatment of EIVA.

Methods: Group A – 2041 athletes (0.67 boys, 7–19) years. They had been directed to paediatric cardiologist because of symptoms or innocent heart murmurs. All athletes had no structural heart disease group B – preparticipation group included 257 highly trained competitive athletes, which had been examined in preparticipation study. They were asymptomatic, without structural heart disease. A and B group underwent investigation protocol: 12 leads ECG, echocardiography and stress test.

There were 18 patients in group C (control group) with heart diseases: 8-arrhythmogenic right ventricular cardiomyopathy (ARVC), 10-hypertrophic cardiomyopathy (HCM).

Results: In group A 10/2041 (0.49%) had EIVA: 7 EI ventricular tachycardia (EIVT), 3 EI premature ventricular contractions (PVC). During follow up (13–61 months) 3/10 patient died. One patient had complete regression of EIVA; others are on antiarrhythmic drugs.

There were 2/257 (0.78%) athletes in group B with EIVA. First had EIPVC. After 38 months follow up EIPVC disappeared. Second patient had complete regression of EIVT after four months.

In group C 8/18. One (1/7) patient died (4 years after diagnosis) in severe heart (right ventricle) failure.

Conclusions: Preliminary results showed that incidence of EIVA was higher in preparticipation group (2/257) comparing with group A (10/2041). Incidence of sudden death in apparently healthy athletes (3/10) was significantly higher than in patients with cardiomyopathies (1/18, $p < 0.05$).

EIVA may occur in asymptomatic, apparently healthy young athletes. Current status of preparticipation cardiovascular screening of young athletes is poor. Complete noninvasive assessment, including stress test can be effective in early diagnosis of exercise induced ventricular arrhythmias in highly trained competitive athletes. That can be good direction in prevention of sudden cardiac death in young athletes.

P6

Prevention of inadequate shocks in children and adolescents, treated with implantable cardioverters

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Objectives: Implantable cardioverters (ICD's) are available for the treatment of life threatening ventricular arrhythmias in children and adolescents. Devices have been optimised recently. Programming is based on experience in adults. Inadequate shocks (IS) are a major problem. Last generation ICD's can continue rhythm analysis during condenser-charging (CADC) and prevent shock if sinusrhythm resolves. Previous devices are “blind when charging” (BWC), there is only a short period of redetection thereafter. One extrasystole during redetection can lead to shock. In Medtronic-devices, the feature “progressive episode therapies” should improve safety.

Methods: Since 2000 in our institution 6 ICD's were implanted to 6 patients (9 3/12 to 17 11/12).

Diagnoses: HOVM n = 2, DCM n = 2, cardiac fibroma n = 1, arrhythmogenic cardiomyopathy n = 1.

Histories: Syncope n = 2, torsades de pointes n = 1, ventricular fibrillation (VT) n = 2.

1 patient (HOVM) received prophylactic ICD-implantation.

Devices (all Medtronic): GEM-II-DR (n = 1, 2000, BWC), GEM-III-DR (n = 2, 2001, BWC), Marquis-DR-7274 (n = 2, 2002–2003, BWC), Intrinsic-7288 (n = 1, 2004, CADC). All with atrial and ventricular leads.

Results: Cumulative postimplantation patient-time: 201 month.

3 patients received 29 shocks: 15 inadequate shocks in 2 patients (IS, 5 episodes), 14 adequate shocks in 3 patients (AS, 13 VF, 1 ventricular tachycardia, 12 episodes).

IS occurred in the first 2 patients. In these “progressive episode therapy” (PET) was enabled previously. PET means: next therapy during the same episode is always equal/higher than before. Two series of shocks (up to 6) were seen for sinus tachycardia after a first IS. Since 2002 PET is disabled in all our devices. Only one IS was delivered thereafter to a patient with a BWC-Device. The patient with the CADC-device had 3 episodes of VF with recovery of sinus rhythm during charging. In all 3 episodes therapy was discontinued. All 13 episodes of VF have been detected and effectively defibrillated.

Conclusion: In our small series we could show that specific programming, especially deactivation of PET and the introduction of devices, capable to continue rhythm-analysis while charging the condenser, is essential for preventing inadequate shocks in young patients. There is a need for further investigation on ICD-programming in this age group.

Basic Science and Genetics (see also OP22-3-4)

P7

Mutations in KCNA5 encoding the alpha-subunit of the K⁺ channel Kv1.5 cause sudden cardiac death

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Introduction: Cardiac arrhythmia is a prominent cause of sudden death. The cardiac action potential is the result of a well orchestrated opening and closing of a multitude of ion channels. Arrhythmia may result when one of the ion channels are mutated, e.g. long QT syndrome (LQTS). Until now seven types of LQTS have been described. However, it is only in about half the cases a genetic defect can be identified. It is thus reasonable to assume that mutations in other ion channel genes involved in the cardiac action potential, may explain LQTS.

Methods: In a group of LQTS patients from Scandinavia referred to Statens Serum Institut for molecular-genetic workup we screened for mutations in the gene KCNA5, coding the Kv1.5 alpha-subunit of a potassium ion channel. 88 patients were screened for mutations in the coding region of KCNA5 using single strand conformation polymorphism analysis and DNA sequencing. In these patients no disease-causing mutations had been identified by mutation screening of the coding regions in known LQTS genes.

Results: One patient was found to be heterozygous carrier of a missense mutation P91L inherited from the mother. This patient died suddenly at the age of 25, despite treatment with beta-adrenergic blockers (Atenolol 75 mg daily). The mother was asymptomatic and had normal QTc interval (<440 ms). The mutation thus

exhibits reduced penetrance. The electrocardiogram of the patient showed with an atypical LQTS pattern different from that seen in LQTS caused by mutations in *KCNH2*, *KCNQ1* or *SCN5A*. The P91L mutation was not found in 200 Danish controls.

The functional characterization of the P91L mutated Kv1.5 ion channel, revealed a significant decrease in inactivation current. A faster inactivation will result in a reduced I_{Kur} current, leading to a prolonged repolarisation and increased QTc-interval. This explains, why the mutation can cause both LQTS and sudden cardiac death. **Conclusion:** We have identified a mutation in *KCNA5* associated with LQTS and sudden cardiac death. *KCNA5* should be mutation screened in cases of sudden cardiac death, sudden infant death syndrome, sudden adult death syndrome and LQTS. Furthermore, drugs blocking Kv1.5 should be used with care.

P8

Effect of dexamethasone on the myocardial expression of cytokines and heat shock proteins in human neonates

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Introduction: Cardiac surgery with cardiopulmonary bypass (CPB) stimulates the synthesis of the proinflammatory cytokines such as TNF-alpha, IL-6, IL-8, and antiinflammatory cytokines such as IL-10. This study was intended to analyze the effect of preoperative administration of dexamethasone on gene expression of pro- and antiinflammatory cytokines and heat shock protein in the myocardium.

Methods: Neonates (n = 22) scheduled for arterial switch operation, were double blinded randomized to receive dexamethasone (n = 11) (1 mg/kg) or saline (n = 11) given intravenously 2 hours before induction of anesthesia. Biopsies were taken from the right atrial appendage immediately before initiation of CPB. Myocardial gene expression and synthesis of TNF-alpha, IL-1beta, IL-6, IL-8, IL-10, and of heat shock proteins HSP32, HSP90, and HSP70 were detected by quantitative real time RT-PCR and by Western blot.

Results: Pro- and antiinflammatory cytokines as well as HSPs were expressed at mRNA-level. IL-6 and HSP70 were also expressed at protein level. Expression of mRNA encoding for TNF-alpha, IL-1beta, IL-6, IL-8, IL-10, and HSP32 were lower in neonates treated with dexamethasone than in the others. In contrast, expression of HSP70- and for HSP90-mRNA and protein levels of IL-6 and HSP70 were not different between both groups.

Conclusion: Our study shows for the first time expression of pro- and antiinflammatory cytokines and of HSPs in the myocardium of human neonates undergoing cardiac surgery. Dexamethasone given before cardiac surgery is associated with a reduction of cytokine expression at induction of CPB. This might provide myocardial protection.

P9

Individualised preoperative prediction of children developing effusions and oedema after cardiopulmonary bypass surgery by serological and routine laboratory data

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Introduction: Postoperative effusions and oedema and capillary leak syndrome in children after cardiac surgery with cardiopulmonary

bypass constitute considerable clinical problems. Overshooting immune response is held to be the cause. In a prospective study we investigated whether preoperative immune status differences exist in patients at risk for post-surgical effusions and oedema, and to what extent these differences permit prediction of the postoperative outcome.

Methods: One-day preoperative serum levels of immunoglobulins, complement, cytokines and chemokines, soluble adhesion molecules and receptors as well as clinical chemistry parameters such as differential counts, creatinine, blood coagulation status (altogether 56 parameters) were analysed in peripheral blood samples of 75 children (aged 3–18 years) undergoing cardiopulmonary bypass surgery (29 with postoperative effusions and oedema within the first postoperative week).

Results: Preoperative elevation of the serum level of C3 and C5 complement components, tumour necrosis factor- α , percentage of leukocytes that are neutrophils, body weight and decreased percentage of lymphocytes (all $P < 0.03$) occurred in children developing postoperative effusions and oedema. While single parameters did not predict individual outcome, >86% of the patients with postoperative effusions and oedema were correctly predicted using two different classification algorithms. Data mining by both methods selected nine partially overlapping parameters. The prediction quality was independent of the congenital heart defect.

Conclusions: Indicators of inflammation were selected as risk indicators by explorative data analysis. This suggests that preoperative differences in the immune system and capillary permeability status exist in patients at risk for postoperative effusions. These differences are suitable for preoperative risk assessment and may be used for the benefit of the patient and to improve cost effectiveness.

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P10

Familial myxoma associated with Carney complex and a PRKAR1A mutation: diagnostic and prognostic significance

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Introduction: Carney complex (CNC) is a multiple neoplasia syndrome featuring cardiac, endocrine, cutaneous and neural tumours as well as a variety of pigmented lesions of the skin and mucosae. It is inherited as an autosomal-dominant trait (MIM 160980). In most patients CNC is caused by inactivating mutations of the tumor suppressor gene PRKAR1A, coding for type 1-alpha regulatory subunit of protein kinase A. So far, there does not seem to be a specific genotype-phenotype correlation. Routine genetic investigation of families is still not recommended.

Method: A 17 yrs old boy was admitted to hospital and operated on for left atrial myxoma without systemic manifestations. It was classified as familial because of recurrent myxoma in the mother (operations at 32 and 35 yrs of age) who had also recurrent breast

fibroadenomatosis. Familial myxoma and concomitant skin, scleral and mucosal (lip and buccal) pigmentations in the mother and sister fulfilled the clinical criteria for CNC diagnosis. A genetic investigation in search of mutation of the PRKAR1A gene was undertaken in patient, parents and sister. Analysis on the submitted genomic DNA of the patient with sequence analysis of PCR-amplified fragments for each exons 2–11 of the PRKAR1A gene was performed.

Result: A heterozygous deletion of 2 basepairs c.578_579delTG in exon 4B was found. The deletion begins in codon Val164 causing a frameshift with a premature termination codon 4 codons downstream. The mutation is subject to nonsense mRNA decay (NMD) and has been previously described in other patients. The same mutation was established in mother and sister.

Conclusion: This is the first genetic investigation of a Bulgarian CNC family. It proved the clinical diagnosis and has implications for the clinical follow-up of an affected relative with no current tumor manifestations. CNC should be suspected in patients with myxoma and genetic investigation of family members is of benefit for the patients and physicians.

P11

Role of S100B in brain cell culture under conditions of deep hypothermia

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Introduction: Increased concentrations of the astrocytic protein S100B in serum and cerebrospinal fluid in association with hypothermic perfusion of cardiopulmonary bypass have been associated with a higher incidence of postoperative neurological dysfunction. In the CNS, beneficial effects of pico- or nanomolar S100B concentrations have been shown, while micromolar S100B levels lead to detrimental effects. However, the role of S100B in hypothermia-associated neuroregeneration has not yet been investigated. Therefore, we have analyzed the impact of nanomolar S100B administration on hypothermia-treated primary astrocytes, BV-2 microglial cells, primary neurons and organotypic brain slice cultures subjected to dynamic changes of temperature.

Methods: Brain cells and organotypic brain slice cultures were pre-treated with nanomolar S100B concentrations and incubated according to a hypothermia protocol mimicking temperature changes during cardiac surgery in children: deep hypothermia (2 h at 17°C, phase 1), slow rewarming (2 h up to 37°C, phase 2), normothermia (20 h at 37°C, phase 3).

In all cells, release of the proinflammatory cytokine IL-6 was investigated. In brain slices, axonal outgrowth modulation was analyzed microscopically.

Results: Deep hypothermia induces the secretion of the pro-inflammatory cytokine IL-6 by astrocytes, microglial cells and neurons. Application of S100B reduces hypothermia-induced IL-6 release by microglial cells and neurons. In contrast, S100B synergistically increases hypothermia-induced IL-6 secretion by astrocytes. In brain slice culture, S100B significantly suppressed hypothermia-induced axonal outgrowth.

Conclusion: These data may suggest that S100B inhibits neuroregeneration by suppressing neuronal cell activation and axonal outgrowth under non-physiological conditions of deep hypothermic perfusion of CPB.

P12

Genetic evaluation of Congenital Heart Disease by genealogical research in São Miguel Island, Azores (Portugal)

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In well defined populations, parental consanguinity and familial aggregation suggest that genetic factors contribute to congenital heart disease (CHD), the most frequent of all clinically significant birth defects. Recently, we have shown that São Miguel Island (Azores, Portugal) has a high average incidence (9.20%) of CHD. This observation may be related to the population structure of the rural area, which has an average of 1508 inhabitants, and to the high endogamy (60%). In order to investigate this hypothesis and for future molecular studies, we are currently (1) assessing the genetic contribution of children affected with complex CHD in São Miguel Island, through a structured family questionnaire, and (2) building a biobank of samples collected from patients (DNA, RNA and cells) and parents (DNA and RNA) only after their informed consent.

In this study, all CHD children from São Miguel Island belong to the Azorean registry of CHD, which has complete clinical and personal information of 288 individuals until 2003. The family questionnaire includes queries for factors increasing the risk for CHD (maternal diabetes mellitus, alcohol and drug abuse by the mother during pregnancy, viral infections of the foetus and genetic conditions), and a detailed family history to construct the ascending genealogy of, at least, three generations.

Until now we have assessed the familial aggregation, by genealogical research, of 19 CHD patients in 7 localities of the island. Four familial clusters with a total of 13 patients were identified. One is a consanguineous family (F = 0.004) with 4 siblings (1 dysplastic aortic valve + Ao Ins, 1 ASD, 1 TA, and 1 PA+VSD), and the other three families have the following affected children: 2 siblings (PS and ASD+PS) and 1 first cousin (VSD), 3 first cousins (2 VSD and 1 VSD+PDA), and 2 first cousins (VSD) and 1 third cousin (VSD+PS). The remaining 6 patients are sporadic cases, 3 belong to endogamic families.

This ongoing genetic evaluation is essential to future molecular studies, in order to identify the possible relation between the CHD aetiology, specially recessive genes, and the genetic structure and characteristics of the São Miguel population.

P13

Duration of nitric oxide bound hemoglobin in patients with pulmonary hypertension using electron paramagnetic resonance (EPR) spectroscopy

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Introduction: Pulmonary hypertension is associated with many congenital or acquired heart diseases and often involves NO-inhalation therapy. When relaxation of the vascular smooth muscle is the desired and achieved effect, there is always the concern that excess NO may enter the bloodstream and be transported as nitrosylhemoglobin with possible undesirable systemic consequences. In addition to forming nitrosylhemoglobin by reaction

with deoxyhemoglobin, NO also reacts with oxyhemoglobin to produce methemoglobin and nitrate. Clinically safe levels of NO delivery have, in part, been established by measuring methemoglobin concentrations in the blood of experimental volunteers and patients. These earlier studies, employing a near-infrared differential absorption method, have not adequately addressed the issue of possible nitrosylhemoglobin content.

Methods: We used a novel electron paramagnetic resonance approach, which is sensitive to both nitrosylhemoglobin and methemoglobin and we began to investigate the change in blood hemoglobin species of pediatric cases receiving NO-inhalation therapy. We so far studied 4 pediatric patients with pulmonary hypertension receiving NO doses between 5 and 30 ppm from 3 to 6 days.

Results: In the case of one patient who received 30–50 ppm NO for more than 24 hours, there was some indication for the presence of nitrosylhemoglobin in both arterial and venous blood. However, this was at least an order of magnitude less than the NO-dependent increase in methemoglobin levels. Moreover, the nitrosylhemoglobin content was below the detection limit in the majority of cases. Surprisingly, when NO delivery was stopped, our measurements show baseline methemoglobin levels of 0.2% relative to total heme – ca. 0.7% is a more usually quoted number. To date, the highest level of methemoglobin we have measured in a patient (who was on 30 ppm NO for 5 days) was 1.2%. This number also seems to be unexpectedly low.

Conclusions: To our knowledge, this is the first time that an electron paramagnetic resonance approach to the quantitation of nitrosylhemoglobin and methemoglobin levels has been used in human patients with a view to guiding appropriate NO therapy.

P14

Clinical manifestations and diagnosis of Noonan and LEOPARD syndrome in paediatric cardiology practice – peculiarities may matter

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Introduction: Diagnosis of Noonan syndrome (NS) and LEOPARD syndrome (LS) is still based on clinical signs. Differentiation between them may be difficult. Cardiological manifestations are a major sign in a predominant number of cases. We searched for peculiar clinical manifestations in a paediatric cardiology clinic cohort of patients.

Methods: Fifteen patients were included: 12 with NS, 2 with LS and 1 with an unclear phenotype that could fit both syndromes. Previously diagnosed by a clinical geneticist were 4/15; the rest were suspected or diagnosed by a paediatric cardiologist during outpatient consultation (4/11) or inpatient perioperative (5/11) and periprocedural (2/11) assessment (for the female patients Turner syndrome was ruled out). The diagnosis of NS or LS was made at a median age of 5y (0,3–15,5) and at median 3,6 y (0,1–14,8) after the cardiological diagnosis. Intraoperative findings in 7/15 pts were also analysed.

Results: Typical facial dysmorphism was present in 13/15; thoracic deformity in 10/15; short stature in 5/15, inguinal hernia/cryptorchidism in 8/15. Splenomegaly or hepatosplenomegaly was found in 5/15; this was correlated with iron-deficiency anemia.

One had congenital, and two had postoperative chylothorax. Cardiological manifestations were quite variable: Two had hypertrophic cardiomyopathy (HCM) with mild biventricular obstruction (BVO); the rest (13/15) have congenital heart defects: ASD secundum 5/13 (4/5 with fenestrated membrane, 2/5 concomitant mild pulmonary valve stenosis (PSt), 1/5 with PDA and Ao kinking); severe PSt – 3/13 (in 1 with ASD and Ao bicuspidy/mild stenosis, in 1 with mild LV obstruction; 2/3 with restenosis after balloon valvuloplasty); VSD perimembranous partially closed – 3/13 (1/3 subinfundibular stenosis, 1/3 BVO with excessive LV hypertrophy). There are 2 unusual presentations – aortic valve dysplasia/severe regurgitation – 1/13; Ebstein anomaly with ASD and CoAo – 1/13. Concomitant LSVC is found in 4/13, AV valve dysplasia in 6/13 (invariably present with VSD cases, lobulated MV in 1 case).

Conclusion: NS/LS is underdiagnosed. The finding of higher rate of ASDs with fenestrated membrane, splenohepatomegaly, iron deficiency and postoperative chylothorax needs confirmation. RV obstruction in HCM, BVO, AV valve dysplasia as well as congenital chylothorax should raise the suspicion of NS/LS.

P15

Protective effects of simvastatin on coronary reactivity in swine with acute infection

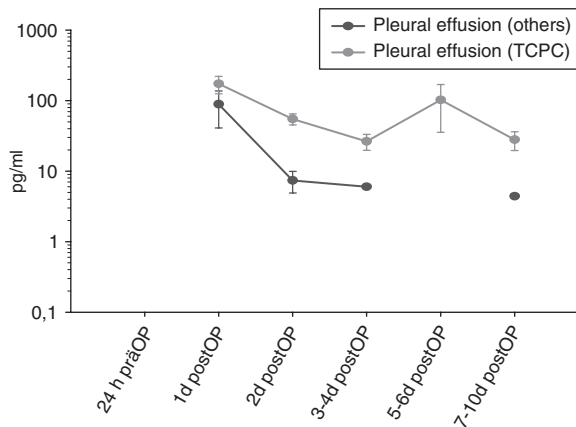
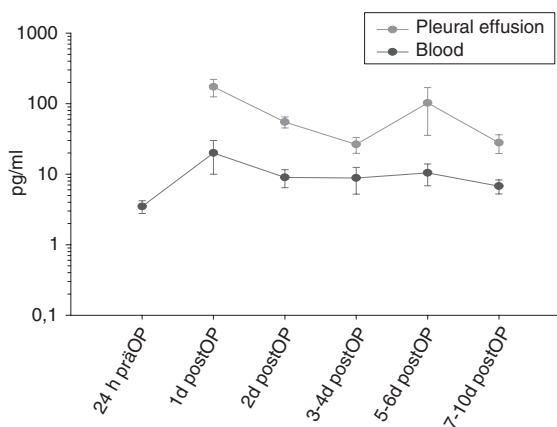
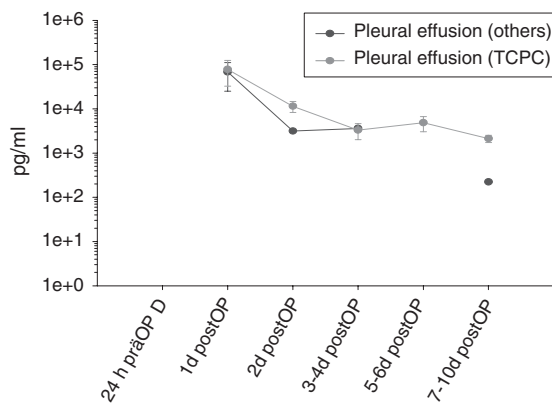
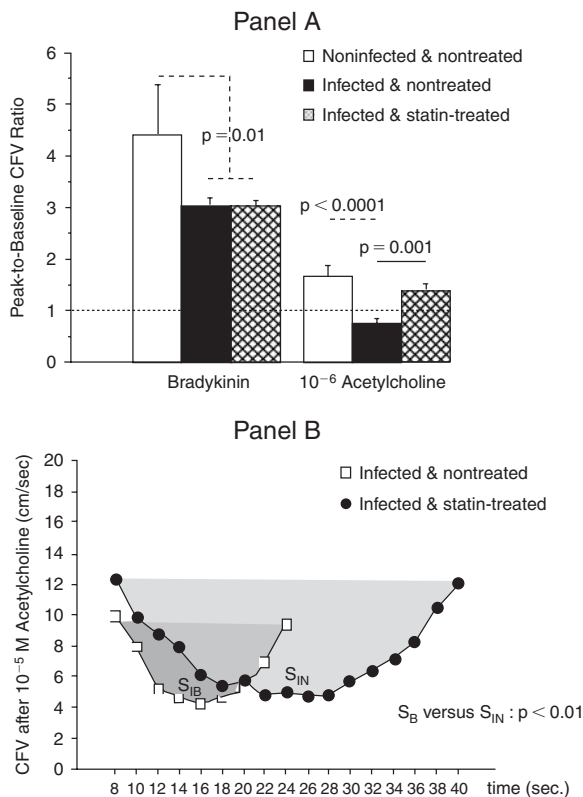
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Background: Mounting evidence supports the hypothesis that atherosclerosis could be exacerbated by acute infection. Perturbation in vascular endothelial function emerges as one important link. We investigated whether simvastatin could protect the coronary arterial function from the adverse effects of acute infection in swine.

Methods: Coronary endothelium-dependent and independent vasomotor responses were assessed by Doppler velocimetry in 12 Chlamydia pneumoniae-infected and 6 sham-infected swine two weeks after intratracheal inoculation. Half of animals from the infection group were pretreated with simvastatin (80 mg daily), while the remaining animals received placebo. The treatment was started 2 weeks prior to inoculation and continued until the end of the study. ANOVA was used for statistical calculations. Data are mean ± SD.

Results: As compared to noninfected animals, peak-to-baseline coronary flow velocity (CFV) ratio after bradykinin was significantly decreased in infected animals regardless of statin treatment ($p = 0.01$; Figure 1/A). Intracoronary 10^{-6} M acetylcholine caused slight dilatory responses in noninfected and infected & treated animals (CFV ratio: 1.6 ± 0.2 and 1.4 ± 0.2 , respectively; $p > 0.1$) while a velocity drop (CFV ratio: 0.7 ± 0.1 ; $p < 0.001$ vs. noninfected and infected & treated), indicating constriction, was observed in infected & nontreated animals (Figure 1/A). 10^{-5} M acetylcholine caused vasoconstriction in all animals, with a significantly more prolonged response in the infected&nontreated group ($p < 0.01$; Figure 1/B). Intracoronary adenosine and SNP induced similar dilatory responses in all groups ($p > 0.5$). There was no differences in markers of systemic inflammation (fibrinogen, amyloid, and CRP) and lipid profile (HDL, LDL and total cholesterol) between the groups ($p > 0.2$).

Conclusion: Acute infection is associated with impairment of the muscarinic and kinin-related reactivity of coronary circulation. This functional abnormality is in part prevented by simvastatin through mechanisms unrelated to reduction of systemic inflammatory markers or lipid-lowering. The vascular protection conferred by simvastatin against the deleterious effects of infection might be of particular importance in children with conventional risk factors for atherosclerosis, such as diabetes mellitus.



P16 Cytokines in serum and pleura effusion of patients after TCPC completion and other cardiac operations

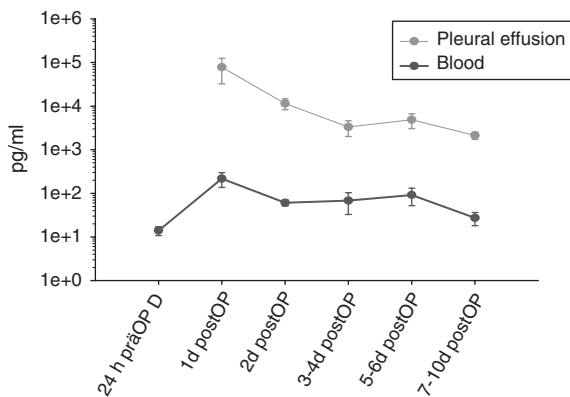
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Introduction: After the Fontan surgery (TCPC) pleura effusions often arise. The pathogenesis is not fully understood yet. Aim of this study was to compare cytokine levels of serum and the effusion fluid to gain information about the etiology of this phenomenon which is still a therapeutical problem.

Methods: Levels of Protein, Erythrocytes, IL-6, IL-8, IL-10, sE-, sL-Selectin and also complement (C3, C3d) were analyzed quantitatively in serum and pleura effusions of 21 patients after TCPC operation (aged: 2,5–5,3 years) according to a definite timetable.

The same parameters we analyzed in 8 patients with other diagnosis as a compare group.

Results: Levels of IL-6 and IL-8 (proinflammatory) in the pleura effusion were significantly higher ($p < 0,05$) than in the serum, whereas the course showed affinities.



Levels of IL-10 (antiflammatory) in the pleura effusion is significantly higher than in the serum at postoperative day 1. In the following time the levels are almost similar in serum and pleura effusion.

Conclusions: The results show a strengthened cytokine reaction in the thorax region after the Fontan type surgery. Analyzed cytokines represent pro- as well as antiinflammatory reactions. This could be the basis for further research aiming to influence the exudation therapeutically. Furthermore, due to the higher concentrations in the effusion, this kind of examination could be more reliable to screen immunological reactions after the Fontan surgery.

P17**Non-invasive diagnostics of genetical background in small infants with congenital heart defects using buccal smears (pilot study)**

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Introduction: 10% of congenital heart defects (CHD) are associated with a syndrome. Two common syndromes are 22q11-deletion and Williams syndrome (WS). Early detection of these syndromes may affect morbidity and prognosis. In these two syndromes typical facial findings develop with age and they are often subtle in newborns and infants. Microdeletions in these syndromes are usually detected by the fluorescence in situ hybridisation (FISH) technique on cultured cells from blood samples. The FISH technique can also be applied on uncultured, non-dividing (interphase) cells from buccal smears.

Aim: The pilot study was designed to validate the procedure of early testing by interphase FISH for deletions 22q11 and 7q11 (WS) applied to buccal smears.

Patients and Methods: The FISH technique was carried out on buccal smears to detect deletions of 7q11 and 22q11 in CHD patients less than one year of age, consecutively referred to the paediatric cardiology clinic during a 3 months period. Premature babies with isolated patent ductus arteriosus and open foramen ovale were excluded.

After obtaining informed consent from the parents, three buccal smears per patient were taken by the paediatric cardiologist. The samples were processed and analysed in the cytogenetics laboratory. The cardiac diagnosis was based on complete echocardiographic study.

Results: Buccal smears of 35 patients were collected. In 3 patients the buccal smears could not be analyzed because of insufficient numbers of epithelial cells. A 22q11 deletion was detected in 1 patient with interrupted aortic arch type-B with VSD.

Conclusions: The pilot study showed that sampling of buccal smears is a non-invasive procedure that is easy to perform is suitable for demonstrating specific chromosomal deletions with the interphase FISH technique in small children.

P18**Brain Natriuretic Peptide levels in children with right ventricular overload due to congenital heart disease**

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Objective: To evaluate the role of Brain Natriuretic Peptide plasma concentration (BNP) and its correlation to hemodynamic right ventricular (RV) parameters in paediatric patients with chronic overload of the right ventricle due to congenital heart disease.

Methods: 36 paediatric patients (mean 4.8 years) with volume or pressure overload of the right ventricle caused by congenital heart disease were studied: 24 patients with surgically biventricular corrected tetralogy of fallot (TOF, n = 14) or pulmonary atresia (PA, n = 10) and 12 patients with preoperative atrial septum-defects (ASD, n = 7) and anomalous pulmonary venous drainage (APVD, n = 5). Measurements of BNP were performed with Triage® from Biosite. Enddiastolic pressure of the right ventricle and peak right ventricular to left ventricular pressure ratio (RV/LVP) were determined with cardiac catheterization and were correlated to BNP plasma concentration.

Results: The 36 patients had a mean BNP of 87.7 (5–316) pg/ml and an enddiastolic pressure in RV of 5.6 (2–10) mmHg and a RV/LVP of 0.56 (0.24–1.03). There was a positive correlation between BNP and RV/LVP ($r = 0.7844$, $p < 0.0001$) in all patients as well as in children with TOF or PA ($r = 0.7472$; $p = 0.0002$)

and in children with ASD or APVD ($r = 0.9148$; $p < 0.0001$). Similarly, a weak correlation was shown between enddiastolic RV pressure and BNP ($r = 0.5947$, $p = 0.0004$). Patients with a RV/LVP below 0.5 offered a maximum BNP of 55 pg/ml, whereas a RV/LVP above 0.75 was equipollent with a BNP of 80 to 316 pg/ml.

Conclusion: There was a significant correlation between RV hemodynamic parameters and BNP in children with RV overload due to different types of congenital heart disease. The monitoring of BNP may provide a non-invasive and safe quantitative follow up of the RV pressure and volume overload in these patients.

P19**Long QT syndrome associated with familial occurrence of patent ductus arteriosus**

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Introduction: Incidence of isolated patent ductus arteriosus (PDA) is about 1 in 2000 live births. Polygenic inheritance has been implicated as its etiology. Long QT syndrome is caused by defect in genes controlling sodium and potassium channels. This can be inherited as autosomal dominant or recessive disorder. Familial occurrence of these two disorders individually has been reported. However, these two disorders occurring together in a family have not been established.

Methods: Case note review of members of a family with patent ductus arteriosus in association with long QT syndrome.

Results: Patent ductus arteriosus was diagnosed in family members of 4 successive generations. The index patient, a 20 year old female, had long QT syndrome and patent ductus arteriosus. Her son had a patent ductus arteriosus. Her twin brother had long QT syndrome and a ventricular septal defect. Her mother had patent ductus arteriosus and died suddenly at the age of 41 years with presumed arrhythmia. Her maternal grandmother had surgery for patent ductus arteriosus. Patients with long QT syndrome had electrocardiographic evidence of QT prolongation, although, we have not managed to do genotyping.

Presence of long QT syndrome associated with PDA occurring together in members of a family is unlikely to be by chance alone, suggesting a possible genetic mechanism. The association of PDA with long QT syndrome may provide insight into the mechanisms underlying both disorders. One postulated hypothesis on PDA closure suggests that the ductal closure may be accomplished by mechanisms through ion channels. Studies on rabbit ductus suggested that increasing oxygen stimulates smooth muscle contraction of the PDA partly by closing oxygen sensitive delayed rectifier potassium channels. As long QT syndromes are channelopathies, there may be a common mechanism for persistence of ductus arteriosus.

Conclusions: We identified occurrence of long QT syndrome in association with patent ductus arteriosus in members of a family. We postulate that there may be a common genetic mechanism for these two disorders occurring together.

Cardiac Imaging (see also OP27-1-6)**P20****Beneficial effect of growth hormone treatment on aortic distensibility in patients with Turner Syndrome**

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Introduction: In Turner Syndrome (TS) an increased risk of aortic dilatation of unknown aetiology exists. Abnormal biophysical

aortic wall properties might play a role. We therefore assessed the biophysical properties and dimensions of the aorta in patients with TS.

Methods: 38 patients (age 19.9 ± 2.1 yr, BSA 1.7 ± 0.2 m²) underwent MRI examination at least 6 months after discontinuation of growth hormone (GH) treatment. Patients had been enrolled in our previous GH dose-response study and were randomly assigned to 1 of 3 subgroups (A = 0.045 mg/kg/d, B = 0.067 mg/kg/d, C = 0.09 mg/kg/d). 27 age and BSA matched controls (age 20.6 ± 1.6 yr, BSA 1.8 ± 0.1 m²) served as reference. Phase velocity encoded flow maps were acquired at four predefined levels to measure aortic diameter and distensibility: level 1/ascending aorta; level 2/descending aorta; level 3/diaphragm level; and level 4/abdominal level. Distensibility was calculated: $D = (A_{\max} - A_{\min}) / [A_{\min} \cdot (SBP - DBP)]$ (D = distensibility, A = aortic area and P = blood pressure). Pulse wave velocity (PWV) between level 1 and 4 was measured.

Results: Patients versus controls: Mean aortic diameter in patients was larger at levels 1 and 3. Aortic distensibility in patients was lower at level 3 and tended to be lower at level 1. PWV in patients was higher.

Between subgroup analysis: No differences for aortic diameters or PWV were found. Aortic distensibility was lower in group A compared to group C at the levels 3 and 4. Distensibility increased at all four levels with increasing GH dose and a significantly positive correlation with GH dose at levels 3 and 4 was found.

Subgroups versus controls: Distensibility in group A was lower at levels 3 and 4, and tended to be lower at level 1. Distensibility in groups B and C was not different from controls.

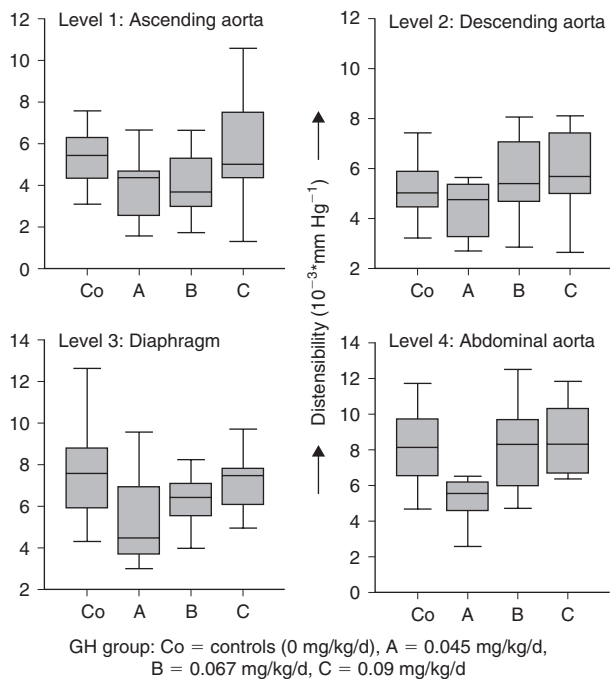


Figure. Aortic distensibility per level of measurement.

Conclusions: At two out of four levels aortic diameter was larger in patients. TS patients showed signs of decreased aortic compliance. Aortic distensibility increased with increasing GH dose and only differed from controls in patients receiving the lowest dose, suggesting beneficial effect of GH on the aortic wall. Aortic distensibility measurements could be a useful tool for detection of cardiovascular disease and/or risk estimation in TS.

P21

Diminished neo-aortic elastic properties following the Ross operation

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Introduction: In young patients with severe anomaly of the aortic valve and/or left ventricular outflow tract obstruction the Ross operation is an established surgical option. The main concern of this procedure is dilatation of the neo-aortic root leading to progression of aortic regurgitation. In order to quantify the potential for pulmonary autograft dilatation, we determined neo-aortic and abdominal aortic elastic properties non-invasively.

Methods: In 6 patients aged 9 to 16 years (mean 12.3 ± 2.9 years) who underwent a Ross procedure for severe valvular aortic stenosis and insufficiency diameter measurements were obtained at the sinuses of Valsalva, the ascending (neo-)aortic and descending abdominal aorta out of M-mode echocardiographic images by a special autocontour finding software developed by our institutions. Investigations were done one day postoperatively to 3,4 years (mean 1,3 years) post surgery. Six age and sex matched healthy persons served as controls. After simultaneous oscillometric blood pressure determination several aortic elastic parameters were calculated automatically.

Results: Patients showed larger mean enddiastolic neo-aortic diameters (29 ± 3 vs. 19 ± 1 mm, $p < 0,001$) than controls. Neo-aortic distensibility was more than 50% decreased in patients (28 vs. $62 \text{ kPa}^{-1} \times 10^{-3}$, $p < 0,05$) paralleled by a reduction of maximum systolic area increase (MSAI, 24 vs. $53\%/100$ ms, $p = 0,001$), wall stiffness index of patients was markedly increased ($10,1$ vs. $3,7$, $p < 0,05$). Descending aortic elastic properties tended to be reduced in patients, but differences were not statistically significant. Early postoperative measurements and measurements obtained at follow up investigations years after operation did not differ significantly.

Conclusions: Our preliminary results show, that the reduction of neo-aortic elasticity can be accurately quantified out of M-mode echocardiographic images in young patients after Ross operation. Correlation of neo-aortic diameter and elasticity changes during follow-up investigations in a larger patient population may help to estimate the potential for neo-aortic dilatation and arterial hypertension, and perhaps gives hints to optimize surgical details of the Ross procedure.

P22

Assessment of the left ventricular wall motion velocities in neonates by tissue Doppler echocardiography

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The aims of the study are to establish normal values for left ventricular motion velocities by TDE in neonates and to compare them with older children.

Fifty term neonates (1–5 days of age) and 54 children (5–16 years of age) were examined by 2-dimensional echocardiography, conventional pulsed wave Doppler echocardiography (CPWDE) and TDE. The peak transmitral early diastolic (E), and the peak transmitral late diastolic flow velocities (A), and the ratio of E/A

were determined. Left ventricular myocardial velocities were assessed along the long axis in the four-chamber view. Sample volumes were placed in the basal and middle part of the left ventricular posterior wall (LVPW) and interventricular septum (IVS). They were also placed in the lateral (MLA) and medial (MMA) sites of mitral annulus. The peak systolic (Sw), the peak early diastolic (Ew) and the peak atrial systolic (Aw) tissue velocities were measured and compared with each other in all segments.

The highest Sw, Ew and Aw were obtained from MLA. In all segments, the mean Sw was found to be significantly lower than the mean Ew and Aw ($p < 0.0001$). The mean Aw was the dominant wave in both annular sites of mitral valve. The mean value of Ew/Aw increased significantly with replacing the Doppler beam from base to the apex in both LVPW and IVS segments. The mean transmitral peak E velocity and the mean value of E/A in neonates were significantly lower than those found in the children group ($p < 0.0001$). However, the mean transmitral A velocity was not different in neonates from older children. Similarly, TDE parameters (the mean Ew, Sw and ratio of Ew/Aw) obtained from MLA and MMA in neonates were significantly lower than those detected in the children group ($p < 0.0001$). However, the mean Aw in the MLA and MMA was not different in neonates from older children.

In this study, we observed that the diastolic and systolic myocardial velocities of the left ventricle in neonates were significantly lower than those found in children group. Decreased myocardial tissue velocities obtained from neonates probably reflect the immaturity of neonatal myocardium.

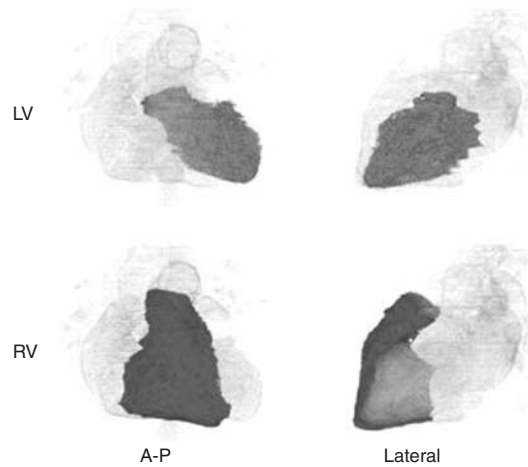
P23

Calculation of right and left ventricular volumes with multi-detector row computed tomography in children

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Background: Multi-detector Row CT (MDCT) of the heart is an interesting new approach for the evaluation of the coronary artery in adults. However, in children, the usefulness of MDCT is mentioned in reference to color imaging cardiac reconstruction without quantification. In this study, we attempt to clarify the applicability of both right and left ventricular volume assessment using ECG-gated MDCT in children.

Method: Study subjects consisted of 16 patients who had definite right and left ventricle (corrected transposition of the great arteries, tetralogy of Fallot, Kawasaki disease etc), aged from 10 months to 18 years (mean 9.4 ± 5.4). After imaging with ECG-gated MDCT (Aquilion16, 16-line multi-detector, Toshiba), CT row data were made with the segmental reconstruction algorithm under retrospective ECG-gating to minimize the time resolution of images. Images were transferred to an online PC-based workstation. Then, we assessed each right and left ventricular diastolic volume by two methods, direct measurement of the ROI area with 3D reconstruction (direct measurement method) and calculation of the cast from three-dimensional anterior-posterior view and lateral view with traditional catheter equation (cast calculation method) (see figure). We calculated the left ventricular volume using cast imaging with the Nakazawa's equation, and the right with the Graham equation. On the other hand, cardiac catheterization was performed in 7 patients in the same period and ventricular volumes were calculated with the same equations utilizing the catheterization data.



Result: The correlations between direct measurement method and cast calculation method in left and right ventricles are excellent ($r = 0.98$ and 0.96 , respectively). The correlations between cast calculation method and volume assessment in catheterization are also good for both ($r = 0.98$ and 0.96). The volume measurement from catheterization was 97% of the 3D direct measurement in the left ventricle, and 73% in the right ventricle ($r = 0.98$ and 0.97 , respectively).

Conclusion: Volume calculation with ECG-gated MDCT is reliable for assessment of right and left ventricle volumes and can be utilized instead of cardiac catheterization.

P24

Quantitative assessment of regional and global longitudinal ventricular dysfunction in patients with hypertrophic cardiomyopathies (HCM) using tissue Doppler imaging (TDI)

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Introduction: Evaluation of systolic and diastolic function in patients with hypertrophic cardiomyopathies (HCM) is limited. We assess and characterize the regional and global ventricular systolic and diastolic function with the novel TDI technique in patients with HCM. **Patients and Methods:** The data of 20 patients with HCM (median age 12, range 2–18 years) who underwent conventional echocardiography and TDI were compared to those of 20 age-matched healthy subjects. In 4 apical views, tissue Doppler derived velocities, strain and strain rate, and the isovolumetric acceleration index (IVA) (m/s^2), a load independent parameter reflecting the systolic function, were measured in all. Isovolumic relaxation (IVRT), contraction (IVCT) and ejection times (ET) at basal and mid segments of the LV, IVS and RV walls respectively were measured from the TDI spectral wall velocities. Tei index ($ICT + IVRT/ET$) and I/H index ($IVRT + ICT/ET + IVRT$) were calculated.

Results: Compared to normal subjects, patients with HCM had significantly reduced mean peak basal and mid-segment LV systolic S ($p = 0.001$, $p = 0.014$) and significantly reduced diastolic E ($p = 0.01$, $p = 0.002$) and A waves ($p = 0.04$, $p = 0.001$). Similar significant results were found at the basal and mid segment of the septal annular side of the mitral valve. The reduction of the wall velocities at the basal and mid segments of the anterior RV wall was less pronounced S ($p = 0.04$, $p = 0.02$), E ($p = 0.06$, $p < 0.001$), A ($p = 0.2$, $p = 0.1$). Regional strain and strain rate values at the mid segments of LV and RV walls were significantly

reduced ($p = 0.01$). The isovolumic relaxation (IVRT) and contraction time (IVCT) was significantly prolonged in HCM patients ($p = 0.004$, $p = 0.001$), resulting in significantly higher calculated Tei index and I/H index.

Conclusion: Significantly altered regional and global systolic and diastolic function was determined using TDI. The longitudinal ventricular alteration of wall velocities was more pronounced in the hypertrophic left than in the right ventricle.

P25

Live 3D echocardiography – visualization of ventricular septal defects (VSD) in complex congenital heart disease (CHD)

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Introduction: Many complex congenital heart defects (CHD) are associated with ventricular septal defects (VSD). For surgical interventions the assessment of size and localization of the VSD and the spatial relationship between the VSD and the adjacent cardiac structures is essential. Due to the high technical and timing effort 3D echocardiography currently plays no major role in the diagnostic evaluation of complex CHD. Live 3D (Philips) in contrast provides 3D visualization in real time and fast acquisition of 3D datasets for further off-line post processing. We report our experience with Live 3D echocardiography in the assessment of VSDs in infants and children with complex CHD.

Methods: In the preoperative diagnostic assessment of 12 patients with complex CHD (DORV, TOF, VSD with posterior malalignment, TGA with VSD) Live 3D echocardiography (Philips Live 3D) was applied in addition to 2D Echo und cardiac catheterization. The 3D data were acquired using a transthoracic and sub-costal window in a bedside setting. In most cases this was possible without sedation.

Results: Live 3D echocardiography permitted fast and easy acquisition of 3D datasets in all patients. The simulation of new cut planes and surface reconstructions from any desired perspective provided both, an anatomical and a surgical view into a virtual heart model. This enabled direct 3D visualization and exact definition of the VSD regarding size, shape and relation to adjacent cardiac structures in all patients. Live 3D was especially valuable for the surgical strategy of intraventricular tunnelling in TGA and DORV and in borderline biventricular correction of VSD with posterior malalignment and LVOTO. Intraoperative findings confirmed the results of 3D echocardiography.

Conclusions: Live 3D echocardiography is easy to apply in paediatric patients without sedation. It is a useful diagnostic tool in determining position, size and shape of VSDs and their relation to adjacent cardiac structures in children with complex congenital heart disease. This information improves the preoperative assessment and gives additional valuable data for the planning of surgical procedures.

P26

Right ventricular Tei index obtained by Tissue Doppler Imaging in heart diseases with different types of overload

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Objectives: To analyze global RV function in heart diseases with different types of RV overload using Tei index obtained by Tissue Doppler Imaging (TDI-Tei).

Methods: Study group consisted of 122 children aged 1 to 196 months (mean 94.6 ± 64.4). They were divided into 4 groups. Group 1: 25 children with significant atrial septal defect (ASD), Group 2: 24 children with severe pulmonary stenosis (PS) (mean pressure gradient 81.3 ± 33.7 mmHg), Group 3: 30 children operated on for tetralogy of Fallot (Post TF) (mean pulmonary regurgitation $+1.7 \pm 0.6$ of 4 grades, mean pulmonary pressure gradient 33.2 ± 12.4 mmHg) and Group 4: 43 healthy children (control group). All patients were in NYHA class 1. There was no statistically significant difference in age and heart rate between the groups.

Tricuspid annular velocities were obtained from the apical 4-chamber view. Using the TDI method, the time interval between the end and the onset of tricuspid annular velocities (a) minus the duration of the systolic wave (b) was divided by b, i.e. $(a - b)/b$.

Results: The values of RV TDI-Tei index are presented on Table:

Group	Min	Max	Mean	SD
1 (ASD)	0.42	1.70	0.80	0.28
2 (PS)	0.11	1.00	0.47	0.23
3 (Post TF)	0.16	0.84	0.44	0.22
4 (Control)	0.20	0.45	0.34	0.06

There was a significant difference of RV TDI-Tei between the control group and each patients group: for Group 1, $t = 3.335$, $p < 0.01$, Group 2, $t = 2.727$, $p < 0.01$ and Group 3, $t = 10.241$, $p < 0.001$. There was a significant difference of RV TDI-Tei between Groups 1 and 3 as well as Groups 2 and 3, $t = 4.757$, $p < 0.001$, but not between Groups 1 and 2, $t = 0.368$, $p > 0.05$.

Conclusions: Global RV function was impaired in patients suffering from diseases with RV volume (ASD) and pressure overload (PS). Most significant impairment was found in children operated on for tetralogy of Fallot (with previous pressure overload and present mild to moderate volume overload). The RV DTI-Tei index is a very sensitive parameter for early recognition of global RV dysfunction.

P27

Malignant arterial hypertension due to renal polar artery stenosis in a male adolescent

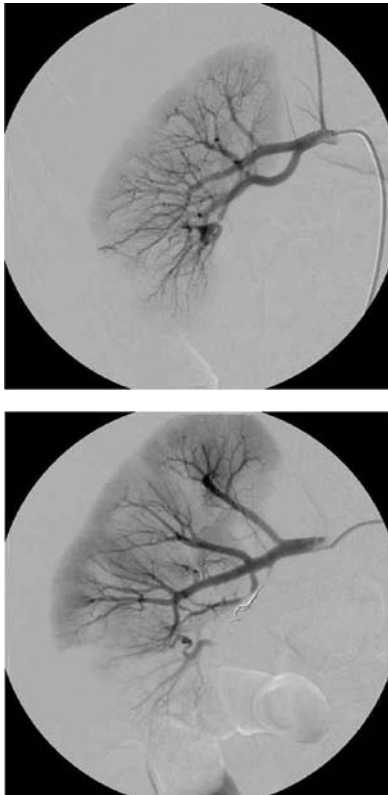
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Introduction: Organic arterial hypertension is more common in children than in adults. Renal artery stenosis follows coarctation of the aorta as the second most frequent cause of surgically correctable AHT.

Case: A 12.5 yr old male was referred after routine medical school examination for investigation of severe arterial hypertension. At admission AHT was confirmed (SBP: 170 mmHg/DBP: 110 mmHg), with good femoral artery pulsations and otherwise normal physical examination. Chest X-ray showed slight cardiomegaly. 2D-echocardiography showed structural normal heart with significant left ventricular hypertrophy (LVM/height 2.7 index: 48.5/g/m 2.7). Blood chemistry, thyroid function, plasma renin, aldosterone, plasma and urinary catecholamines and their metabolites were normal. Imaging studies including abdominal ultrasound with renal doppler, radionuclide imaging without and with captopril were all normal. Carotid doppler flow and CT-scan of the brain were normal. MRI of the kidneys and adrenals was normal and MRA of the renal arteries showed no evidence

for stenosis of the renal arteries and no arguments for fibromuscular dysplasia. There was poor response to a combination therapy of β -blocking agents and ACE inhibitors. Reluctant to accept the diagnosis of essential hypertension in a youngster we decided to perform a classical angiography of the abdominal aorta and renal arteries. This showed a high graded stenosis of a small polar artery of the lower pole of the right kidney. Because of the small calibre of the affected artery interventional embolisation (Figure) was preferred over balloon stenting or surgical angioplasty. 1 week after embolisation tension was dropped to 138/78 mmHg under 25 mg atenolol. Control 2D-echocardiography shows diminishing LV hypertrophy ($LVM/height\ 2.7 = 42\ g/m\ 2.7$).



Conclusions: Although MRA seems to be the accepted first line examination in arterial hypertension of suspected renal origin, we strongly suggest to perform a classical angiography especially in those cases where MRA findings are negative. As all organic causes should always be excluded before accepting the diagnosis of “essential hypertension” especially in a child with AHT, classical angiography remains the “golden standard”. Secondly we confirm that in children with renal artery stenosis PTA and surgical reconstructions are the treatments of choice (25% risk for restenosis)-intra-renal arterial embolisation being reserved for very small lesions.

P28

Which right ventricular dysfunction cause severe pulmonary stenosis?

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Objectives: This study was to assess the impact of severe pulmonary stenosis (PS) on systolic, diastolic and global right ventricular (RV) function using M-mode, Pulse Wave Doppler (PWD) and Tissue Doppler imaging (DTI) parameters.

Methods: Study population consisted of 70 children divided into two groups: Group I: 45 healthy children aged 99.8 ± 65.0 months, and Group II: 25 children with severe pulmonary stenosis aged 73.2 ± 71.7 months, with mean transvalvular pressure gradient 103.5 ± 27.1 mmHg. Systolic RV function was assessed using longitudinal tricuspid annular systolic velocity by DTI (Sm) and amplitude of tricuspid annular longitudinal movement by M-mode (TAPSE). Diastolic RV function was assessed from the ratio of early and late diastolic tricuspid velocities by PWD (E/A) and by DTI (Em/Am). Global RV function was assessed using the myocardial performance index (Tei index) obtained by DTI, as follow: time interval between the end and the onset of tricuspid annular velocities (a) minus the duration of the systolic wave (b) was divided by b, i.e. $(a - b)/b$.

Results: Table shows results of the study.

	Group I	Group II	P- value
Sm (m/s)	0.15 ± 0.02	0.11 ± 0.02	<0.01
TAPSE (mm)	22.12 ± 3.43	18.22 ± 4.22	<0.001
E/A	1.47 ± 0.51	1.15 ± 0.37	<0.05
Em/Am	1.67 ± 0.54	1.40 ± 0.43	<0.05
Tei	0.34 ± 0.06	0.47 ± 0.22	<0.01

Systolic longitudinal velocity and amplitude of the tricuspid annulus (Sm and TAPSE) were significantly reduced indicating systolic RV dysfunction. Diastolic velocity flow profile obtained by PWD as well as tricuspid Em/Am ratio were significantly different between Groups 1 and 2 indicating diastolic RV dysfunction. Tei index was significantly increased in children with severe PS indicating global RV dysfunction.

Conclusions: Severe pulmonary stenosis in childhood produces systolic, diastolic and global RV dysfunction, most probably because RV morphology and function are genetically predisposed for low pressures.

P29

Does real-time Transthoracic 3-D Echocardiography reveal the mechanism of left-sided AV valve regurgitation after AVSD repair?

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Aims: The purpose of this study was to assess the feasibility of real-time 3-D echocardiography data acquisition, and the additional value of real-time 3-D echocardiography for morphology and function of the left-sided AV valve (LAVV) in adult patients after surgical repair of atrioventricular septal defect (AVSD).

Methods: Twenty consecutive patients with surgically corrected partial or complete AVSD were enrolled in this study. The real-time 3-D images were acquired with the Hewlett-Packard Sonos 7500 echo system (Philips Medical Systems, Andover, MA, USA). Image were reviewed off-line with assistance of TomTec Echoview 5.2 software (TomTec, Inc., Munich, Germany) by experienced observers. For analysis of the LAVV “en face” views from a ventricular and atrial position were reconstructed from the 3-D data set.

Results: Three-dimensional reconstruction of the LAVV was feasible for analysis in 17 of 20 patients. The mean time of 3-D acquisition was 15 ± 6 min. The quality of the 3-D images was optimal in 35%, good in 30%, sufficient in 20% and insufficient in 15%. Recognition of the LAVV structures was significantly better looking from a ventricular position than from the atrial position. Accurate identification of the pathology was possible in 85% of the patients. The abnormal position of the LVOT was could be seen from the atrial

position. These results are demonstrated in the RT-3DE images (Figures A to D).

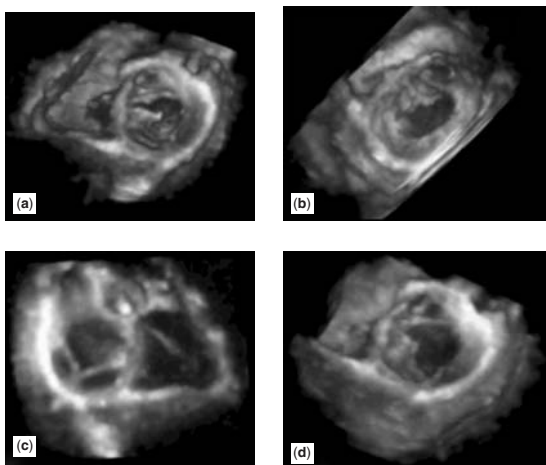


Figure. (a) LAVV in diastolic frame, seen from a ventricular view; (b) LAVV after AV valve repair; (c) LAVV seen from the LA and (d) LVOT that makes a 90° corner between left-sided AV valve and the LVOT.

Conclusion: Real-time transthoracic 3-D echocardiography provides new insight into the dynamic morphology of left-sided AV valve regurgitation and LVOT anatomy after AVSD repair. Because it has become feasible, easy to use in the daily practise and not time-consuming, it should become common practise in all echo laboratories.

P30

Myocardial scarring determined by delayed enhancement MRI at long-term follow-up after operation of left coronary artery from the pulmonary artery (ALCAPA)

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Background: Patients with an anomalous left coronary artery from the pulmonary artery (ALCAPA) improve their decreased left ventricular (LV) function postoperatively. LV functional studies have been carried out using angiography, echocardiography, and scintigraphy for short to mid-term follow-up. However, little is known about the distribution of myocardial scarring. In particular, the distribution of myocardial scarring in long-term follow-up remains unknown. Delayed enhancement magnetic resonance imaging (DE-MRI) is a modern imaging method and is accepted as the goldstandard for detection of LV myocardial scarring. Therefore the aim of this study was to describe the distribution of LV myocardial scarring after successful operation of patients with ALCAPA after long-term follow-up.

Methods: Since 1974, n = 63 patients with ALCAPA have been operated at our center. Of these n = 33 patients are now older than 14 years, and therefore included into this study. LV ejection fraction (LVEF) and LV enddiastolic volume (LVEDV) was determined by MRI. LV myocardial scarring was determined by DE-MRI.

Results: Interim results are available for n = 9 patients, n = 6 additional patients have given their consent to participate in this study and will be included within the next weeks. No scarring was found in n = 2 patients, transmural scarring in n = 3 patients, diffuse or endocardial scarring in n = 4 patients. No specific pattern of scarring could be determined in these patients. The presence of scarring could not be correlated to the operation method, the age at operation, or time after operation. LVEF was $54 \pm 12\%$. LVEDV was 128 ± 28 ml.

Conclusions: Because the size of scar tissue was relatively small, neonatal myocardial remodeling mechanisms may be very different than adult myocardial remodeling mechanisms. Additionally, the individual coronary collateralization seems to be the major determinant factor for the pattern and the size of myocardial scarring.

P31

Prediction of the stretched diameter of atrial septal defect in children

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Introduction: Stretched diameter of atrial septal defect (ASD) measured by balloon sizing is commonly used to select the size of the device for transcatheter closure. The formulas for estimation the stretched diameter of ASD have been reported, however the results for paediatric population were not available.

The aim of the study was to predict the stretched diameter of ASD by means of transthoracic echocardiography (TTE) measurement in children.

Methods and Patients: The study group consisted of 58 children, aged 3–18 years. In all of them the preliminary selection for transcatheter closure was based on TTE. ASD size (TTEASD) was determined as the maximal width of color Doppler flow jet at the defect site. The balloon stretched diameter (TEEASDsd) was measured by transesophageal approach. Multiple linear regression was used for construction of models.

Results: Mean values, standardized deviations and ranges for TTEASD and TEEASDsd were: 11.7 ± 3.7 mm (range: 6–19.5 mm) and 15.3 ± 4.3 (range: 10–26 mm) respectively. Using TTEASD, the predicted stretched diameter can be calculated by means of formula I: $\text{TEEASDsd (mm)} = 1,1 \cdot \text{TTEASD (mm)} + 2.94$. In 50% children discrepancy higher than 10% (TEEASDsd vs predicted value of this parameter) was found. Analogical formula II based on TTEASD and body surface area (BSA) was: $\text{TEEASDsd (mm)} = 1.0 \cdot \text{TTEASD (mm)} + 2.79 \cdot \text{BSA (m}^2\text{)}$. According to formula II in 62% children the stretched diameter was predicted with the error smaller than 10%. Correlation coefficient between TEEASDsd and predicted value of this parameter was 0.90 ($p < 0.0001$).

Conclusions:

1. In children with ASD selected for transcatheter closure the balloon stretched diameter can be predicted using the measurement of the defect size by transthoracic echocardiography.
2. Application the BSA to the formula based on transthoracic measurement of the defect can improve the predictive value of echocardiographic data in children.

P32

Shunt calculation in patients with atrial septal defects (ASD) – three-dimensional colour Doppler imaging versus Fick's method

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Non invasive quantification of cardiac shunts is an important measurement for decision making in paediatric cardiology. During cardiac catheterisation shunts are often calculated using estimated oxygen consumption. This approach however, is not precise particularly in ventilated patients. Three-dimensional (3D) colour Doppler imaging could serve as an alternative method to determine shunt volume in patients with ASD.

Between 2002 and 2004 we studied 12 patients (age 5.7–17.9 yr) who were admitted for interventional ASD-closure by trans-esophageal 3D colour Doppler ultrasound. All patients were ventilated and oxygen consumption was measured directly. Ultrasound data were recorded with a 5 MHz multiplane probe with rotational acquisition during apnoea. 3D datasets were reconstructed with a special software (TomTec). The max diameter of the defect was measured by 2D-echo, the area of the defect by 3D-echo and the shunt across the ASD was calculated from the 3D in the flow convergence region. Oxygen consumption and saturations were measured synchronously. The flow parameters were determined by Fick's method.

The mean maximal diameter of the defect was 15 mm (4–22 mm) in the 2D echo, the mean area (3D-measurement) was 210 mm² (19–362 mm²). The mean ratio of pulmonary-to-systemic flow was 1.79 (1.1–2.9). A mean left-to-right shunt of 1.91/min (4.55–0.25 l/min) was calculated by the 3D-colour measurements. Compared to the determinations by Fick's method (mean shunt 1.98 l/min, 5.23–0.29 l/min) there was a good agreement ($r = 0.95$, $p < 0.01$). The mean difference was $2 \pm 18\%$. The greatest differences was present in patients with larger defects. The shunt calculations with empiric oxygen consumption showed a much higher difference to 3D-calculation with a wider range ($37 \pm 28\%$).

Conclusion: 3D-colour Doppler imaging allows an exact calculation of shunts in patients with atrial septal defects also during ventilation without measurement of oxygen consumption. Compared to the oxymetric calculation there is a underestimation especially in large defects.

P33

Tissue Doppler evaluation of late cardiac effects of anthracycline containing therapy for childhood acute lymphoblastic leukaemia

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Introduction: At present about 80% of children with acute lymphoblastic leukaemia (ALL) will be cured following treatment with multi-drug chemotherapy. A major concern for this growing number of survivors is the risk of late effects of treatment. We aimed to determine whether signs of cardiomyopathy were present in patients treated in childhood with cumulative anthracycline doses of <300 mg/m².

Methods: Evaluation of cardiac function in a cohort of 63 long-term survivors in their first continuous remission following treatment of ALL with multi-drug chemotherapy including anthracyclines was performed using standard M-mode echocardiography and Tissue Doppler Imaging (TDI). Associations between age at diagnosis, cumulative dose of anthracycline, sex, length of follow-up on one hand and deviations from normal values in M-mode echocardiograms on the other were evaluated using univariate and multivariate regression analysis. TDI data were compared to normal values using Wilcoxon's matched-pairs signed-ranks test.

Results: By standard M-mode echocardiography the most significant findings were diastolic dilatation of the left ventricle, thinning of the interventricular septum, decrease of left ventricular mass in females, follow-up dependent dilatation of the left ventricle in systole and follow-up dependent decrease in ejection fraction. TDI abnormalities showed signs of early diastolic dysfunction and myocardial hypertrophy, and were also found in structures that appeared normal by M-mode echocardiography.

Conclusions: This study suggests that even low to moderate doses of anthracyclines might lead to progressive cardiac dysfunction. It is important that children treated with anthracyclines receive life long follow-up for signs of cardiomyopathy.

P34

Feasibility and accuracy of real-time transthoracic 3D echocardiographic assessment of ventricular septal defects

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Background: The aim of this study was to evaluate the feasibility and accuracy of real-time transthoracic 3D echocardiography (RT-3DE) in the determination of the position, size and shape of VSDs.

Methods: Between July and December 2004, 25 patients who were scheduled for surgical closure of a VSD, were enrolled in the study. The VSD localisation, shape and measurements of minimal and maximal diameter from "en face" LV and "en face" RV view were assessed from the 3D data set. These 3D data were compared with measurements and descriptions done by the surgeon during the surgical procedure. RT-3DE was performed with Hewlett-Packard Sonos 7500 echo-system and off-line analysis with TomTec Echoview[®] software.

Results: Acquisition of RT-3DE datasets was feasible in 22 of the 25 (88%) patients. In 3 patients, the quality of the transthoracic 3D echo was too poor to allow 3D reconstruction. The time of 3D data acquisition was 4 ± 2 min. Reconstruction time was 23 ± 16 min. The localization and number of the VSD were determined correctly by RT-3DE in all 22 patients. There was a good correlation between RT-3DE and surgery for the maximal VSD measurements from "en face" RV view ($r = 0.95$) and "en face" LV view ($r = 0.91$).

Conclusion: Real-time 3D echocardiography is feasible for quantitative assessment of VSDs and allows accurate determination of VSD size and localization. After a short learning curve, RT-3DE is applicable in daily clinical practise.

P35

Analysis of right atrial-ventricular interaction in patients with right ventricular pressure overload

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Objective: To assess the interaction of right atrial (RA) and right ventricular (RV) function in patients with chronic RV pressure overload (RVPO).

Methods and Materials: A total of 13 patients with RVPO caused by pulmonary hypertension, tetralogy of Fallot and pulmonary stenosis and 10 controls were studied with MRI. For the RVPO group invasive pressure measurements were available from cardiac catheterization. MRI was based on phasic multislice volume-analysis of the RV and RA and phasic pulmonary blood flow analysis using steady-state free precession and phase-contrast MRI, respectively. Concentric and excentric hypertrophy was determined by RV muscle mass and enddiastolic and endsystolic volumes, respectively. RV systolic function was defined by ejection fraction (EF) and diastolic function as antegrade pulmonary

forward flow in late diastole and by the filling rate of the RV. RA function was classified into percentage reservoir (fraction of maximal and minimal volume extension), conduit (fractional RV filling – (reservoir + pump fraction)) and pump function (fractional filling of the RV during atrial contraction). Data were normalized for body surface area where appropriate.

Results: In the RVPO group pressures (expressed in mmHg) were: 61 ± 22 (RV mean), 4 ± 1 (RV diastolic) and 3 ± 1 (RA mean). Compared to controls the RVPO group showed increased RV muscle mass of the free wall ($p < 0.001$) and slightly enlarged EDV and ESV ($p = 0.09$). Global systolic RV function was impaired ($EF = 42 \pm 11\%$ vs. $54 \pm 8\%$ in controls, $p < 0.01$). Late diastolic pulmonary forward flow pulse was augmented ($p < 0.05$) indicative of restrictive RV physiology. Fractional filling of the RV by atrial contraction was decreased by $19 \pm 7\%$ ($p < 0.01$) and RA reservoir function was decreased by $29 \pm 8\%$ ($p < 0.001$).

Conclusion: RV systolic and diastolic dysfunction due to chronic RV pressure overload is associated with impaired RA reservoir and pump function.

P36

Magnetic resonance 3D visualization of congenital heart disease in infancy

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Introduction: With MRI highly resolved images of coronary arteries, intra-cardiac morphology and extra-cardiac vessels can be obtained in adults with steady state free precession (SSFP) techniques. However, imaging of congenital heart defects in infancy is limited by spatial resolution and fast heart rates. The purpose of this study was to evaluate the feasibility of high resolution three dimensional (3D) imaging of congenital heart defects in free breathing infants using SSFP.



Methods: Ten infants (median age 15.5 months, 3 months to 9.7 years, weight 4 to 24 kg) were sedated. According to patient size head ($n = 7$) or cardiac ($n = 3$) coils were chosen. The systolic ($n = 8$) and diastolic ($n = 10$) rest period of the heart was assessed with a cine fast low angle shot sequence. Heart and great vessels were imaged within the thorax with a 3D navigator gated true fast imaging with steady precession (True-FISP) sequence with a T2 preparation pulse on a commercial 1.5 T scanner (Siemens Medical Solutions, Erlangen, Germany, TE 1.95 to 2.25 ms, flip angle of 110° , 1.0 to 1.25 mm³ isotropic voxels). A scoring system for image

quality was used (1 = non diagnostic; 3 = diagnostic information available; 5 = excellent). Continuous data are reported as median \pm SD (range). A p value < 0.05 was considered significant.

Results: All exams were diagnostic (imaging score > 3) with an overall imaging score of 4 ± 1 (3 to 5). Mean imaging scores in systole were 4.5 ± 0.7 vs. 4.1 ± 0.9 in diastole with no statistically significant difference ($p = 0.5$). Median navigator efficiency was 80%. With a median heart rate (bpm) of 118 ± 23 bpm (75 to 160 bpm) 55 ± 12 ms (43 to 81 ms) per heart beat were needed to acquire image data.

Conclusions: T2 prepared 3D True-FISP sequence allows high resolution imaging with isotropic voxels of the intra-cardiac blood pool and extra-cardiac blood vessels without using contrast agents in free breathing, sedated infants. Image data can be acquired in diastole and systole with similar quality by adjusting the image data acquisition time to the resting period of the heart.

P37

Cardiovascular magnetic resonance for evaluation of congenital heart disease in newborns and infants

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Background: Cardiovascular MRI (CMRI) is increasingly used as advanced diagnostic technique in patients with congenital heart disease (CHD). Its application in the paediatric population remains limited to few centers. We sought to assess the role of clinical application of CMRI and its impact on the management of newborns and infants with CHD.

Methods: Between May 2002 and December 2004, 38 CMRI studies were performed in 34 infants, median age 2 months, range 1 day–11 months, for initial evaluation of CHD in 18 and after cardiac surgery in 20 patients. Underlying diagnoses included aortic arch anomalies in 11, complex CHD in 10, pulmonary atresia with ventricular septal defect in 4, truncus arteriosus in 3, tumors in 2 and other CHD in 4. Indication for CMRI were unclear or suspected findings at echocardiography, needing further investigation. The anatomical structures assessed included the pulmonary arteries in 20 cases, the aorta and its branches in 15, the pulmonary veins in 10, the systemic veins in 4, the ventricles in 4 and the diaphragm in one. CMRI was performed under general anaesthesia in 33 and sedation in 5 patients. Sequences used were cine gradient echo imaging in 97%, contrast-enhanced angiography in 92%, and phase contrast flow measurements in 50% of the examinations. Thus functional evaluation was performed additionally to anatomical imaging in 24/38 (63%) of the examinations.

Results: All CMRI studies were diagnostic and provided definite anatomical delineation of the CHD. The information obtained was crucial for further management in 21/34 (61%) patients, including planning surgery in 19, planning an intervention in 7 and ruling out a significant vascular anomaly in 7. CMRI obviated cardiac catheterisation in 15 and lung perfusion scan in 9 cases (70%). No further imaging was required in 71% of the cases; catheterisation was still required for haemodynamic testing in 3 patients and for an intervention in 8.

Conclusions: In newborns and infants CMRI is an accurate, safe and non-invasive technique for advanced anatomical and functional evaluation of CHD. Complex vascular anomalies or complex CHD represent the main indication for CMRI. Further invasive examinations may be limited to selected cases.

P38**Evaluation of cardiac function of cirrhotic children with conventional and tissue Doppler echocardiography**

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Patients with cirrhosis of the liver may have several cardiovascular abnormalities including latent cardiomyopathy, hyperdynamic circulation, and arteriovenous communications causing arterial hypoxemia.

Objective: To evaluate the systolic and diastolic function of cirrhotic children with conventional echocardiography and Tissue Doppler imaging (TDI) and to document associated cardiovascular abnormalities.

Study Design: 20 children with liver cirrhosis (8.6 ± 5.6 years) were examined by conventional echocardiography and TDI. The relative wall thickness (RWT), LV mass index (LVM/h^{2.7}), and myocardial velocities obtained by TDI were compared with age-matched control group. Contrast echocardiography with agitated saline was made in 16 patients.

Results: Ejection and shortening fractions of the left ventricle determined by M-mode measurements and diastolic function evaluated by mitral inflow velocities were normal in cirrhotic children. The left ventricular mass index (LVM/h^{2.7}) was significantly greater in cirrhotic cases but the relative wall thickness was not different from the control group. The early to late relaxation velocity ratio (e/a) determined by TDI for the interventricular septum was significantly lower in the cirrhotic group (1.76 ± 0.6 vs. 2.5 ± 0.45 , $p < 0.001$). Systolic and diastolic myocardial velocities in the left ventricle were not different from the control group. None of the patients had cyanosis. Pulmonary arteriovenous fistulae was shown by contrast echocardiography in two of 16 patients.

Conclusion: LV hypertrophy (eccentric) as evidenced by increased LVM and normal relative wall thickness was present in cirrhotic children. TDI revealed subclinical changes in diastolic function of IVS. These findings emphasize the importance of the cardiac evaluation of cirrhotic children for the possible association of a latent cardiomyopathy.

P39**The assessment of regional cardiac function in children with moderate chronic renal failure**

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Introduction: Cardiovascular disease has been recognized as the most important cause of death in adults with end stage renal disease. Nevertheless, children having an impaired renal function but who are not yet in dialysis have not been studied so far; they might particularly benefit from the early detection of cardiac dysfunction since therapy could be commenced before irreversible myocardial damage occurs. Strain/Strain rate imaging is a technique known to be more sensitive for detecting myocardial abnormalities before they are noticeable using standard echocardiographic methods. Pathology studies have demonstrated that the atherogenic process begins early in childhood. Increased intima media thickness is a marker of early atherosclerosis.

Objectives: To assess myocardial function in children with moderate renal failure; and to determine whether early markers of atherosclerosis are present at this stage of the disease.

Methods and Results: Twenty-nine patients and twenty-one controls were studied. The patients were all in the early to moderate

stages of renal failure. Ten of the patients were hypertensive or on medication to lower blood pressure. Standard transthoracic echocardiograms as well as myocardial velocity imaging studies, which allowed the calculation of myocardial velocities, strain rate and strain, were performed. The blood pressure was higher in the patients' group (106.5 ± 13.0 vs. 99.1 ± 11.8 , $p = 0.05$). A higher fractional shortening and ejection fraction were found in the patients. Annular motion, at the three measured points, was significantly reduced in the patients' group ($p < 0.001$). The analysis of the longitudinal function of the left ventricle revealed a reduced peak systolic strain at the mid septal and at three lateral segments in the patients. The peak systolic strain rate was significantly lower at the basal and mid segment of the left ventricular lateral wall. No difference in the intima media thickness was seen between patients and controls.

Conclusions: In patients with moderate renal failure, a higher blood pressure, a normal radial systolic function, a normal diastolic function and a decreased longitudinal systolic function are seen. On the basis of these results a close and thorough monitor of cardiac function is warranted to start therapy before irreversible damage occurs.

P40**Lung perfusion scintigraphy in patients after correction of tetralogy of Fallot**

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Lung perfusion abnormalities (LPA) are frequently observed in patients with tetralogy of Fallot (TOF). They can be of primary origin or occur as a result of surgery. There are several diagnostic modalities used clinically to assess LPA. Among others lung perfusion scintigraphy is a non invasive, sensible and easy accessible method.

Material and Methods: 110 patients (49 men and 61 women) from 6–28 years (14,6) after surgical repair of TOF were studied. In 33 cases palliative surgery (Blalock–Taussig shunt) was done prior to complete repair. Mean age was 15 ± 8.2 years. Lung perfusion scans with use of ^{99m}Tc macroaggregates of albumin were analyzed semiquantitatively with assessment of relative uptake and regional perfusion defects.

Results: Asymmetric pattern of pulmonary perfusion was observed in 65 (59,1%) patients. Appearance of perfusion asymmetry was equal in patients after primary surgical repair and in those who underwent palliative shunt prior to correction. There was no prevalence of relative hypoperfusion of right or left lung in both groups of patients. Regional perfusion defects were observed in 44 (40%) cases. There was no difference in frequency of regional perfusion defects in patients after primary surgical repair and in those who underwent palliative shunt prior to correction and they appeared more often ($p < 0.05$) in right than in left lung in both groups of patients. There was a significant correlation between age at surgical repair and prevalence of regional perfusion defects appearance.

Conclusions: Asymmetric lung perfusion and regional perfusion defects are frequent findings in patients with TOF. There is no significant difference in appearance of LPA in patients after primary surgical repair and in those who underwent palliative shunt prior to correction. Correction of TOF at early age decreases the risk of regional perfusion defects but has no impact on asymmetry of pulmonary perfusion.

P41**Important echocardiographic parameters in early detection of cardiac involvement of patients suffering from thalassemia major**S. Mehralizadeh¹, N.M. Noori²¹Semnan University of Medical Sciences, Semnan, Iran; ²Zahedan University of Medical Sciences, Zahedan, Iran

Introduction: Cardiac involvement is one of the most common causes of mortality and morbidity in patients suffering from thalassemia major. In this study the echocardiographic parameters which would predict the cardiac involvement in patients at an early stage were determined.

Methods: The study was designed as a case control study on 80 patients suffering from thalassemia major from September 2002 to December 2003 at a pediatric hospital. The M-mode and Doppler examination were performed to measure the following parameters: isovolumic ventricular relaxation time (IVRT), deceleration time (DT), pre-ejection period to ejection time (PEP/ET), and myocardial performance index (MPI) and the results were compared with the control group who were at similar age and sex. Data were analyzed by *t*-students test and correlation coefficient.

Results: Mean age of the patients was 14.3 ± 2.3 and age of the control group was 14 ± 2.6 years. Mean ejection fraction in the case group was 55.7 ± 7.2 and 62.8 ± 7.7 in control ($p > 0.05$). Mitral valve DT in case group was 126.21 ± 22.4 and in control group was 95.3 ± 11.7 ($p < 0.05$). DT of mitral valve in case group was 144.27 ± 30 ($p < 0.05$).

Mean right ventricular IVRT in case group was 128.18 ± 21.62 and in control group was 98.32 ± 15.16 ($p < 0.05$). Tricuspid valve DT in case group was 134.87 ± 25 and in control group was 144.93 ± 20 ($p < 0.05$). PEP/ET in the left heart in case group was 0.32 ± 0.06 and in control group was 0.28 ± 0.004 ($p < 0.05$). PEP/ET in the right heart in case group was 0.31 ± 0.06 and in control group was 0.26 ± 0.04 ($p < 0.05$). MPI in the right ventricle in case group was (0.59 ± 0.12) in comparison to control group (0.41 ± 0.12) was increased 87% in the patients ($p < 0.001$). Also MPI in left ventricle in case group was 0.49 ± 12 in comparison to control group 0.4 ± 0.09 and was increased 73% in patients ($p < 0.001$).

Conclusion: The data show that IVRT in both ventricles regressed to the same extent, also decreased DT and increased PEP/ET in the right heart shows earlier right sided failure. Increased MPI in both ventricles show systolic and diastolic malfunction in both ventricles at an early stage.

Coronary Arteries and Morphology (see also

OP22-5)

P42**Inhaled nitric oxide in respiratory distress syndrome (RDS) of the newborn lamb improves cardiac index and right coronary blood flow**A. Berg, A. Nordh, G. Oskarsson, D. Ley, V. Fellman, E. Pesonen
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Introduction: Respiratory distress syndrome (RDS) is associated with pulmonary hypertension. Increased pulmonary blood pressure further complicates the respiratory function by causing reduced perfusion of the already poorly ventilated lung. A low ventricular output, and an increased ventricular pressure may compromise perfusion to the myocardium and lead to right cardiac dysfunction. The aim of this study was to evaluate the acute hemodynamic effects of inhaled nitric oxide treatment in a lamb model of RDS and pulmonary hypertension.

Methods: Ten surfactant-treated preterm sheep with gestational age 125 days were delivered by cesarean section and supported by pressure-limited mechanical ventilation. Right ventricular pressure was measured with a balloon catheter (4-F). Cardiac index and coronary blood flow was measured with transthoracic echodoppler cardiography. The animals were treated with inhaled NO (40 parts per million) for 15 min.

Results: Inhalation of NO was associated with an immediate and rapid decrease in systolic right ventricular pressure. Cardiac index increased from 3.6 ± 1.2 (mean + SD) to 4.6 ± 1.1 ml/min ($p < 0.001$) after NO treatment. Right coronary blood flow increased from 15.3 ml/min to 28.6 ml/min ($p < 0.001$). There was no significant increase in left coronary blood flow during treatment. Oxygenation improved significantly in all sheep.

Conclusions: Inhaled nitric oxide improves right coronary perfusion in newborn lambs with RDS and elevated pulmonary pressure. The effect of NO on right myocardial perfusion seems to be a result of reduction in right ventricular pressure and increase in cardiac index.

P43**Evaluation of myocardial perfusion by magnetic resonance imaging in children with congenital or acquired coronary artery disease**E.R. Valsangiacomo Buechel¹, U. Bauersfeld¹, C.J. Kellenberger², J. Schwitzer³¹University Children's Hospital Zurich, Division of Paediatric Cardiology; ²University Children's Hospital Zurich, Division of Diagnostic Imaging; ³University Hospital Zurich, Department of Cardiology, Zürich, Switzerland

Introduction: Abnormal myocardial perfusion may occur in children after inflammatory disease or cardiac surgery for congenital heart disease (CHD) and congenital coronary artery anomalies. Detection of myocardial ischemia by perfusion magnetic resonance imaging (pMRI) in adults has been demonstrated to be very accurate. We sought to assess the feasibility of evaluating myocardial perfusion by pMRI in children and to compare the results with coronary angiography (CA).

Methods: A hybrid echo-planar pulse sequence with saturation recovery preparation was used for assessing contrast medium first-pass (Gd-DTPA-BMA, 0.1 mmol/kg, 5 ml/sec) in the myocardium under pharmacological stress (adenosin 0.14 mg/kg/min i.v.). Mean duration of examination, including evaluation of myocardial perfusion and ventricular function, was 66 ± 11 min; the maximal heart rate under vasodilatation was 95 ± 18 bpm. Three examinations were performed in general anesthesia, one under conscious sedation. Coronary artery disease (CAD) was defined at CA if at least 50% narrowing occurred in ≥ 1 coronary vessel.

Results: Nineteen consecutive patients, median age 13 yr (range 3.5–18.2 yr) underwent pMRI between January 2003 and December 2004. Underlying diagnosis was CHD in 8, inflammatory disease in 5, cardiomyopathy in 2, congenital coronary artery anomalies in 1 and others in 3 children. Six patients had undergone coronary surgery during repair of CHD, 2 had an aorto-coronary bypass. PMRI was diagnostic in all cases and no complications were observed. PMRI depicted normal myocardial perfusion in 14 patients and abnormal in 5; in 3 cases abnormal first pass indicated a stenosis of a coronary artery, in one a diffuse subendocardial hypoperfusion was related to severe myocardial hypertrophy. Another patient after myocarditis presented abnormal perfusion in scar tissue of a hypokinetic region and CA showed absence of CAD.

Twelve patients underwent CA with a median time interval of 19 months (range 1 d–6 y) between pMRI and CA. The findings of both examinations were concordant in all 12 cases.

Conclusion: PMRI is feasible in children, shows high agreement with CA results and may add haemodynamic information to the anatomic findings provided by CA. PMRI may be useful in selecting patients requiring invasive investigation.

P44

Determination of myofiber orientation in human cardiac specimen using Magnetic Resonance Diffusion Tensor Imaging

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Introduction: Within the left ventricular (LV) cardiac wall muscle fibers are oriented in a characteristic helixlike pattern, which is similar across various animal species. Measured transmural helix angle courses typically range from +60° at the subendocardium to -60° at the subepicardium, although a large variation between measurements exists. Accuracy of fiber angle determination is hampered by the employed histological techniques, which only allow in-plane measurement of fiber angles. Magnetic Resonance Diffusion Tensor Imaging (MR-DTI) circumvents this problem but has until now only been employed in fresh formaldehyde-fixed animal hearts.

Aims: To assess whether Magnetic Resonance Diffusion Tensor Imaging (MR-DTI) can be used to determine three-dimensional myocardial fiber orientation in the myocardium of long-term formaldehyde-fixed or ethanol-glycerin preserved heart specimens from human anatomical collections.

Methods: Human hearts, either fixed in 10% formaldehyde (n = 3) or preserved in 90% ethanol-10% glycerin (n = 3) were analyzed at a room temperature of 20°C. ¹H MR-DTI measurements were performed in a 4.7 Tesla magnet interfaced to a Varian NMR spectrometer. The long axis of the left ventricle (LV) was visually aligned with the centerline of the magnet bore. Diffusion data were measured in 3-mm-thick adjoining slices.

Results: The out-of-plane components of the fiber orientation within each LV cross-sectional plane are easily recognized and determined in specimens preserved either way. More axially oriented fibers are found in the subepicardium, the subendocardium and the papillary muscles. Midwall fibers run predominantly in the circumferential direction. The quality of the results was 1) inversely related to the age of the specimen and 2) better for formaldehyde-fixed hearts than for the ethanol-glycerin preserved heart specimens. The latter is probably due to unequal distribution of water after ethanol fixation.

Conclusions: MR-DTI can be used to determine cardiac myofiber direction in formaldehyde-fixed and ethanol-glycerin preserved intact heart specimens and is therefore a promising technique to investigate heart specimen from anatomical collections.

Fetal Cardiology (see also OP22-6-8)

P45

Left and right ventricle Tei-index in normal fetuses in comparison to those with heart defects or arrhythmia

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Objectives: To establish normal value of Tei-index (TI) (isovolumetric time/ejection time) throughout pregnancy for right and

left ventricles in fetuses with normal cardiovascular system and to compare them with fetuses with CHD or arrhythmia.

Methods: The Doppler waveforms of the LV and RV inflow and out-flow tracts were recorded. The LV isovolumic contraction time (ICT), isovolumic relaxation time (IRT) and ejection time (ET) were measured and TI was calculated using the formula (ICT + IRT)/ET. Student *t*-test and Spearman's correlation test were used for statistic analysis. Cardiovascular score (CVS) was used to evaluate fetal heart failure. All measurements were obtained by 2 independent observers. **Results:** 237 measurements in 132 fetuses, between 13 and 38 weeks were obtained. Fetuses were divided into 5 groups: 1 – normal; 2 – heart defects (AVSD, HLHS, SV, other); 3 – bradycardia; 4 – premature atrial contraction; 5 – supraventricular tachycardia (Table 1). There were not statistically significant difference between maternal age and weeks of pregnancy among all groups.

Table 1.

Group	1 – normal	2 – CHD	3 – brady	4 – PAC	5 – SVT
Mothers' age	30,46	29,06	30,67	27,46	29,29
SD	5,86	4,65	7,09	3,66	5,44
Weeks of preg.	25,58	30,45	29,58	30,12	30,18
SD	5,87	4,89	4,60	5,35	6,08

CVS was 10 in group 1; 6–10 in group 2; 8–10 in group 3; 9–10 in group 4; 8–10 in group 5. Results of TI are shown in Table 2. In fetuses with arrhythmia TI was measured during sinus rhythm periods.

Table 2.

Group	No of LV measurement			No of RV measurement		
	LV-TI	SD		RV-TI	SD	
1	65	0,5152	0,1002	60	0,5385	0,1066
2	27	0,6073	0,1098	29	0,5874	0,1394
3	7	0,5114	0,1095	5	0,5180	0,1057
4	64	0,5181	0,1095	61	0,5417	0,1275
5	19	0,5111	0,1094	11	0,5555	0,1364

TI in normal fetuses was $0,52 \pm 0,1$ for LV and $0,54 \pm 0,1$ for RV and was constant throughout pregnancy. Similar values were obtained for fetuses with PAC, SVT and bradycardia. Higher LV-TI: $0,61 \pm 0,11$ and RV-TI: $0,59 \pm 0,14$ were in fetuses in group 2 and difference was statistically significant (LV-TI $p = 0,0004$ and RV-TI $p = 0,0595$). Those results, however, need further evaluation due to small and non-homogenous group.

Conclusions:

1. Normal TI was significantly higher in comparison to children's TI and already published fetal TI by Falkensammer et al. in 2001.
2. LV-TI was similar to those published by Friedman et al. in 2003.
3. LV-TI is easier to evaluate than RV-TI.
4. Fetuses with arrhythmia have normal TI during sinus rhythm periods.
5. Evaluation of ventricular function using TI in fetuses with CHD needs further investigation.

P46

Outcome of in utero versus postnatally diagnosed major congenital heart disease: a multi centre Swiss study

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Introduction: Switzerland has a population of 7 million with 70–75,000 live births per year. Assuming an incidence of congenital heart

disease (CHD) of 0.7–0.8%, 490–600 affected newborns would be expected per year, of which 230–260 haemodynamically significant and prenatally detectable CHD. The aim of this prospective study was to analyse the outcome of prenatally detected CHD and compare it with the postnatally diagnosed cohort.

Methods: Prospective study of all prenatally diagnosed major CHD during a period of 2 years time (1.7.01–30.6.03) in 7 Swiss tertiary fetal cardiology centres and prospective assessment of all haemodynamically relevant and prenatally detectable CHD of children born during the same period of time in these centres.

Results: 94 fetuses with major CHD were detected. 22 (23%) had Single ventricle, 30 (33%) conotruncal, 7 (7%) valvar, 28 (30%) septal defect and 7 (7%) other malformations. Gestational age at time of diagnosis was <24 weeks in 32, >24 weeks in 54 and unknown in 8. In 70 (74.5%) cases parents opted for postpartal treatment, in 22 (21%) treatment was denied. Intrauterine death occurred in 2. In the no treatment group pregnancy was terminated in 14/22 cases, in 8/22 comfort care was given after birth. In the treatment group 52/70 newborns survived >1 year, 18/70 (10 without, 8 with treatment) did not survive. The overall survival was 55.3%. CHD was detected in 306 patients postnatally, 21 (7%) had single ventricle malformation, 93 (31%) conotruncal malformation, 39 (13%) valvar abnormalities, 120 (40%) septal defect and 26 (9%) other malformations. 266 (87%) were alive >1 year, 40 (13%) died, 19 without intervention, 11 postoperatively and 10 not CHD related.

Conclusions: Most parents opted for treatment of prenatally diagnosed CHD. However this could be biased because of late diagnosis during fetal life. Outcome of prenatally detected CHD is worse than postnatally diagnosed CHD. The reason for this could be a higher percentage of severe CHD (single ventricle) in the prenatal group.

P47

Dynamics of septum primum in fetuses with intrauterine growth restriction

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Introduction: The “septum primum” mobility is a diastolic cardiac phenomenon and can be related to left atrial pressure, which is modified in intrauterine growth restriction (IUGR).

Objective: Fetuses with placental insufficiency leading to IUGR and fetuses with normal growth for gestational age (NG) whose mothers had systemic arterial hypertension (SAH) or not were evaluated to test the hypothesis that the linear displacement of the “septum primum” is reduced in that fetuses with IUGR.

Methods: A controlled transversal study which reviewed the ratio between the linear displacement of “septum primum” and the left atrial diameter (excursion index–EI). It has been compared among 3 groups: 27 fetuses with IUGR (group I), 35 fetuses with NG whose mothers had no SAH (group II) and 24 fetuses with NG whose mothers had SAH (group III). The atrioventricular flow velocities and the umbilical artery resistance index (IR) were also compared among those 3 groups.

Results: In fetuses with IUGR and gestational age more than 30 weeks, the mean of EI was 0.38 ± 0.05 . It was significantly minor ($p < 0,001$) than in group II (0.51 ± 0.06) and in group III (0.49 ± 0.07). At that gestational age, it was observed a significant converse correlation between EI and IR ($r = 0.427$, $p = 0.002$). There was no correlation between EI and atrioventricular flow velocities.

Conclusion: The mobility of “septum primum” is reduced in fetuses with IUGR and that fetuses with more than 30 weeks of gestational age, when compared to fetuses with NG with or without maternal SAH. These findings can show the left ventricle diastolic function anomaly and placental insufficiency.

P48

Prenatal diagnosis of double inlet left ventricle associated with truncus arteriosus and interrupted aortic arch

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Introduction: Most of congenital heart diseases have been detected prenatally. However, some uncommon associations with major neonatal impact have not yet been described.

Methods and Results: A 29-year-old G3P2 woman was referred at 18 weeks gestational age for fetal heart defect. Her personal and family history is negative. Fetal echocardiography showed a double inlet left ventricle (DILV) associated with a truncus arteriosus (TA) type II. No extracardiac anomaly was visualized. Fetal karyotyping was normal and there was no 22q11 microdeletion at FISH analysis. On follow up scan at 23 weeks, the presence of an interrupted aortic arch (IAA) was suspected. The truncus gave rise to 2 separate pulmonary arteries and to the right innominate artery (RIA) in a straight course. The arch drew a peculiar curve and there was a long distance between the RIA and the left carotid artery (Figure).



Postnatal echocardiogram confirmed a DILV and TA type II. At 24 hours of life, IAA type C was confirmed by constriction between the RAI and the left carotid artery at ductal closure. Prostaglandins were started. The neonate underwent first stenting of the aortic arch and bilateral pulmonary arteries banding. Reconstruction of the aortic arch, including removal of the stent, together with a bidirectional superior cavopulmonary anastomosis was performed at 6 months. The child is currently well at 8.5 months of age. Retrospective review of the fetal echocardiograms showed a lower origin of the transverse arch very close to the emergence of the pulmonary arteries, prior to the take off of the RIA. As such, the arch was lying on the roof of the atria.

Conclusions: We report the first case of prenatal diagnosis of DILV associated with TA and IAA. IAA associated with TA might be suspected prenatally when the arch does not draw an harmonious curve, when the distribution of the neck vessels is abnormal and when the arch is positioned more caudally. In this rare condition, the 6th embryonic aortic arch is indeed persisting rather than the 4th as usually. Prenatal detection of IAA is of most importance given the risk of cardiogenic shock at ductal closure.

P49

A limited ability to increase coronary artery blood flow in fetal heart failure

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Background: Coronary circulation can accommodate marked increases in blood flow in response to increased oxygen demand. The fetal heart may compensate intrauterine fetal circulatory failure by increasing myocardial blood flow. However, data on fetal coronary flow velocity patterns are lacking. This study was designed to evaluate resting coronary blood flow velocity in normal fetuses and fetuses with heart failure using Doppler echocardiography.

Methods: A total of 107 fetuses, 92 normal fetuses (30 ± 4 weeks) and 15 fetuses (29 ± 4 weeks) with findings of heart failure (enlargement of fetal heart, significant tricuspid regurgitation, or hydrops fetalis), were studied. The flow signal in the left anterior descending coronary artery (LAD) was detected by color Doppler echocardiography using a short-axis view at the aortic sinus level. LAD flow measurements were also performed in neonate 1–2 hours after birth. Measurements of maximum peak velocity (MPV), average peak velocity (APV), and flow velocity–time integral (FVI) were performed automatically using the analysis package of a ultrasound unit.

Results: LAD flow signals were detected in 19/92 (21%) normal fetuses and in 7/15 (47%) fetuses with heart failure. The mean MPV, APV, and FVI in normal fetuses were 47 ± 5 cm/sec, 30 ± 4 cm/sec, and 5.9 ± 1.2 cm, respectively. Compared with neonates (MPV; 17 ± 3 cm/sec, APV; 11 ± 3 cm/sec, FVI; 3.7 ± 0.8 cm), the mean MPV, APV, and FVI in normal fetuses were significantly higher ($p < 0.01$). Compared with normal fetuses, the mean MPV (50 ± 7 cm/sec), APV (33 ± 4 cm/sec), and FVI (6.3 ± 1.1 cm) in fetuses with heart failure were tended to be higher but not statistically significant.

Conclusion: Fetal LAD flow is greater than that in neonates, which suggests that the fetal heart compensates its relatively hypoxic environment by increasing myocardial blood flow. Fetuses with heart failure have an impaired myocardial blood flow response to cardiovascular stress. Thus, a limited ability to increase myocardial blood flow during conditions of increased myocardial oxygen demand may play a potential role in the pathogenesis and progression of fetal heart failure.

P50

Foramen ovale pulsatile flow: morphological and functional correlation in fetuses of diabetic mothers

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Introduction: Flow through the foramen ovale (FO) has a vascular profile during fetal life. The pulsatility index (PI) has been used to assess flow impedance and left ventricle diastolic function, especially in fetuses with myocardial hypertrophy due to maternal diabetes.

Objective: To test the hypothesis that the foramen ovale pulsatility index (FOPI) is correlated with “septum primum” mobility (SP) and pulmonary venous flow PI (PVPI), parameters used to analyse fetal left ventricle (LV) diastolic function, and with the thickness of the interventricular septum (TIVS), a morphological factor, in a sample of fetuses of diabetic mothers.

Methods: Fifty-six fetuses of mothers with previous or gestational diabetes were evaluated by a diastolic fetal function investigation protocol. The excursion index of “septum primum” (EISP) and TIVS were analyzed by two-dimensional echocardiography, as previously described. The FOPI and pulmonary venous flow were obtained by pulsed wave Doppler by the ratio [maximal velocity (systolic or diastolic) – minimal velocity (pre-systolic)/mean velocity]. For statistical analysis purposes, it was used the Pearson’s correlation with a level of significance of 0.05.

Results: Maternal age was between 17 and 43 years (mean = 31.6 ± 6.7 years) and gestational age was between 24 and 36 weeks (mean = 32.1 ± 3.3 weeks). Data are presented as mean ± sd and amplitude. FOPI: 2.76 ± 1.17 (1.21–6.88); PVPI: 1.47 ± 0.88 (0.60–4.80); TIVS: 0.36 ± 0.21 (0.24–0.61); EISP: 0.49 ± 0.12 (0.27–0.60). A significant positive correlation was observed between FOPI and TIVS ($r = 0.649$, $p < 0.0001$) and between FOPI and PVPI ($r = 0.331$, $p = 0.013$). There was a significant inverse correlation between FOPI and EISP ($r = 0.428$, $p = 0.001$).

Conclusion: In fetuses of diabetic mothers, the foramen ovale pulsatile flow is correlated with pulmonary venous flow, LV parietal thickness and “septum primum” mobility. Myocardial hypertrophy due to maternal diabetes has influence in LV diastolic function and, consequently, in the left atrial dynamics, with reflection in the behavior of flow through the foramen ovale.

P51

Preliminary experience with national data base for fetal anomalies

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Objectives: To present concept and early experience with national data base for fetal cardiovascular pathology which was built to evaluate present detection rate, possibilities of prenatal treatment, and outcome of fetuses with different cardiac pathologies.

Methods: Database was built by two experienced fetal cardiologist in co-operation with computer-scientist experienced in building medical data bases. Patients data was coded by the computer to protect their personality. Information concerning referring physician, reason for fetal echocardiography, obstetric ultrasound results, diagnosis, pregnancy outcome and follow-up in 30th day and 12th month were added to the base. AEPC code was used for diagnosis.

Results: There were 16 centers registered in the database, which were divided into three categories: C – full fetal cardiology service compliant with AEPC recommendation (3); type B – at least one cardiologist with Polish fetal cardiology certificate (3); type A – screening centers (10). 325 different fetal cardiac pathologies were registered in the data base in 2004. 93% of them were diagnosed in three C centers and one B center. Preliminary results are as followed: 234 heart defects, 40 SVT or AF, 7 TTTS, and other anomalies like: CHB, ectopia cordis, conjoined twins. The most common CHD was HLHS (22), followed by VSD and AVSD. It was difficult to count precisely those defects due to different codes used for them. It has not been possible to evaluate pregnancy outcome, as not all were finished yet.

Conclusions:

1. It is possible to built national fetal database however all fields must be carefully prepared.
2. AEPC cardiac code is too long and contained too many details for using it for the national base, so special edition for such purpose should be prepared.
3. Preliminary results showed that less experienced centers mixed structural heart defects with fetal functional abnormalities so further training is necessary.
4. Evaluation of pregnancy and neonatal outcome let us to more precise parental counseling as well as comparison with neonates with same pathologies without prenatal diagnosis.
5. Close co-operation between physician and computer-scientist is essential.

P52

Diagnosis of restrictive ductus arteriosus and foramen ovale. A challenge for the right ventricle in utero

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Introduction: Premature closure of the ductus arteriosus (DA) in utero is a well known complication of cyclo-oxygenase inhibitor treatment in pregnant women. Premature closure of the foramen ovale (FO) in utero is described in complex cardiopathy, but rarely described with normal heart morphology. We describe 2 cases of premature closure of the DA and 2 cases of restrictive FO in utero and their follow-up after birth.

Cases:

1. Echography at 29 weeks gestation showed no congenital heart disease, but a complete closure of the foramen ovale (FO) with dilatation of the right sided heart chambers, hypertrophy and good function of the right ventricle (RV). The DA was open without restriction. Follow-up showed progressive RV dysfunction leading to delivery at 32 weeks gestation.
2. Sonography at 26 weeks gestation because of a small aorta demonstrated dilatation of the right sided heart chambers, small aorta without stenosis, hypoplasia of the aortic arch, 2 muscular VSDs and a restrictive FO. A stable evolution allowed delivery at 38 weeks gestation.
3. Vitality sonography at 41 weeks gestation showed hypertrophy and dilatation of the RV with poor systolic function, no DA could be visualised leading to caesarean delivery.
4. Echocardiography at 30 weeks gestation demonstrated RV dilatation and hypertrophy, with diminished contractility and severe restriction of the flow on the DA, tricuspid and pulmonary regurgitation. Reduced vitality of the foetus was noted leading to caesarean section delivery at 32 weeks gestation. All infants had good primary adaptation at birth. Every newborn

demonstrated severe RV hypertrophy and dilatation, persistent elevation of the pulmonary pressure for weeks, ECG signs of severe RV hypertrophy and anomaly of the repolarisation in the right precordial leads that persisted for many months.

However in all cases the RV hypertrophy regressed completely.

Conclusion: Premature closure or restriction of the FO and of the DA are entities that can occur without complex heart malformation and can lead in utero to severe dysfunction of the RV and necessitate premature delivery.

P53

Feasibility and usefulness of real time 3D echocardiography (RT3D echo) in the fetus

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Aim: We performed RT3D echo in 9 fetuses, to test feasibility and usefulness of this new technique.

Method: The patients were randomly selected among pregnant women who underwent a fetal 2D-echocardiography to rule out CHD. GA varied from 19 to 34 weeks. We used a Sonos 7500 equipment with 2–4 MHz probe. Full-volume acquisitions were stored in the hard disk of the machine and further elaborated off-line. We evaluated the heart anatomy, fetal face, limbs and genitalia.

Results: Three to 8 full-volume acquisitions were performed in each patient, lasting 4–8 sec. each. Off-line elaboration of the 3-D images required from 20 to 40 minutes. Heart: a cardiac malformation was present in 4 (1 TAC, 1 Aorto-LV tunnel+VSD, 1 TOF and 1 PA+IVS). RT3D echo confirmed the 2-D echo diagnosis in all and gave better understanding of the spatial position of the anatomical structures. Face: in 4 cases the fetal face was depicted clearly and no genetic syndrome was suggested in 3. In the 4th case, a small chin with prominent forehead and an abnormal profile suggested a DiGeorge phenotype. In 5 cases, we could not separate the profile of the face from the adjacent placenta, and the physiognomy could not be visualized. Limbs: in the 5 fetuses in whom we attempted we could clearly visualize arms and legs, as well as hands and feet, and bone abnormalities could be excluded. Genitalia: genitalia could be clearly studied in all the fetuses, and major abnormalities like hypo and epispadias could be excluded in the males.

Conclusions: RT3D echo was feasible in all 9 fetuses, lengthening the examination time by only a few minutes. It adds a better understanding of spatial relations of the cardiac structures in malformed hearts. Furthermore, it permits a thorough examination of physiognomy, small parts and genitalia, identifying fetuses in whom a genetic syndrome is more likely to be present. The lack of a sculpting tool to permit separation of adjacent curved surfaces, like the placenta and the fetal face, and the long elaboration time are the major draw-back to routine clinical use.

General Paediatric Cardiology (see also

OP22–9–11)

P54

Biochemical markers and myocardial damages in the patients with Kawasaki disease

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Purpose: To investigate the relationship between biochemical markers and myocardial damages in chronic stage, some biochemical

markers and dual isotope single photon emission computed tomography (SPECT) and endomyocardial biopsy (EMB) were compared in the patients with Kawasaki disease (KD). Patients and method: They included 10 patients with giant coronary aneurysm (G-AN) and 20 patients with coronary artery lesions (CAL). Ages ranged 2 to 18 years. Selected biochemical markers in this study were high-sensitive C-reactive protein (hsCRP), myoglobin, Creatin Kinase MB (CK-MB), troponin T (TnT), heart-type fatty acid binding protein (H-FABP), ANP and BNP. These markers were sampled from coronary sinus and valsalva sinus of the aorta at cardiac catheterization. Histopathology of endomyocardial biopsy was evaluated with histomorphometric method by computer assistance. A defect score (DS) for SPECT images was interpreted as normal: 0, mildly decreased: 1, moderately or severely decreased: 2, complete defect: 3. the difference in DS between TL and BMIPP was defined as the mismatch score (MS).

Results: Myocardial changes on EMB at chronic stage showed various histopathological findings such as fibrosis, degeneration, disarray and inflammatory cell infiltration in the KD patients with CAL, including suggested chronic myocarditis. Accumulation of myelin bodies in the myocytes, disarray of myofibrils, vacuoles and microangiopathy were also found as ultrastructural changes.

TL/BMIPP discrepancy was found both in KD with G-AN and those with CAL. In the cases with TL/BMIPP discrepancy, ultrastructural changes revealed massive myelin bodies.

Conclusion: The incidence of abnormal values were found 22% in H-FABP, 30% in myoglobin, 30% in BNP and 9% in hsCRP. Myocardial changes in the patients with KD include fibrosis, hypertrophy of myocytes, degeneration of myocytes and postmyocarditic changes even in late stage. Discrepancy of dual SPECT image suggested that myocardial changes in long-standing Kawasaki disease might reflect not only myocardial ischemia but also disordered myocardial fatty acid metabolism following myocarditis. This finding suggests that a more severe chronic inflammatory process might play a role in the development of stenosis or obstruction of coronary artery disease and myocardial changes. Further studies are needed to investigate the role of biochemical markers in the view point of initiation and progression of CAL and myocardial damages.

P55

Clinical and genetic characteristics of Russian families with long QT syndrome

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The aim of this study was to determine phenotype-genotype correlations in families with LQTS, association between the localization of mutations and phenotype in these patients and to evaluate influence of age and gender on the probability of sudden death.

Methods and Results: 94 unrelated Russian families in which probands had prolonged QTc on ECG were clinically evaluated using family and medical histories, ECGs, Holter recordings, treadmill. We have tested 60 families with LQTS for mutation in 5 genes: KCNQ1 (exons 2,3,4,5,6,7,14), KCNH2 (exons 2,6,7,10), SCN5A (exons 17,26,28), KCNE1 and KCNE2 using PCR-SSCP analysis and then direct sequencing. Mutations were founded in 60% families: KCNQ1 in 45%, KCNH2 in 10%, SCN5A in 1,7%, KCNE1 in 1,7%. In 1 family were founded mutations in 2 genes. The occurrence of the LQTS among directly related family members was 71,9%. Patients with KCNQ1 mutations have an early age at the first syncope, but not patients with KCNH2 mutations ($6,3 \pm 4,7$ and $9,6 \pm 5,4$ years respectively, $P < 0,05$). In patients with KCNH2

mutations arrhythmic syncope often occurred in association with emotional and especially acoustic stimuli, in patients with KCNQ1 mutations with exercises the combination of exercises and emotional stress and especially swimming. The QTc was significantly prolonged during exercise in patients with KCNQ1 mutations but not in patients with KCNH2 mutations. Some HRV parameters were differences between patients with KCNQ1 and KCNH2 mutations. Phenotype was more severe in patients with 2 mutations. LQTS families with mutations in C-terminal region of KCNQ1 and KCNH2 had a milder phenotype. In childhood, the occurrence of SD was somewhat higher in male than female LQT1 family members. In adulthood (16-40 yrs), the occurrence of SD was higher in female than male with LQT2.

Conclusions: It has being discussed that the phenotype LQTS probably varies by and specific mutation, amount mutations (patients with 2 mutations have phenotype more severe) and gene (including a direct functional association between a polymorphism and a mutation in the gene). Age and gender have different genotype-specific modulating effects on the probability of sudden death in LQTS patients.

P56

Effects of body position on oxygen saturation and respiration in patients after the Fontan operation: platypnea and orthodeoxia

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Introduction: Platypnea-orthodeoxia is an uncommon syndrome characterized by dyspnea and deoxygenation accompanying a postural change to upright position from a recumbent one. It has been noted that this syndrome is associated with pulmonary arteriovenous fistulas, intra-atrial shunts and cardiac dysfunction. Although these problems are not rare in Fontan patients, there are few reports to address platypnea and orthodeoxia in this population. The aim of this study was to assess whether platypnea and orthodeoxia occur in Fontan patients.

Methods: We divided 14 Fontan patients into 2 groups: 8 patients who had pulmonary arteriovenous fistulas and/or intra-atrial shunts (group A) and 6 patients who had neither pulmonary arteriovenous fistulas nor intra-atrial shunts (group B). They were compared with 9 controls (group C). By applying ventilatory gas analysis and a pulse oximeter, arterial oxygen saturation, minute ventilation per body weight and ventilatory equivalent for carbon dioxide were measured in the supine and then sitting positions.

Results: In group A, 1 patient had platypnea and 3 patients had orthodeoxia (changes in the saturation from the supine to the sitting position were -4% to -7%) accompanied with slight hyperpnea. All of 4 had both pulmonary arteriovenous fistulas and intra-atrial shunts. Contrary, patients in group B had neither nor orthodeoxia. Group A showed the saturation was significantly lower and the minute ventilation was significantly higher in the sitting position than in the supine position ($p < 0.05$). The other groups showed no significant difference in the saturation or the minute ventilation between the 2 positions. All groups showed the ventilatory equivalent was significantly higher in the sitting position than in the supine position ($p < 0.05$ to 0.01).

Conclusion: We demonstrated platypnea and orthodeoxia in Fontan patients with pulmonary arteriovenous fistulas and intra-atrial shunts. We believe platypnea and orthodeoxia should be regarded as a complication in Fontan patients with pulmonary arteriovenous fistulas and/or intra-atrial shunts. Arterial oxygen saturation should be measured in both recumbent and upright positions in those patients.

P57

Is 24-hour Blood pressure associated with physical activity level in children with type 1 diabetes?

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Introduction: Hypertension is a common complication of type 1 diabetes mellitus (DM1) and may develop during childhood. Increased blood pressure (BP), especially during the night, is a strong predictor of early renal structural changes in DM1. The main purpose of this study was to measure ambulatory 24-hour BP in children and adolescents with DM1, and to evaluate its relationships with physical activity and aerobic capacity.

Methods: This cross-sectional study included 24 patients with DM1 and 24 matched healthy controls (age 11.3 ± 2.4 years). None of the patients with DM1 had microalbuminuria. We measured 24-hour systolic and diastolic BP and heart rate using a Diasys Integra[®] monitor, and calculated standard deviation scores (SDS) using reference values of the German Working Group on Pediatric Hypertension. We also assessed maximal aerobic capacity (peak VO_2) by a treadmill test; past 12-month physical activity by questionnaire; 7-day physical activity count by accelerometer; body composition by dual-energy x-ray absorptiometry; fasting blood lipid levels and diabetes control.

Results: Groups had similar gender, age, height, weight, body mass index, percentage of body fat, and pubertal stage. There were no significant differences between groups for mean 24-hour heart rate, past 12-month physical activity, 7-day activity count, peak VO_2 , or blood lipids levels. Children with diabetes had significantly higher mean 24-hour systolic and diastolic BP (+0.89 and +0.56 SDS, resp.), daytime diastolic BP (+0.52), and night-time systolic BP (+0.59) than healthy controls. In patients with DM1, night-time systolic BP was negatively correlated with physical activity ($r = -0.46$, $p < 0.05$), while night-time diastolic BP was positively correlated with duration of diabetes ($r = 0.51$, $p < 0.05$).

Conclusions: Our study confirmed that children and adolescents with DM1 have higher 24-hour BP compared to non-diabetic controls, and that it is associated with low physical activity and number of years since diagnosis. We conclude that children with this condition should be encouraged to participate in regular physical activities, to prevent the rise of night-time BP that usually precedes renal structural changes.

P58

Cardiac strangulation – a rare complication of permanent epicardial pacing

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Introduction: We present a rare complication of permanent epicardial pacing and its diagnosis with chest x-ray and angiocardiology.

Case Report: A male newborn had complex congenital heart disease with common atrium, ventricular septal defect, left atrial isomerism with polyspleny (Ivemark syndrome), bilateral superior vena cava without vena anomoma and hemiazygos continuation. Because of severe bradycardia due to absent sinus node and complete atrioventricular block the patient required temporary cardiac pacing for postnatal stabilization. At the age of three weeks he had surgical repair (atrial septation and vsd closure) and cardiac pacemaker implantation with a bipolar epicardial electrode on the right ventricle for permanent VVI pacing. After 8,2 years there were

signs of impending battery depletion and the patient was hospitalized for exchange of the pulse generator. The patient was acyanotic and had no complaints. Growth and body weight were on the third percentile for age and length, respectively. Performance of the pacing system was regular. Chest x-ray showed an atypical course of the pacing lead ascending left upward from the right ventricle, crossing the left ventricle and descending dorsally to the abdominal pacemaker pocket. Suspected cardiac strangulation could be clearly demonstrated by left heart angiocardiology. Compromise of the coronary arteries was excluded by arteriography. Impression of the left ventricle had been missed on two dimensional echocardiography although it could be clearly visualized. Consequently, the patient underwent removal of the pacer and the strangulating wire and implantation of a new epicardial dual chamber pacing system.

Discussion: Our case underlines the importance of the correct placement of the electrode in epicardial cardiac pacing and the assessment of growth related changes. If MRI is contraindicated due to permanent cardiac pacing, cardiac catheterization permits excellent visualization of the electrode's interaction with the cardiac chambers and the coronary arteries as well as its effects on cardiac performance.

P59

Increased natriuretic peptide type B after ventricular unloading in children with univentricular heart defects with right compared with left ventricular morphology

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Children with univentricular heart defects have systemic ventricles of either left (LV) or right ventricular (RV) morphology. A systemic ventricle with RV morphology is not designed to supply the systemic circulation and may therefore be more vulnerable to overload and dysfunction.

Aim: To evaluate plasma concentrations of BNP as marker of ventricular overload in children with univentricular heart defects with right compared with left ventricular morphology.

Methods: Blood samples for BNP were obtained during regular pre-operative investigations or out-patient check-ups. Ventricular function and AV-valve regurgitation were evaluated by echocardiography. Twenty-three children without heart disease aged two weeks to 8.3 years served as a control group for BNP measurements. The reference interval for BNP was 0–18.4 ng/L.

Results: Thirty-two children (19 boys, 13 girls), with univentricular heart defects were included. Ten children aged 0.5–0.9 years, (4 LV, 6 RV morphology) had undergone a first palliative operation (Stage I), 13 children aged 1.6–3.7 years (9 LV, 4 RV morphology) had undergone ventricular unloading by means of a bidirectional Glenn at 6 months of age (Stage II) and 9 children aged 5.2–13.6 years (7 LV, 2 RV morphology) had undergone a complete TCPC at 2–3 years of age (Stage III).

All children had normal ventricular function and no or trivial AV-valve regurgitation, on echocardiography.

The BNP levels were higher in the Stage I group: median 31.6 ng/L (8.3–122) than in the Stage II: 6.7 (0.0–16.0) Stage III: 9.0 (0.0–46.9) and control groups 4.7 (0.0–17.7) ($p = 0.0001$). In the Stage I group the BNP levels were similar in children with LV and RV morphology: 40.9 (19.8–122) and 31.6 (8.3–90.0) respectively ($p = 0.67$). BNP levels in the Stage II and III groups were higher in children with RV morphology than in children with LV morphology: 11.2 (9.6–16.0) and 5.0 (0.0–46.9) respectively ($p = 0.01$). No correlations were observed between the BNP levels and oxygen saturation or treatment with diuretics or ACE inhibitors.

Conclusion: In children with univentricular hearts BNP levels were higher in children with RV morphology after ventricular unloading. This may imply an increased risk for development of heart failure in children with systemic ventricles of RV morphology.

P60

Serum lipids including non-high density lipoprotein cholesterol levels in Turkish school-children 7 to 18 years of age

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Introduction: Cardiovascular diseases are the most common causes of death in adults in Turkey like worldwide. Dyslipidemia is an independent risk factor for atherosclerotic coronary diseases. Measurement of serum non-high density lipoprotein-cholesterol (non-HDL-C) level has been proposed for screening program because of non-HDL-C includes both cholesterol-rich and triglyceride-rich atherogenic apolipoprotein-B containing lipoproteins and the measurement do not require overnight fasting. The purpose of this study was to evaluate serum non-HDL-C levels and their relationship with other coronary risk factors in children. This study also aimed to provide the prevalence of dyslipidemia according to non-HDL-C levels in Turkish children.

Methods: A randomly selected 2896 school-children (1467 girls, 1429 boys) aged between 7–18 years, residing in urban and rural parts of Eskisehir, Turkey, were enrolled. Serum total cholesterol (TC), triglyceride (TG), high density lipoprotein-cholesterol (HDL-C) levels were analyzed. Serum low density, very low density and non-high density lipoprotein cholesterol (LDL-C, VLDL-C and non-HDL-C) levels were calculated.

Results: Serum non-HDL-C, TC and TG levels were higher in girls than boys especially in the 7–10 year-old age group. Serum TC and HDL-C levels were higher in urban area than rural area while serum TG levels were higher in rural area. No statistical difference was observed between urban and rural areas for serum non-HDL-C and LDL-C levels. In girls, serum non-HDL-C levels positively correlated with age and other lipid parameters except HDL-C levels which were inversely correlated. In boys, serum non-HDL-C levels correlated with the same parameters as girls and also correlated with total body fat percentage, weight, height and smoking. The prevalence of dyslipidemia according to serum non-HDL-C levels was higher (13.2%) in girls than boys (8.9%) ($p < 0.0001$). Dyslipidemia was most prevalent at 7–10 year-old girls (15.7%). The dyslipidemia prevalence according to non-HDL-C levels was similar with dyslipidemia prevalence according to serum LDL-C levels.

Conclusions: The prevalence of dyslipidemia in children is considerably common in our population. Non-HDL-C level is an appropriate tool for detecting dyslipidemia in childhood. Early detection of dyslipidemia and long-term prevention of atherosclerosis by controlling the risk factors including elevated non-HDL-C level, should begin in childhood.

P61

Williams–Beuren syndrome with obstruction of the left coronary ostium without supravalvular stenosis of the aorta leading to death

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Introduction: Williams–Beuren syndrome is a well known syndrome associated with vascular stenosis usually located at the level

of the pulmonary arteries and at the aortic supravalvular region. Cases of stenosis of the coronary arteries are described so as progressive stenosis of the coronary ostium as consequence of the progression of the aortic supravalvular stenosis. We describe the case of an infant with complete obstruction of the left coronary ostium without aortic supravalvular stenosis.

Case Report: A 9 month old boy was referred to our centre because of a dilated left cardiomyopathy. He was examined, for the first time at the age of 3 month, by paediatrics cardiologist, because of a systolic murmur. The investigation demonstrated severe peripheral pulmonary stenosis typical of Williams–Beuren syndrome, so as slight hypoplasia of the aortic arch without coarctation. The left ventricle (LV) showed a normal systolic function and both coronary arteries were visualised and depicted as normal. At 9 month, the echocardiography showed a severe left ventricular cardiomyopathy with an ejection fraction of 15%. At our institution we confirmed the founding of decreased LV function, the peripheral pulmonary stenosis and no aortic supravalvular stenosis, but founded that the flow in the left coronary artery was inverted. To insure the diagnosis of a possible aberrant left coronary artery, a cardiac catheterisation was decided. After the anaesthesia induction and intubation, with a drip of noradrenalin, severe dropping of the ST segment occurred. Rapidly ventricular arrhythmias began, with ventricular fibrillation and finally electromechanical dissociation. The CPR was immediately undertaken, with defibrillation and adrenaline. The CPR was stopped after 60 minutes. The autopsy demonstrated a complete absence of the left coronary ostium and a severe narrowing of the right coronary ostium, with severe endofibroelastosis of the left ventricle. The aortic supravalvular region was free of significant stenosis, but at microscopy showed a fibrosis of the wall of the aorta.

Conclusion: In Williams–Beuren infant a narrowing or complete obstruction of a coronary ostium could develop also without significant aortic supravalvular stenosis and then could be overlooked if no regular echocardiographic and ECG controls are established.

P62

Myopericarditis associated with Campylobacter jejuni infection: a case report

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Background: Campylobacter jejuni is the most commonly recognised cause of bacterial gastroenteritis worldwide. An association between Campylobacter jejuni and myocarditis has not been described in paediatric literature till today.

Case Report: A 16 year old white male presented with a 5 day history of diarrhea, headache and abdominal pain. At the day of admission he suffered from constant retrosternal pain associated with shortness of breathing. Laboratory investigations revealed normal blood counts and serum electrolytes. Troponin T was elevated to 1.7 ng/ml (reference range < 0.1), creatin kinase was 1432 U/L (reference range < 170) and CK-MB was 141 U/L (reference range < 24). C-reactive protein was elevated to 132 mg/L (reference range < 8). Electrocardiogram showed a significant ST-elevation in the lateral leads. Transthoracic echocardiography revealed a moderately reduced left ventricular function. Based upon clinical presentation and laboratory results the diagnosis of myopericarditis was made. Campylobacter jejuni was isolated from stool cultures; antibodies against Campylobacter jejuni were detected in blood using complement-binding reaction. For this

reason clarythromycin was initiated at a dose of 500 mg twice daily perorally. Stool cultures were negative for other bacterial or viral agents such as salmonella, shigella and yersinia, rota virus and adenovirus. Serological testing revealed no evidence for infection with cardiotropic viruses. Enteric and Norovirus infection was ruled out by polymerase chain reaction. Soon after the initiation of antibiotic therapy the patients' clinical condition improved significantly, intermittently bloody diarrhea persisted for 48 hours. Laboratory tests, electrocardiogram and echocardiogram normalised during the 7 day hospital stay. The patient was discharged from the hospital in excellent condition.

Conclusion: Myopericarditis is a rare but severe complication of *Campylobacter jejuni* infection. It should be considered as a diagnosis in patients presenting with diarrhea and chest pain or elevated cardiac enzymes.

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Limited autopsy rate in pediatric patients with cardiac diseases

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Introduction: It is well known that autopsies can result in unexpected findings in a significant number of patients, even when there was no doubt about the cause of death. Most patients in a pediatric cardiology department are well known patients, and it is hypothesized that unexpected findings at autopsy are relatively infrequent.

Methods: Retrospective review of all patients that died before the age of 18 years during a 7-year period from February 1996 until March 2003. Included were all patients below the age of 18 years that had a cardiac abnormality, either congenital or acquired, as main diagnosis.

Results: The population during the 7-year period consisted of 5600 patients being followed. A total of 1470 operations were performed. Of the total number of patients 48 died within 30 days of operation (3.2%). During the 7-year period 189 patients died. In 38/189 patients, the parents or legal guardians consented in autopsy (20%). Main diagnoses were hypoplastic left heart syndrome (N = 10), tricuspid atresia (N = 3), pulmonary atresia (N = 4), transposition of the great arteries (N = 2), cardiomyopathy (N = 5), primary pulmonary hypertension (N = 2), and different other monoventricular and biventricular cardiac anomalies. In 20 patients the autopsy results were completely similar to the findings as suspected before death. In the other 18 patients there were new or unexpected findings, which partly might have influenced therapy. This included thrombotic occlusion of a Blalock Taussig shunt (N = 3) or Glenn shunt (N = 1), pulmonary bleeding (N = 1) or bronchopneumonia (N = 3), abnormal anatomy of the coronary arteries (N = 3), partial abnormal pulmonary venous drainage (N = 2), and significant abnormalities of the central nervous system (N = 2).

Conclusions: Even in closely monitored pediatric cardiac patients autopsies led to new findings in a considerable percentage. In our series substantial discrepancies exist between clinical diagnoses and findings at autopsy. However, we found a low number of only 20% autopsies performed. Since the substantial number of new findings at autopsy underscores the fact that autopsy may be used as a tool for quality management to analyze diagnostic discrepancies all efforts should be undertaken to increase the number of autopsies in the field of pediatric cardiology.

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Cardiac involvement in the mucopolysaccharidoses – retrospective analysis

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The mucopolysaccharidoses (MPS) are lipid storage diseases, secondary to a deficiency of the enzymes necessary for glycoaminoglycans (GAG's) metabolism.

It has various systemic manifestations, including cardiac involvement. The cardiac complications are progressive and may be the cause of death. Rarely patients present with acute cardiomyopathy or fibroelastosis in the first year of life. The valvular lesions result from GAG's deposits and affect all of the cardiac valves and can lead to cardiac failure. Coronary ostia thickening manifests as angina or myocardial infarction. Tricuspid and pulmonary valvular insufficiency are worsened by the pulmonary hypertension secondary to chronic hypoxia, which results from airway obstruction and lung disease.

The authors carried out a retrospective analysis of 23 patients with MPS followed up at Coimbra's Paediatric Hospital, including sex distribution; MPS type; age at first and last echocardiogram and respective findings; therapeutic options and mortality.

The results obtained were as follows: 11 boys and 12 girls with the following MPS types; type I (6); type II (2); type III (7); type IV (2); type VI (5) and type VII (1). Of the 20 patients that had echocardiograms, 17 had underlying changes, namely, mitral and aortic pathological changes in 12 and 11 patients respectively, left ventricular hypertrophy in 11 patients and pulmonary hypertension in 8 patients. Seven patients died. At present 5 patients are medicated.

The findings are consistent with those in the medical literature. Echocardiography is a sensitive method for the diagnosis and follow up of the cardiac anomalies associated with this pathology. An annual echocardiogram is recommended to exclude valvular anomalies, cardiomyopathy, cor pulmonale and cardiac failure.

P65

Idebenone treatment for Friedreich's ataxia: a three years open trial

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Purpose: Friedreich ataxia (FA) is associated with a progressive hypertrophic cardiomyopathy. Idebenone, a free radical scavenger, has been shown to produce an improvement in myocardial function and a reduction in left ventricular mass index (LVMI) after one year of therapy in patients with FA. The long-term effects remain to be described. We aimed at determining whether the beneficial effect of Idebenone on myocardial function and the regression in LVMI persisted over a three years period.

Methods: LVMI was calculated. Myocardial function was assessed measuring longitudinal peak systolic strain and strain rate at the basal, mid and apical segments of the interventricular septum and LV lateral wall in seven FA patients with hypertrophic cardiomyopathy and normal fractional shortening (age: 8.5–27.6 years). They were studied at baseline, at 12 months, at 24 months and at 36 months after starting with Idebenone (5 mg/kg/day).

Results: Table. There was a reduction in LVMI after one year of therapy, which remained virtually unchanged after three years. An

improvement in myocardial function at 12 and 24 months was seen. Nevertheless, deterioration was noticed at 36 months.

Table. Results.

	Peak systolic strain rate	Peak systolic strain	LVMI
Baseline	-1.02 ± 0.21	-12.3 ± 3.4	127.8 ± 28.6
12 months	-1.50 ± 0.51*	-18.4 ± 5.2*	110.3 ± 26.3*
24 months	-1.38 ± 0.31*	-17.3 ± 4.4*	111.3 ± 29.2*
36 months	-1.10 ± 0.16 ^{§,†}	-14.3 ± 3.7 ^{§,†}	116.1 ± 28.0

*p < 0.05 vs. Baseline; [§]p < 0.05 vs. 12 months; [†]p < 0.05 vs. 24 months.

Conclusions: The beneficial effect on myocardial function seems not to be sustained beyond two years of therapy. On the other hand, LVMI decreases and remain unchanged throughout the three years follow-up. These findings could be explained by a higher sensitivity of deformation indices (strain and strain rate), to detect subtle changes in myocardial function.

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Long term outcome after the Fontan-type operations

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The purpose of the study was to assess a long term outcome of the patients who underwent Fontan operation for functional univentricular physiology and to determine the quality of life.

We analysed retrospectively the data of 34 children, present age 4 to 23 years (mean 12,8), who underwent Fontan operation between 1988–2000 (age at the operation ranged from 12 months to 15 years, mean 6 years). 23 children underwent different palliative procedures prior to Fontan-type operations. Altogether 26 children underwent the complete Fontan procedure. Follow-up ranges from 3 to 20 years (mean 8 years).

Results: 5 (15%) patients died in the follow-up. Actual survival at 5, 10 and 15 years after surgery is 87%, 87% and 84% respectively. Capillary oxygen saturation ranges from 89–92% at rest, 10 children have got hepatomegaly. On x-ray a heart silhouette was enlarged (CI > 0,6) in 18 from 34 pts. Arrhythmias were present in 19 (56%) children. Transient sinus bradycardia was registered in 12. 4 patients (pts) had supraventricular tachycardia, 2 others atrial flutter/fibrillation all had to undergo medical antiarrhythmic treatments. 3 children on Holter-ekg had a premature monomorphic ventricular ectopy. On echo examination 12 pts have a significantly enlarged right atrium and in 17 of them the shape (geometry) of hemodynamic single ventricle is changed with the significant dysfunction in 3. Diagnostic cardiac catheterisations were performed in 10 pts, in 4 of them cardiological interventional procedures were conducted. The NYHA class was assessed during the final examination and most (25/29) pts were assigned to class I, and 4 to class III. 4 of our pts are employed, 19 attend school (four have got individual school lessons), 4 are on disability payment because of cardiological state and 3 others are in pre-school age. On the basis of the history data 19 follow-up pts have moderate daily/sports activity (it means: exercise 1–4 days/week).

Conclusion: The correlation between the results of the medical studies and the self-perceived state of health is very complex and further multi-centric investigation is required for our better understanding of the quality of life after congenital heart defects operations.

P67

Diagnostic value of contemporary myocard biopate analysis on the diagram of diagnostic flow in primary cardiomyopathies in children

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Introduction: The purpose of this study was to show the importance of myocard biopate analysis using different methods in the flow diagram for diagnosis of primary cardiomyopathies in children.

Methods: In the clinical evaluation of the types of cardiomyopathies we followed the guidelines of the Task Forces on Cardiomyopathies of the WHO/ISFC. The specimens were analysed by light microscope (Dallas criteria) in all patients (pts), 13 by immunofluorescence, 8 by immunohistochemical method, 7 by electron microscope, and 5 by PCR method where DNA and RNA of cardiomyopathic viruses was used.

Results: We identified 121 children (50 females and 71 males) as having cardiomyopathy, giving an average occurrence for all of 3,881 for each 10,000 patients examined in our outpatient clinics. The dilated cardiomyopathy (DCM) was indentified in 52 pts (42.9%), hypertrophic cardiomyopathy (HCM) in 43 pts (35.5%) and restrictive cardiomyopathy (RCM) in 6 pts (4.8%). We placed 11 pts (9.0%) in the group of specific cardiomyopathies. In 9 pts (7.4%), it was impossible to classify the cardiomyopathy. Most of those with DCM had been diagnosed prior to the age of 3 years (RR 1.9, 95% CI 1.4–2.47). There were no statistically significant differences in the incidences of DCM as compared to HCM (Z 0.923, p < 0.1779), but we encountered a significantly lower occurrence of RCM (Z 6.044, p < 0.001). The biopsy of endocard and myocard was done to confirm the etiology of primary cardiomyopathy in 22 pts, 12 males and 10 females age 1 to 17 (average age 9.5 yr). Out of 10 pts with DCM, 4 pts had myonecrosis as a consequence of acute myocarditis and 6 showed signs of late inflammatory processes, as a consequence of chronic immunologic myocarditis. In 4 of them rebiopsy proved complete healing. In 5 pts with HCM the diagnosis was confirmed histologically. Out of 4 pts with RCM due to inflammation, in 3 pathohistological findings proved diagnosis and in one showed primary amiloidosis. In one patient pathohistological finding showed fibroelastosis, in one heart tumor (fibroma).

Conclusion: The comprehensive analysis of myocard biopate is essential in favour for further treatment of patients with cardiomyopathies.

P68

Atrial Natriuretic Peptide (ANP) and B-Type Natriuretic Peptide (BNP) in children with congenital heart disease after cardiac surgery

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Introduction: Children with congenital heart defects suffer from severe overload of the heart muscle. After surgical correction cardiac overload connected with a so called stable heart insufficiency often remains. Atrial Natriuretic Peptide (ANP) and B-Type Natriuretic Peptide (BNP) are useful markers to diagnose congestive heart failure in adult patients. However, there is no detailed knowledge about plasma ANP/-BNP and their gene expression in the heart muscle of children suffering from congenital heart defects. No data exist at which postoperative time the myocardium adapts to the corrected blood flow.

Methods: In this prospective study blood samples were taken from 73 children (age: mean 22 months) at the day before cardiac surgery and at discharge from the intensive care unit (median: 11th day after operation). Plasma ANP and BNP levels were determined by an immunoradiometric assay and correlated with clinical symptoms of heart failure. Gene expression of the natriuretic peptides was measured quantitatively by TaqMan-PCR in heart muscles specimens from 38 children.

Results: Compared to normal values ANP and BNP levels were increased in all children with congenital heart defects prior to surgical intervention. There was no significant correlation between preoperative ANP or BNP values and clinical symptoms of heart failure. Compared to preoperative values ANP and BNP levels remained high in all groups even weeks after surgical intervention despite of improved clinical condition. The difference between pre- and postoperative values was not significant. However, the correlation between preoperative plasma ANP and BNP values was highly significant, likewise the correlation between postoperative plasma ANP and BNP values. There was a significant correlation between mRNA-ANP and mRNA-BNP and also between TATA-mRNA-BNP-Ratio in the right atrium and preoperative BNP-values. No correlation was found between gene expression and the clinical score of heart insufficiency.

Conclusion: We conclude that in infancy natriuretic peptides are more sensitive parameters in the diagnosis of myocardial overload/insufficiency than clinical scores. Our results support further the hypothesis that the adaptation of the heart to the new pressure and blood flow conditions needs months to years even after a successful operation.

P69

Long term follow up cardiac abnormalities in female adolescents with anorexia nervosa

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Objectives: Anorexia nervosa (AN) is a life-threatening eating disorder, with significant risk for sudden death due to severe cardiac complications. The aim of this prospective study was to evaluate the cardiac abnormalities in female adolescents with anorexia nervosa and to examine the long term results and reversibility of the detected cardiac abnormalities.

Methods: We prospectively studied eleven female adolescents (13,5–17 years old) with AN diagnosed according to DSM IV criteria. On admission they were all on a weight-losing course with the mean body mass index (BMI) of $13,71 \pm 1,54$ (11,38–17,05) kg/m². The mean follow up duration was $2,45 \pm 1,17$ (1–4,5) years. All the patients reached normal weight after treatment. The control group was composed of 12 healthy, age matched, of normal weight adolescent girls. The patients with AN and control group underwent a complete clinical examination, electrocardiographic and echocardiographic evaluations. These evaluations were repeated at the last visit of completely cured AN patients, at least one year later from the recovery.

Results: Patients with AN had lower heart rate and blood pressure than control group and these were increased to normal levels found in control group after refeeding. QT and QTc were significantly longer and R waves amplitude in V6 were significantly lower in the patients with AN than in the control group. QT and QTc dispersions were significantly greater in AN patients compared to

control group. Left ventricular mass (LVM) and LVM index (LVMI) was significantly lower in AN group. At least one year after recovery, there was a significant decrease in QT, QTc, QTd, QTcd. Although in AN patients, R wave amplitudes in V6 increased in control ECGs; they did not reach to the levels found in control group. Control echocardiograms of AN patients showed an increase in LV diameters and cardiac mass. There was a strong negative correlation between LVM and QT dispersion.

Conclusions: The adolescent girls with AN had significant structural and functional cardiac abnormalities in comparison to control group. All these abnormalities were reversible except low R wave amplitude in V6.

Adolescent and Adult Congenital Heart Disease (see also OP22-12, OP23-1)

P70

Ebstein anomaly: cardiopulmonary exercise test in the evaluation of exercise capacity and degree of echocardiographic index of progression of this malformation

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Introduction: Ebstein anomaly is characterized by displacement of part of tricuspid ring in the direction of apex of the heart and inappropriate attachment of valvular cusps resulting in significant decrease in right ventricular function and tricuspid regurgitation.

Aim of the Study: Estimation of physical capacity measured with spiroergometry in adult patients with Ebstein syndrome and its possible correlation with echocardiographic index of anatomical progression of the malformation.

Material and Method: Twenty patients were studied aged 24 to 63 years (mean 40,3 years). Control group consisted of 19 healthy persons aged 22 to 61 years (mean 39,9). Echocardiographic examination: Index of progression of Ebstein's/EGE/malformation was calculated – quotient of right ventricular area and atrialized right ventricle and sum of right and left ventricular area and left atrium. Following degrees of progression of the malformation/EGE/were set: I < 0,5, II: 0,5–0,9, III: 1,0–1,49, IV > 1,5. Maximal physical effort was measured on moving track according to modified Bruce's protocol, resting spirometry measured FVC, VE, FEV1 and peak VO₂. VE/VCO₂ slope index was analyzed.

Results: Following parameters in the studied group were decreased compared to control group: VO₂ max – $21,9 \pm 5,4$ ml/kg/min vs $33,6 \pm 8,3$ p = 0,00001, peak VO₂ w 1/min – $1,7 \pm 0,6$ vs $2,5 \pm 0,9$ p = 0,002, maximal heart rate at the peak of exercise – HR max $158,0 \pm 18,9$ beats per minute vs $177,7 \pm 15,4$ p = 0,001, systolic pressure at peak of exercise – $145,7 \pm 14,4$ mmHg vs $171,1 \pm 23,3$ p = 0,0003, VE – $71,3 \pm 17,01$ /min vs $93,8 \pm 37,1$ p = 0,02, VE/VCO₂ slope, was higher than in control group ($40,1 \pm 8,1$ vs $26,9 \pm 3,6$) (p = 0,00001). In 75% of studied patients exceeded 34.

Parameters of pulmonary function – FVC $4,5 \pm 1,0$ vs $4,6 \pm 1,1$. FEV1 – $3,5 \pm 0,6$ vs $3,6 \pm 0,9$ l, did not differ between groups. Number of patients in each EGE group: I-0, II-9, III-6, IV-5 patients. VO₂ (ml/kg/min) in group II $24,5 \pm 3,9$ were higher than in III $17,2 \pm 5,2$, p = 0,007 and IV $22,9 \pm 4,7$, p = 0,05. HR max in group II $169,1 \pm 12,5$ bpm was higher than in IV $146,6 \pm 20,5$, p = 0,03 and III: $150,8 \pm 19,0$, p = 0,05.

Conclusions:

1. Physical capacity among adult patients with Ebstein syndrome is significantly decreased.
2. Physical capacity in this group decreases with degree of echocardiographic progression of the malformation.

P71**Liver dysfunction after Fontan operation**

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Objectives: The Fontan status shows during the follow-up an ongoing decline of cardiovascular and extracardiac functions. Aim of our study was to evaluate indexes of liver function in Fontan patients and their correlation to anatomy, type of intervention and hemodynamic status. **Method:** We evaluated PE, ECG, 2D-Doppler Echocardiography, 24 hrs Holter monitoring, 2D-Doppler liver Ultrasound, and the following blood tests: full blood count, AST, ALT, gammaGT, bilirubin, protein profile, ALP, LAD, PT, PTT, Factor 5, and faecal alfa1 antitrypsin content. A liver disease score (LDS) based on the presence and degree of liver enlargement, abnormal liver function tests and ultrasound parameters (0 = normal value, 1 = mild alteration, 2 = marked alteration, range 0–12) was used, and correlated to the anatomy, type of surgery and hemodynamic data.

Results: 34 patients (20 males) were enrolled in the study. Mean age at operation was 3,2 yr. (0,9–14,4), at evaluation 14,7 yr. (4,1–26,7), mean follow-up 11,5 yr. (1,7–23,3). Seventeen were affected by TA, 5 by HLHS, 4 by PA+IVS, 2 by unbalanced DORV, 2 by Holmes heart, and 4 by miscellaneous lesions. An atriopulmonary anastomosis was performed in 8, a total cavo-pulmonary anastomosis in 26. Thirty were in NYHA functional class I/II, 4 in class III. None of the patients had a LDS score = 0 (completely normal liver function), 4 being the mean score of the group (range 1–9), main alterations regarding gammaGT, bilirubin, clotting profile, and portal Doppler pulsatility index. Faecal alfa1 antitrypsin content was elevated in 4 patients (12%) 2 of whom with marked hypoalbuminemia. No correlation was found between LDS and anatomy and type of operation. Length of follow-up correlated with alterations of liver enzymes and of clotting profile. A significant inverse correlation was found between heart rate and LDS ($p = 0,038$) and cardiac index and LDS ($p = 0,02$).

Conclusions: Liver dysfunction seems to be the rule in Fontan patients. The longer the follow-up the more pronounced the hepatopathy, and mainly dependent from the cardiac index, which, in this physiology, is strictly related to the heart rate. Therefore, surgical techniques preserving the sinus node function and warranting higher heart rate are recommendable.

P72**Cardiac autonomic dysfunction is prognostically adverse in adult patients with congenital cardiac disease**

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Background: Cardiac autonomic dysfunction is prognostically adverse in a variety of cardiovascular cohorts, but its prognostic implications in

adult patients with congenital cardiac disease (CCD) are unknown. The objective of the current study was to assess the prognostic value of heart rate turbulence (HRT) and heart rate variability (HRV) in this cohort.

Methods: 43 patients with CCD, aged 13–72 years, were included in this prospective clinical study. Parameters of HRT (Turbulence onset = TO, Turbulence slope = TS) and HRV (standard deviation of all normal-to-normal intervals = SDNN, standard deviation of mean values for all normal-to-normal intervals over 5 minutes = SDANN, square root of the mean square differences of successive RR intervals = RMSSD and HRVTI = HRV triangular index) were calculated from a Holter-ECG. In addition serum brain natriuretic peptide (BNP) was measured and clinical functional class was determined. A combined endpoint of all cause mortality or cardiac arrest was used.

Results: During follow-up (27 ± 9 months) 5 patients died and another 2 were successfully resuscitated. Patients who died or were resuscitated had significantly higher values for BNP (997.7 ± 227.4 vs. 111.3 ± 237.2 pg/ml, $p \leq 0.001$) and TO (0.007 ± 0.008 vs. -0.018 ± 0.035 , $p = 0.002$) as well as significantly lower values for TS (1.6 ± 1.0 vs. 9.7 ± 8.7 , $p < 0.001$), SDNN (61.7 ± 31.6 vs. 154.3 ± 82.2 , $p < 0.001$), SDANN (44.4 ± 26.1 vs. 140.8 ± 82.2 , $p < 0.001$), RMSSD (18.8 ± 9.6 vs. 34.8 ± 19.0 , $p = 0.021$) and HRVTI (13.1 ± 6.1 vs. 38.5 ± 20.4 , $p < 0.001$) compared with event-free survivors. On univariate analysis, BNP value ($p = 0.002$), uric acid ($p = 0.0045$), cortisol ($p = 0.0003$), TS ($p = 0.0135$), SDNN ($p = 0.004$), SDANN ($p = 0.005$), HRVTI ($p = 0.009$), abnormal TO or TS ($p = 0.007$, $p = 0.002$) as well as abnormal TO and TS ($p = 0.0001$) were associated with impaired prognosis. On multivariate analysis abnormal TO and TS was found to be the strongest independent risk stratifier (HR 61.5, $p < 0.001$).

Conclusion: Our data indicate that HRT and HRV predict survival in unselected CCD patients with various diagnoses. In addition, our results suggest that HRT may even be a stronger prognostic predictor than established markers of cardiac autonomic dysfunction like HRV. The combined use of HRT, HRV and markers of neurohormonal activation like BNP may further improve the prognostic value and warrants further investigation.

P73**Effects of aerobic exercise training after the Fontan operation: comparison between children and adult patients**

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Objective: It has been recently documented in the literature the positive effect of aerobic training on exercise performance in children after the Fontan operation (Am J Cardiol 2005; 95(1): 150–2). The aim of our study was to investigate whether the same beneficial result can be achieved in adult patients.

Method: Ten patients, $8,9 \pm 2$ years old (F1) and 15 patients, $19,5 \pm 4,1$ years old (F2), respectively 4 to 11 and 13 to 21 years after the Fontan operation, were evaluated with a cardiopulmonary maximal exercise test before and after an exercise training program. The exercise training lasted for 8 (F1) and 5 months (F2) respectively, with 10 group teaching sessions followed by individual training at home twice a week for 30–45 minutes. A wristband heart rate monitor, set with a specific target heart rate range, was used to control the intensity of exercise. The exercise program

was characterized by aerobic training with an exercise level between 50–70% of maximal oxygen consumption. Results Only 4 F2 pts, and all 10 F1 pts completed the exercise training program, all with no adverse events. In F1 group the training resulted in an improvement in oxygen consumption, as measured by Mets ($p = 0,03$) and maximal oxygen consumption ml/min ($p = 0,001$), a decrease of the heart rate curve ($p = 0,009$) and an increase of the oxygen pulse curve during submaximal exercise ($p = 0,0001$). Exercise duration and maximum heart rate did not change significantly. In F2 group exercise duration increased from 578 to 659 sec ($p = 0,032$), maximal heart rate increased from 168 to 181 bpm ($p = 0,10$), Mets increased from 13,45 to 15,13 ($p = 0,07$), while the maximal oxygen consumption, the heart rate and oxygen pulse curves during submaximal exercise did not change significantly.

Conclusion: We can conclude the compliance to the exercise program was good in F1 group but very poor in the adults. Furthermore, while in children the training resulted in an improvement of the aerobic capacity, in F2 group only the performance parameters improved, while the parameters of cardiovascular function did not change.

P74

Procreation and pregnancy in patients with congenital heart diseases

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The improvement in the treatment of the congenital heart defects (CHD) prolongs the survival time and it gives rise to the perspectives of better quality of life. Increase of the population of women in the age of procreation and accompanying problems became the inspiration to the trials, which aimed at testing the influence of the defect on procreation and the pregnancy in patients with CHD.

We analysed retrospectively 98 pregnancies of 46 women with CHD and compared the results with the demographic data.

The frequency and the type of the CHD were as follow: ASD – 35%, ToF – 17,5%, VSD – 13%, AS – 11% and others – 24%. The surgical or interventional treatment were performed in 56%, the next 44% were untreated.

The level of education of the patients with CHD was significantly higher than average. 33% were active at work, 34% had disability payment, 33% were unemployed.

15 pregnancies have been terminated by abortion. 78% of deliveries have been on time. Vaginal births were conducted in 76% of deliveries and cesarean section in 22% (10 of them not from the cardiological reasons). 36% of the pregnancies were accounted for the high risk pregnancies. 85 children were born and 46% of them underwent the cardiological consultation. The fertility was 1,82. The women with ToF, AS and VSD have got the lowest fertility but others with ASD II have got 2,5 which exceed the demographic data.

Conclusions:

1. The patients with CHD have higher education level than the average.
2. 33% of them are active at work.
3. There is no difference in the fertility of our group to compare with the demographic data.
4. There is still low rate of the cardiological consultations of the newborns of the mother with CHD.
5. The kind of the congenital heart defect is the main factor which influence the fertility, course of the pregnancy and the way of the delivery.

The women with CHD might be pregnant, but the pregnancy may be associate with a few serious problems and because of that it requires a very special medical care.

P75

Adult patients with congenital heart disease – supraventricular arrhythmias

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Nowadays most patients (P) with congenital heart diseases (CHD) reach adulthood. In some cases complications such as supraventricular arrhythmias emerge.

The aim of the study was estimation of frequency of supraventricular arrhythmias among adult patients with CHD. Group of 1327 patients was analyzed, aged 18–27 years (mean $29,3 \pm 10,4$). In this group 26 different types of congenital heart diseases were diagnosed. Patients were under control of Congenital Heart Diseases Outpatients Clinic for Adults at Ist Cardiology Clinic, Medical University in Poznan since 1993 till 2004. Presence of significant arrhythmias was diagnosed using ECG examination during visit in the outpatients clinic, regional hospital, family doctor's office or Holter examination. Significant supraventricular arrhythmias (SVE) included nonsustained supraventricular tachycardia (at least 5 QRS complexes with frequency above 100/min) or atrial flutter/fibrillation (FA/FLA) according to common criteria.

FA/FLA and SVE were observed altogether in 96P (7,2% of studied population). FA/FLA in 33P (2,5% of all P) and SVE in 63P (4,7% of all P). Supraventricular arrhythmias were present most often in patients with: Ebstein syndrome – 45% of population (mean age 41yr), DTGA – 35,2% P (22,0 yr), DORV – 30% P (23,0 yr), LTGA – 25% P (23,5 yr), Tricuspid art. – 22,2% P (26,9 yr), ASDI 15,7% P (25,3 yr), ToF – 13,6% P (28,8 yr), CoAo – 7,5% P (46,3 yr) (complex anomalies). Less frequently in ASD – 7,1% P (44,7 yr), VSD – 6,9% P (26,8 yr), CNSZP – 7% (32,1 yr) (simple anomalies). Supraventricular arrhythmias were present more often ($p = 0,008$) among not operated P: 4,9% vs 9,0%. Mean age of patients with supraventricular arrhythmias was $32,3 \pm 12,0$ years. P with supraventricular arrhythmias were older compared to those without arrhythmias. Mean age for FA/FLA was $46,7 \pm 15,3$ vs $29,2 \pm 10,1$ years ($p = 0,00001$), and for SVA – $35,3 \pm 13,2$ vs $29,0 \pm 10,3$ years ($p = 0,00001$).

1. Supraventricular arrhythmias consist a common clinical complication among adult patients with congenital heart diseases.
2. Significant supraventricular arrhythmia is present most often in patients with more complex heart anomalies, older patients and those not operated in the past.

P76

Fontan operation – a bridge to transplantation? twenty-five years experience with the Fontan procedure

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Introduction: Since the Fontan operation was introduced in 1971, the technique and its modifications have been applied in most

patients with a functionally single ventricle. The first Fontan operation in Göteborg was performed in 1980. Between 1980 and 1988 another 13 patients were operated upon with the atriopulmonary connection. The first total cavo pulmonary connection was performed in 1988. Up to the end of 2004, 146 patients have been operated upon with the Fontan procedure at our institution with a total survival rate of 90%. The extracardiac conduit was introduced at the end of 1998 and since then all patients have been treated with this technique.

Results: The 30 days mortality was 4%. Eight patients (5%) have died later. The causes of these deaths were protein-losing enteropathy (PLE) three years after surgery in one patient. Malignant arrhythmias in one patient and in combination with PLE in two cases, 23, 21 and 22 years after surgery, respectively. Massive thrombus formation in the extracardiac conduit and pulmonary arteries three months after surgery was the cause of death in one patient. One teenage girl died three months postoperatively due to multiorgan failure. One boy died in a traffic accident three years after surgery. Another boy was operated upon with the lateral tunnel technique in 1995. He developed PLE and cardiac failure and was therefore heart transplanted in 1998 with a total resolution of the PLE. Unfortunately, he died due to acute rejection 4 years later. One girl, operated upon with the atriopulmonary connection in 1985, developed hepatic cell cancer and died in 2004. She had been infected with Hepatitis C at the operation. Another now 21 year old male, operated in 1988 developed severe cyanosis due to intrapulmonary arteriovenous malformations and was heart transplanted successfully in 2003.

Conclusion: The three-staged Fontan procedure is the "Golden standard" all over the world with good immediate surgical results and good quality of life during childhood and young age. The morbidity and mortality still progresses with time and perhaps will the Fontan procedure in the future be a bridge to transplantation.

P77

The left atrial function in patients after corrective surgery of left sided congenital heart defects.

A tissue Doppler study

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Background: Left atrium (LA) plays an important role for compensating hemodynamics when left ventricular (LV) abnormal relaxation exists through the aging process. Patients with left sided congenital heart defects (CHD) and LV volume and/or pressure overload frequently suffered from abnormal postoperative LV relaxation and contraction. Whether the LA in this group of patients keeps the ability of compensation is unclear.

Methods: Twenty patients with postoperative left sided CHD, thirty age matched normal controls, 15 aged subjects (mean age 53 ± 10 years vs 26 ± 14 years in normal controls, $p < 0.001$) were included. LA deviation in late diastole (LAdev) was derived from mitral flow Doppler profile: $A \text{ VTI} / (E \text{ VTI} + A \text{ VTI})$. Mitral annular systolic (S'), early diastolic (E') and late diastolic (A') peaks of motion at the LV lateral wall were measured by tissue Doppler imaging.

Results: There were significant reduction of E' ($p < 0.001$) and significant elevation of A' ($p = 0.009$) and LAdev ($p = 0.002$) in the aged group when compared to the normal control group. In patients after corrective surgery of left sided CHD the S' ($p = 0.01$), E' ($p = 0.008$) at LV lateral wall were significantly reduced while there was no significant difference in A' when

compared to the control group. The LAdev in patients with postoperative left sided CHD was significantly lower than that in normal group ($p = 0.022$).

Conclusion: Abnormal LA function measured with tissue Doppler imaging may contribute to the lower compensatory performance of abnormal LV relaxation after corrective surgery of left sided CHD.

P78

Plasma concentration of brain natriuretic peptide is correlated to subjective and objective Quality of Life in adolescents with congestive heart failure due to congenital heart defects

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Objective: To investigate the relationship of the plasma concentration of BNP to parameters of congestive heart failure (CHF) other than hemodynamic measures.

Methods: Comparison of BNP plasma concentration with parameters of spirometry (peak VO_2) and Quality of Life (QoL) questionnaire in 24 adolescents (14–18 years) with stable CHF (NYHA I–III) due to various congenital heart defects. Plasma concentrations of BNP were measured with TRIAGE[®] from Biosite. Quality of Life was measured with the validated Quality of Life questionnaire SF 36. Maximal oxygen uptake (peak VO_2) was measured in those 20 children who were able to carry out spirometry with a stationary spirometric device.

Results: Mean BNP plasma concentration in the 24 adolescents with CHF was 213 (8–1100) fmol/ml. Mean total score of SF 36 in all patients was 57,4 (34–82) points. Mean peak VO_2 was 18,2 (12–23) ml/min/kg in 20 patients. There was a negative correlation of the SF36 total score to the BNP plasma concentration ($r = -0,89$; $p < 0,05$; $n = 22$) and a negative correlation to peak VO_2 ($r = -0,72$; $p < 0,05$; $n = 20$). The BNP plasma concentration was also negative correlated to peak VO_2 ($r = -0,65$; $p < 0,05$; $n = 20$).

Conclusions: The BNP plasma concentrations were correlated to a broad range of both subjective and objective parameters of Quality of Life. If BNP levels are also related to prognosis remains to be determined and requires a broader database. Nevertheless, this easily applicable bloodtest should be part of the assessment of all paediatric patients with CHF.

P79

Sudden death in athletes occurs also in the under 18 population: reducing risk by pre-participation screening

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Sudden death (SD) of athletes <35 years, engaged in competitive sports is a well-known and much feared occurrence. The incidence of SD is higher in athletes (~2/100000/year) than in non-athletes (RR 2,5:1), the cause is cardiovascular in over 90%. To prevent sudden cardiac deaths (SCD), athletes are submitted to varying pre-participation screening protocols (PPSP). This study

reports on SCD in sport in the medical literature and aimed at achieving a generally acceptable PPSP endorsed by the consensus meeting (CM) of, and recommended by the IOC.

A systematic review of the literature identified causes of SCD, gender, age, underlying cardiac disease and type of sport and examining PPSP's in use. Methods necessary to detect pre-existing cardiac abnormalities were discussed to formulate a plan for a feasible and safe PPSP for the CM of the IOC (http://www.olympic.org/uk/organisation/commissions/medical/full_story_uk.asp?id=1182).

SCD occurred in 1101(1966–2004) reported cases in athletes under 35 years, 50% had congenital anatomic heart disease and cardiomyopathies and 10% had early onset athero-sclerotic heart disease. 40% occurred in athletes <18 yrs, 33% <16 yrs; female/male ratio was 1/9. In almost all sports sudden death was reported; most frequently involved were soccer (30%), basketball (25%) and running (15%). The pre-participation screening tests, if present at all, were of varying quality and content. The IOC CM accepted the proposed “Lausanne Recommendations” based on this research and expert opinions (http://multimedia.olympic.org/pdf/en_report_886.pdf).

Conclusion: SCD occurs more frequently in young athletes than expected and is predominantly caused by pre-existing congenital cardiac abnormalities, which can frequently be detected by application of a standardized approach, including a detailed family history, focused cardiac examination and 12 lead ECG. The high occurrence of SCD in patients <18 years of age and the fact that congenital abnormalities play such a substantial role suggest that SCD falls well within the realm of paediatric and congenital cardiologists, who should therefore be more involved in dealing with the problem. The aim of our study, a generally acceptable PPSP, has been achieved by the IOC acceptance of the “Lausanne Recommendations”, but authors realize that this is just a small step in the prevention of SCD in young athletes.

P80

Psychological follow-up long-term after the Fontan procedure

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Introduction: In contrast to objective measurements of reduced exercise capacity and reports of sequelae we want to present a study of the subjective clinical function and psychosocial outcome.

Material and Methods: Twenty patients with different forms of univentricular hearts, who were operated upon with the Fontan procedure between 1980 and 1991, were included in the study. There were 10 atriopulmonary connections and 10 total cavo pulmonary connections. The median age at study was 17.5 years and the median follow-up time 11.5 years.

We used the ability index, which we think represents a useful assessment of quality of life and the ability to adapt to physical problems.

To measure psychosocial outcome we used the I think I am Scale (ITIAS) and the Global Assessment of Functioning-Scale (GAF).

The areas of investigation were: Intellectual function, self-esteem, behavioural-emotional problems, overall function in daily life and presence of psychiatric diagnosis.

Measures of cardiac impairment, academic/occupational functioning and peri-operative course were also included.

Results: Intellectual functioning was lower than the norm for those younger than 16 years. Three individuals met the criteria for mild mental retardation and one for moderate mental retardation.

Four patients had emotional problems. A co-occurrence of mental retardation was over represented in this group.

Twelve individuals were well functioning. Seven had minor to moderate problems and one individual had major problems. Overall function in daily life was not affected by cardiac impairment.

Two individuals in the younger group scored in the clinical range on “Internalising problems” (withdrawal, anxious/depressive problems).

Mean score in self-esteem was on par with the norm of the general population. Those younger than 16 years had significantly lower scores than the older patients. Those who showed academic/occupational impairment had a tendency towards lower self-esteem.

Conclusion: The patients scored lower than expected on measures of intellectual functioning and this was particularly pronounced in the group younger than 16 years.

Various aspects of mental well being show that the majority were functioning well.

Self esteem was significantly lower for those younger than 16. This may be related to age and improves with increasing age.

P81

Transition of brain natriuretic peptide concentration during pregnancy in adult patients with congenital heart disease

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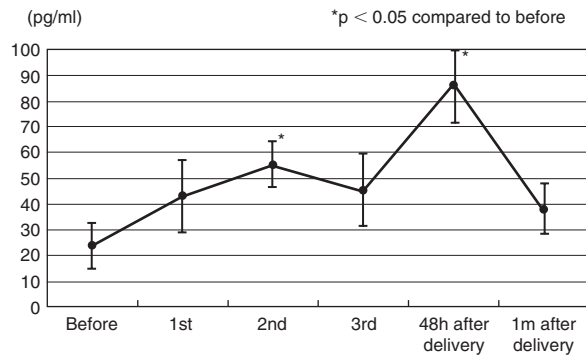
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Background: Hemodynamic changes during the pregnancy may influence on general condition or cardiac function, especially in women having cardiac residuals. Recent studies demonstrated that brain natriuretic peptide (BNP) is sensitive hematological marker of cardiac condition.

Methods: Plasma concentration of BNP was prospectively followed in 22 pregnancies in 20 women before pregnancy (n = 16), 1st, 2nd, 3rd trimester, 48 hours after delivery, and 1 month after delivery (n = 22). Cardiac symptoms (palpitation, peripheral edema, etc) echocardiographic values including left ventricular myocardial performance index (MPI) were also examined at the same period.

Results: There were 15 women with repaired tetralogy of Fallot, 5 with repaired ventricular septal defect, 2 with repaired coarctation of the aorta. Median age at repair was 5.6 years old, ranging from 4.3 to 14.2 years. Median age at pregnancy was 24.9 years old, ranging from 19 to 32 years, and about 18.9 years after the corrective surgery. Based on the NYHA classification, 16 women were assessed class I, and 4 as class II. Medications were not used prior to the pregnancy. BNP level was significantly increased at the 2nd trimester. This elevation was transiently resolved at the 3rd trimester, however, the further elevation was demonstrated at 48 hours after the delivery. Although the correlation between BNP level and MPI was not observed, women with cardiac symptoms were significantly higher BNP level compared to women without symptoms (87.4 ± 12.3 vs. 43.6 ± 10.7 , $p < 0.01$, at 48 hours after the delivery).

Conclusion: Transition of BNP level can play an important role as noninvasive parameter during the pregnancy in adult congenital heart disease.



Heart Failure, Heart Transplantation and Pulmonary Hypertension (see also OP23–2–5)

P82

Efficacy of ventricular assist devices in children

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Ventricular assist devices are successfully used in the treatment of end-stage cardiac failure in the pediatric population. This retrospective study evaluates early and late results of the implantation of ventricular assist device systems in children as bridge to recovery or bridge to transplant.

38 patients (pts) received assist devices, with ages ranging from 2 days to 23 years. There was size differences with weights ranging between 2.7 and 75 kg. 26 pts were supported with ECMO with 8 pts weighing less than 3 kg, 7 pts with Medos, 2 pts with Berlin Heart and 3 pts with Novacor. Pts were supported with an average of 4.2 ± 3.2 days (ECMO), 18.2 ± 8.0 days (Medos), 14.1 ± 19.6 days (Berlin Heart) and 8.3 ± 11.8 days (Novacor). Diagnosis were in 22 pts congenital heart diseases and in 16 pts acquired heart disease. Indications for implantation of the ECMO were postcardiotomy heart failure in 18/26 pts, reanimation in 3/26 pts and non-operation related cardiac failure in 5/26 pts, the indication for the use of the Medos, Berlin Heart and Novacor assist device was bridging to transplant in DCM in all pts.

Primary myocardial recovery was only observed in 12/26 of the ECMO pts. 11/38 pts underwent transplantation (27% of the ECMO pts (5/18), 28% of the Medos pts (2/7), all Berlin Heart pts (2/2) and 67% of the Novacor pts (2/3)). 20/38 pts (52.6%) were discharged and are long-term survivors.

These results demonstrate the efficacy and necessity of an assist program at a centre for pediatric heart cardiology.

P83

NT-pro BNP as a potential marker for acute anthracycline cardiotoxicity in children

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Introduction: Anthracycline-induced cardiotoxicity may appear many years following therapy in a substantial number of patients. The natriuretic peptides were found to be potential markers for anthracycline-induced cardiotoxicity in adults. We evaluated

N-terminal pro B-type Natriuretic Peptide (NT-proBNP) as a marker for acute anthracycline-induced cardiotoxicity in children. **Methods:** Twenty-three consecutive pediatric patients, newly diagnosed with cancer, were enrolled in the study. All patients received anthracycline-containing chemotherapy. Serial measurements of plasma NT-proBNP level were taken before and after each anthracycline-containing course. Echocardiogram was performed before initiation of treatment and at the end of the study. Fifty-four healthy age-matched children served as controls.

Results: Plasma levels of NT-proBNP were normal before therapy (150 ± 112 pg/ml, mean \pm SD, $p = 0.13$ vs control) and increased significantly after the first anthracycline dose to 327 ± 321 pg/ml ($p = 0.02$ vs baseline and <0.0001 vs control). This increase was attributed mainly to a sub-group of patients who received more than 25 mg/m² doxorubicin in the first dose. No significant increase was observed on subsequent courses. In 14 patients (61%), the highest NT-proBNP level occurred after the first anthracycline dose. Sixteen patients (70%) had NT-proBNP levels above the upper limit of normal (350 pg/ml) during the therapy period.

All patients had normal echocardiogram and none developed heart failure.

Conclusions: NT-proBNP increases significantly after first anthracycline course in pediatric cancer patients receiving 25 mg/m² doxorubicin or more. This increase is not associated with clinical or echocardiographic evidence of cardiac dysfunction. This subset of patients may be at risk for subsequent cardiac compromise.

P84

Is N-terminal-pro-B natriuretic peptide a useful parameter in patients with a bidirectional Glenn shunt?

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Introduction: Assessment of early congestive heart failure (CHF) and ventricular function is difficult in patients with a bidirectional Glenn shunt (BDG).

Purpose of the Study: to test the hypothesis, that plasma levels of N-terminal-pro-B natriuretic peptide (NT-pro-BNP) in children with a BDG correlate with clinical signs of heart failure.

Patients and Methods: NT-pro-BNP plasma levels of 24 children (median age: 28 months, range: 7.8–93.1 months) with a BDG (median time after operation: 23.8 months, range 3.1–56.8 months) were measured using an automated enzyme immuno assay (Roche Diagnostics). All patients had a complete clinical and echocardiographic examination by a pediatric cardiologist. CHF was considered if at least two of the following criteria were fulfilled: cardiomegaly in x-ray, more than mild AV insufficiency or decreased ventricular function at echocardiography and dyspnea, tachypnea, tachycardia, hepatomegaly or failure to thrive at clinical examination. 15 patients had Norwood stage I (14 hypoplastic left heart syndrome, 1 tricuspid atresia and transposed great arteries), 8 patients had a BT-shunt (2 tricuspid atresia, 2 pulmonary atresia and intact ventricular septum, 1 TGA and pulmonary atresia, 1 double outlet right ventricle and straddling tricuspid valve, 1 unbalanced complete AV-channel and pulmonary atresia and 1 pulmonary atresia, VSD and straddling AV-valve) prior to the BDG. One patient with tricuspid atresia had no prior surgery.

Results: Signs of CHF were present in 14/24 patients. In patients with CHF the NT-pro-BNP levels were significantly higher (median 874, range 137–3784 pg/ml) than in patients without CHF (median 150, range: 31–366 pg/ml).

Conclusion: Plasma NT-pro-BNP levels correlated with clinical and echocardiographic signs of CHF in patients postoperative BDG. NT-pro-BNP seems a useful and sensitive tool in detecting CHF in these patients. We speculate that measurement of plasma NT-pro-BNP levels may be helpful in monitoring the effect of various treatments for CHF in children with BDG.

P85

Is N-terminal-pro-B natriuretic peptide useful in the long-term management of patients after Fontan operation?

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Introduction: Ventricular function is critical in the long-term management of patients with Fontan physiology. Early and minor deteriorations are difficult to assess.

Purpose of the Study: To test the hypothesis that plasma levels of N-terminal-pro-B natriuretic peptide (NT-pro BNP) in children after Fontan operation correlate with clinical signs of heart failure (CHF).

Patients and Methods: NT-pro-BNP plasma levels of 22 children (median age: 5.4 years, range: 3.6–15.1 years) after Fontan operation (median time of follow up: 1.67 years, range 0.61–13.5 years) were measured using an automated enzyme immuno assay (Roche Diagnostics). All Fontan patients had a complete clinical and echocardiographic examination by a pediatric cardiologist. CHF was considered if at least two of the following criteria were fulfilled: cardiomegaly in x-ray, more than mild AV insufficiency or decreased ventricular function at echocardiography and dyspnea, tachypnea, tachycardia, hepatomegaly or failure to thrive at clinical examination. 10 patients had hypoplastic left heart syndrome, 6 had single ventricle, 4 had tricuspid atresia, 4 had double outlet right ventricle with transposed great arteries, 2 pulmonary atresia with intact ventricular septum, 1 double outlet right ventricle and straddling mitral valve.

Results: 5/22 patients after Fontan operation had signs of CHF. In patients with CHF the NT-pro-BNP levels were significantly higher (median 248.95, range: 125.2–1561 pg/ml) than in patients without CHF (median 94.3, range: 19.5–300.5 pg/ml).

Conclusion: Plasma NT-pro-BNP levels are a useful tool in detecting CHF in patients postoperative Fontan operation. In the future plasma NT-pro-BNP levels may be useful in monitoring the effect of various treatments for CHF in children postoperative Fontan procedure.

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Conversion from cyclosporine A to tacrolimus after heart and heart lung transplantation in children

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In a prospective study we investigated the effects of conversion from Cyclosporine A (CsA) to tacrolimus (TAC) in pediatric recipients of cardiac allografts. Side effects of CsA led to a switch in the immunosuppressive regimen.

22 heart (HTx) and 3 heart lung (HLTx) transplanted patients (pts) with stable graft function were assigned to the conversion to

TAC. Indications for the switch to TAC were severe hypertrichosis in 7 pts, gingival hyperplasia in 5 pts, renal insufficiency in 5 pts, hypertonia in 3 pts, hyperlipidemia in 3 pts and atopic eczema in 2 pts. Demographic data: n = 25, 15 boys and 9 girls, weight 47.5 ± 20.9 kg, age 10 ± 7.5 years (yrs), follow-up time 23.4 ± 4.5 months. Diagnosis leading to transplantation were dilative cardiomyopathy: n = 8, restrictive cardiomyopathy: n = 3, Kawasaki Disease: n = 1, idiopathic pulmonary hypertension: n = 1, congenital heart disease: n = 12.

Renal insufficiency was evaluated in values of serum creatinine and creatinine clearance, atopic eczema was assessed by calculating the Scord score, hypertrichosis by calculating the Ferriman-Galway-Index. TAC was introduced directly with doses adjusted to a range of 8–10 ng/ml. Concomitant immunosuppressive therapy, consisting of mycophenolate mofetil and low dose steroids in the heart-lung-transplanted patient was maintained after the switch. Hypertrichosis (Ferriman-Galway-index) and gingival hyperplasia had strongly resolved in all pts 3 months after the switch. Renal function improved in terms of a decreased serum creatinine 3 months after the switch. Hyperlipidemia and hypertonia improved 3–6 months after the switch. Atopic eczema disappeared in 1 pt and remained unchanged in the other one.

Conversion from CsA to TAC in pediatric heart transplanted pts is effective. CsA related side effects improved within a few months, resulting in a better quality of life and in an improved cardiovascular risk profile.

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Induction therapy with daclizumab in pediatric heart transplantation

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Daclizumab, a humanized monoclonal antibody, is a new immunosuppressive drug which binds with high affinity to the Tac subunit of the IL-2 receptor complex. Effective immunosuppression with Daclizumab in adult patients encouraged the initiation of the administration of Daclizumab as induction therapy in pediatric heart transplantation.

Sixteen patients (9 boys, 7 girls, age 8 ± 7 yrs, BMI 1.75 ± 0.52 m²), received Daclizumab as induction therapy in a dosis of 1 mg/kg intravenously perioperatively and on day 7 and 21 after orthotopic heart transplantation. Additional immunosuppression was cyclosporine (CsA, n = 14) or tacrolimus (TAC, n = 2), mycophenolate mofetil (MMF) and prednisolone. Prednisolone was tapered rapidly in the first 6 months after heart transplantation.

The administration of Daclizumab was not associated with any side effect. Owing to the blockade of the IL-2 receptor the dosage of calcineurin inhibitors could be reduced leading to less renal and hepatic toxicity. Instead of aiming at CsA trough levels of 350–400 ng/ml/TAC trough levels of 12–15 ng/ml in the first weeks after transplantation we reduced to 250 in the CsA group and to 10 in the TAC group. CD25+ T-lymphocytes began to be re-expressed after 2–3 months after administration of Daclizumab.

In a mean follow-up time of 26 ± 11.5 months no acute or chronic episode of rejection could be experienced. The incidence of opportunistic infections was not elevated (5 bacterial, 4 viral and 3 fungal infections which responded well to adequate treatment). No de novo malignancies, especially no lymphoproliferative disease (PTLD) was noticed. Actually patient and graft survival is 100%.

Our results show that immunoprophylaxis with Daclizumab induction therapy in pediatric heart transplantation is safe, effective and well tolerated and does not lead to increased opportunistic infections or malignancies. The reduction of calcineurin inhibitors led to less calcineurin related side effects and raised the quality of life of transplanted patients.

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New insights in hemodynamic testing of pediatric heart transplantation: study on 20 patients

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Introduction: Two mechanisms of heart rate control in patients after heart transplantation are in discussion: sympathetic reinnervation vs. regulation by catecholamines. The latter shows an increase in peripheral vascular tone with only moderate rise in heart rate in orthostatic challenge; the first is characterized by normal response to tilt testing.

We studied 20 children after orthotopic heart transplantation during orthostatic stress using a new continuous blood pressure screening test.

Patients: 20 children (5 female, age 15.8 ± 3.1 yr, weight 54.1 ± 19.6 kg, height 162.6 ± 12.5 cm) 5.79 ± 3.75 yr after orthotopic heart transplantation. Immunosuppression consisted of Tacrolimus (18 patients) or Cyclosporin A (2 p), Mycophenolic acid (18 p) or Azathioprine (2 p).

Methods: The 15 minutes lasting screening test included a 1st phase with the patient supine after which psychological stress was induced by spelling exercises (2nd phase). The last phase consisted of tilting the patient. Parameters recorded: beat-to-beat blood pressure by a finger cuff; ECG. Parameters calculated: heart rate variability following the frequency domain method (HF 0.3 Hz = vagotonus; LF 0.1 Hz = sympathotonus); baroreceptor sensitivity (msec/mmHg).

Results: Heart rate increased from 90 ± 10 bpm to 93 ± 11 (phase 2) and 105 ± 9 (phase 3). Systolic bp increased from 116 ± 14 mmHg to 121 ± 15 mmHg, decreased to 108 ± 20 mmHg. Diastolic bp remained unchanged with 73 ± 8 ; 78 ± 9 ; 72 ± 13 mmHg. The ratio of LF/HF was 2.0 ± 1.6 ; 2.1 ± 1.5 ; 2.5 ± 2.0 . Baroreceptor sensitivity was calculated with 4.3 ± 4.3 , 2.3 ± 2.8 and 2.7 ± 2.1 ms/mmHg.

Discussion: All patients showed a marked rise in heart rate within 60 seconds of orthostatic stress. This finding was independent of age, time since transplantation, medication or heart rate at rest. The diastolic bp remained unchanged suggesting reduced vasoconstriction and decreased systolic bp indicated a reduced cardiac preload. So we hypothesized that in all patients there is a sympathetic reinnervation. The calculations on baroreceptor sensitivity as well as heart rate variability were not reliable due to short duration of the test.

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Effects of intravenous dual endothelin-1 receptor blocker tezosentan and inhaled iloprost on acute pulmonary hypertension secondary to meconium aspiration in a porcine model

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Introduction: Acute pulmonary arterial hypertension is associated with acute lung injury (ALI) and acute respiratory distress syndrome

(ARDS). Effective pharmacological therapy is limited. Selective endothelin-A receptor blockade and inhaled nitric oxide have been shown to be effective in animal models of acute lung injury induced acute pulmonary hypertension. In this study we compared pulmonary artery pressure of 18 animals receiving a new intravenous dual ET-1 receptor blocker tezosentan or inhaled Iloprost to that of controls in a pig model of acute pulmonary hypertension secondary to meconium aspiration.

Methods: Acute pulmonary hypertension was induced in 18 ventilated and instrumented pigs (age 4 weeks, mean bodyweight 20 kg) by instillation of human pooled meconium in a 20% solution, hemodynamic and gas exchange parameters were recorded at 30 minute intervals. Six animals received tezosentan at minute 0 and 90, 6 animals received inhaled iloprost by means of an ultrasonic nebulization device at a dose of $5 \mu\text{g}$ over 5 minutes every 20 minutes, 6 animals served as controls.

Results: Meconium instillation induced an increase of mean pulmonary artery pressure (PAP) from mean 20 mmHg to 34 mmHg (70%), without significant intergroup difference.

Animals receiving tezosentan had a significant decrease of mean PAP (33 ± 4.0 mmHg to 24.7 ± 2.1 mmHg, $p = 0.001$).

In animals receiving inhaled iloprost mean PAP tended to decrease (33.6 ± 3.1 mmHg to 31.5 ± 3.4 mmHg).

In the control animals mean PAP increased from 34.6 ± 3.2 mmHg to 38.0 ± 5.7 mmHg.

This was of significance compared to both treatment groups ($p < 0.001$ for tezosentan and $p = 0.045$ for inhaled iloprost). There was no significant change and no significant intergroup difference of cardiac index, mean capillary wedge pressure, arterial pO_2 and arterial pCO_2 .

Conclusions: The intravenous dual endothelin-1 receptor blocker tezosentan and inhaled iloprost are effective in the treatment of pulmonary hypertension in this porcine model of acute pulmonary hypertension secondary to meconium aspiration.

P90

Safety and efficacy of bosentan in paediatric patients with pulmonary arterial hypertension: retrospective case series

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Background: In adult patients with pulmonary arterial hypertension (PAH) in WHO functional class III and IV, the oral dual endothelin ETA/ETB receptor antagonist bosentan (Tracleer) increases exercise capacity, improves WHO functional class and hemodynamics, and delays time to clinical worsening. Furthermore, long-term data on bosentan demonstrate maintenance of efficacy and safety. In paediatric patients, 12-week bosentan treatment (BREATHE-3 study) in 19 children aged 3–15 years resulted in haemodynamic improvement and was well tolerated.

Methods: This was a retrospective observational study in paediatric patients who were seen at 5 European centres specialised in the treatment of PAH. Paediatric patients received bosentan alone or a bosentan-based regimen with variable follow-up periods. Dosages were largely in accordance with the BREATHE-3 protocol, with a target dose of bosentan 31.25 mg (10 – 20 kg body weight), 62.5 mg (>20 – 40 kg), or 125 mg (>40 kg) twice daily.

Results: The present interim analysis comprises 22 children (14 males; 18 <12 years, 4 >12 years; 13 with idiopathic PAH, 9 with PAH associated with congenital heart disease). At baseline, 1 patient was in WHO functional class I, 9 in class II, 8 in class III, and 2 in class IV (data from n = 20 patients available). Median PAH duration was 30 months. 14 patients were taking concomitant epoprostenol or iloprost, 17 anticoagulants, and 4 calcium channel blockers. After a median treatment duration of 198 days on bosentan, 6-minute walking distance increased from a baseline value of 377 ± 111 m by 29 ± 99 m at the end of follow-up (n = 16). 85% of patients stabilized or improved in WHO functional class (n = 20). Two patients died, 1 after lung transplant and 1 due to worsening right heart failure. Bosentan was generally well tolerated. **Conclusions:** Keeping the methodological limitations of this study in mind, bosentan appeared to be well-tolerated and effective in this paediatric patient population. Prospective studies are needed to confirm these results.

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Pulmonary arterial hypertension post bone marrow transplantation for leukemia

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Background: According to the Third World Symposium on Pulmonary Arterial Hypertension (PAH), chemotherapy is considered to be one of the possible risk factors for patients developing PAH. However, no literature has been sufficiently document the risk and effective treatment in this condition. We described our experience diagnosed and treated children with PAH after chemotherapy and bone marrow transplantation (BMT).

Method: Apart from the baseline cardiac evaluation, all children underwent for BMT at our institute routinely have echocardiogram every 6 month. Children with elevated systolic right ventricular pressure with symptoms suggested PAH were included in our study. Cardiac catheterization was performed to confirm diagnosis of PAH along with pulmonary vasodilator testing with aerosolized iloprost. Then they would be treated with combined pulmonary vasodilators. **Result:** First, a 16 year-old male developed PAH 10 months after chemotherapy and BMT for relapsed acute lymphocytic leukemia. His functional class and oxygen saturation had been declined over the past 1 month with an episode of syncope (NYHC III–IV and oxygen saturation 88% in room air). Cardiac catheterization showed severe PAH, mean pulmonary arterial pressure 57 mmHg. After iloprost inhalation, the mean pulmonary arterial pressure was decreased 45% while his arterial oxygenation increased to 98% in room air. Significant improvement in his functional status (NYHC II) and oxygen saturation (92–98%) was obtained with combination of iloprost and sildenafil treatment.

The second case was a 16 year-old female post BMT for chronic myeloid leukemia. Five months after transplantation, she developed PAH with presenting symptoms of edema and dyspnea on exertion (NYHC II). Cardiac catheterization at baseline showed precapillary pulmonary arterial pressure of 38 mmHg. After acute vasodilator testing, the mean pulmonary pressure was decreased 42%. She has had an improvement in her exercise capacity and functional class (NYHC I) after sildenafil and beraprost treatment.

Conclusion: This report is a supporting document that PAH is considered as one of the complication of chemotherapy and bone marrow transplantation for leukemia. Combined pulmonary vasodilators treatment has a beneficial effect in improve patient's condition and functional status after acute pulmonary vasodilator testing.

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The use of aerosolized iloprost in infant with postoperative pulmonary hypertension

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Background: Pulmonary hypertension is considered to be one of the serious complications after an open-heart surgery. Current medical management of moderate-to-severe pulmonary hypertension after cardiac surgery is using inhale nitric oxide. However, the apparatus required for delivery of the nitric oxide is expensive and complicated. We recently evaluated the use of aerosolized iloprost, a prostacyclin analogue, as an alternative treatment for postoperative pulmonary hypertension in infant.

Methods: After identified infant at risk for postoperative pulmonary arterial hypertension, we directly inserted a catheter into their pulmonary artery for pressure monitoring intra-operatively. Children with moderate-to-severe postoperative pulmonary hypertension were including in this study. They received initial conventional management of pulmonary hypertension including using hyperventilated mechanical ventilator with enriched inspired oxygen, deep sedation, corrected metabolic acidosis and avoid using pulmonary vasoactive agents. If their pulmonary pressure remained elevated with signs of low output and hypoxia, aerosolized iloprost, 25 ng/kg/min, would be given via the endotracheal tube connected to the ventilator.

Result: We recently included the 3 consecutive infants (age 11, 10 and 1 month) with postoperative pulmonary hypertension in this study. They underwent for the cavopulmonary anastomosis, ventricular septal defect closure and rerouting of the obstructed total anomalous pulmonary venous return in univentricular heart. Their mean pulmonary arterial pressure were 28, 48 and 45 mmHg while their arterial saturation were 67%, 85% and 61% despite they were hyperventilated with 100% oxygen. All of them were given aerosolized iloprost 25 ng/kg/min with immediate pulmonary vasodilator response. The mean pulmonary arterial pressure was declined to 22, 35 and 37 mmHg and the oxygen saturation was increased to 78%, 95% and 72%. Their ongoing postoperative pulmonary hypertension was exclusively treated with iloprost. All infants were able to tolerate wean off ventilator with uncomplicated extubation and finally discharged home.

Conclusion: We reported our initial experience using aerosolized iloprost as an alternative treatment for postoperative pulmonary hypertension in infant. In this setting, iloprost has comparable efficacy as nitric oxide in managing postoperative pulmonary hypertension with less expensive and less complicated delivery apparatus.

Interventional Cardiology and New Technology (see also OP23-6–9)

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3D Reconstruction to optimize interventional and angiographic strategies in congenital heart disease

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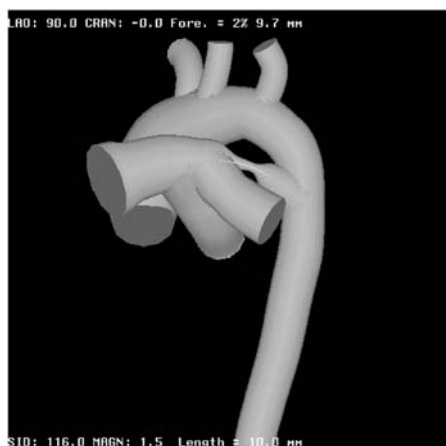
Introduction: A 3D reconstruction algorithm using standard biplane angiography to visualize coronary arteries in adults has previously been developed and validated. Like coronary arteries,

the vasculature in congenital cardiac anomalies is often complex and difficult to visualize using conventional 2D imaging such as echocardiography or biplane angiography. The purpose of this study was to determine the feasibility of adapting this 3D algorithm to model other complex vasculature such as the pulmonary arteries or great vessels in a pediatric setting.

Methods: Biplane angiography from children undergoing routine cardiac catheterization was used. No additional angiographic images were obtained other than those that were required for diagnostic purposes. These biplane angiograms were then post-processed using the 3D reconstruction algorithm to reconstruct 3D models of the vasculature in congenital heart disease.

Results: 3D reconstruction of branch pulmonary arteries (7 cases), and the vasculature in patients with hypoplastic left heart syndrome (7 cases) and persistent ductus arteriosus (23 cases) were produced using this algorithm. These models could then be freely rotated to provide better spatial resolution of the area of interest. An angiogram and 3D reconstruction of a patient with a persistent ductus arteriosus is pictured.

Conclusions: 3D reconstruction of the branch pulmonary arteries and vasculature in complex congenital heart disease such as hypoplastic left heart syndrome from standard pediatric digital biplane angiography is feasible. Modeling of complicated vasculature without the need for an additional MRI procedure can be performed with this method. Furthermore, these 3D constructs can be used to optimize angiographic and interventional strategies by calculating the optimal viewing angles of a particular region of interest to minimize foreshortening or overlap. These optimal views can in turn be used for future interventions to hopefully limit the exposure to radiation or contrast.



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The solysafe septal occluder for atrial septal defects – animal testing of the improved design

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Introduction: For patients with an atrial septal defect, closing the defect with transcatheter technique has evolved to be the first line choice of therapy. We have previously reported on animal results of a new device, called SolySafe™. The first report dealt with the initial design constructed of 8 metal wires (Phynox), one plastic wire holder at each end and a polyester membrane in the middle. In animal testing, we showed that it could be safely introduced and placed in the atrial septal defect, and had a high closure rate. Due to a few wire fractures, we improved the design with two polyester membranes, one on each side of the septum. This design greatly improves the ease of implantation. The second report dealt with the initial results of this improved design including the first 3 animals to reach an age of 6 months post implantation. Since then, we have gathered more experience with this design.

Methods: Our device was tested in a swine model. An atrial septal defect was created with standard transseptal technique using static balloon dilation. The device was implanted under guidance with intracardiac echocardiography and fluoroscopy. In this study, we have concentrated on placing the device in a “non perfect” position, i.e. close to the ascending aorta. The animals were then reevaluated with monthly fluoroscopy and at sacrifice (6 months post implantation) with section of the heart to detect any signs of loss of device integrity.

Results: In 24 animals, the redesigned device was implanted in good position. The procedures were without immediate complications and all the animals had uneventful recoveries. So far, 12 animals have been followed to sacrifice at 6 months post implantation without signs of wire fractures. Sacrifice of the remaining 12 test animals is still pending.

Conclusions: We believe this device to be a promising new design for the closure of atrial septal defects. Its very low profile and self-centering properties make it an interesting alternative to existing devices. With this improved design, the risk of wire fracture seems to be very low. We believe the device is ready for a human trial.

P95

Percutaneous closure of ventricular septal defects in children

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Introduction: Percutaneous VSD closure has been recently introduced as alternative to surgical treatment.

Methods: Between Jan 00 and Sept 04, 104 patient (pts) underwent percutaneous VSD closure. Sixty-two pts were aged <12 years. VSD was mid-muscular in 15 pts, apical in 4 pts, high muscular in 3 pts, perimembranous in 37 pts. All pts had echocardiographic signs of left ventricle volume overload. Twenty-three subjects were symptomatic. Seven subjects had significant post-surgical residual VSD. The Amplatzer muscular VSD occluder (mVSD) and the eccentric VSD occluder (pmVSD) were used.

Results: Mean age at procedure was 4 ± 2.8 years (range 0.5–12 yrs). Mean weight was 18 ± 8 kgs (range 3.5–45 kgs). Mean

QP/QS was 2.1/1 (range 1.5–4). Procedure was successful in 59/62 pts. Mean fluoroscopy and procedure times were 30 ± 17 and 102 ± 60 min, respectively. The median size of the VSD was 8 mm (range 4–14 mm). In 22 pts a mVSD device was used, while in 37 cases a pmVSD device was implanted. Multiple defects were closed in three subjects by implanting two devices.

Complications: No death occurred. Device embolization occurred in 4 patients. In three the device was recaptured percutaneously and the defect closed by using a larger device. In one case the pt was sent to surgery. Periprocedural complete AV block occurred in two subjects: in one pt during the procedure (procedure aborted and pt sent to surgery) and in one subject 24 hours after closure (pace-maker implantation). No significant aortic, mitral or tricuspid regurgitation occurred. A mild to trivial intraprostatic residual shunt was showed in three pts Median follow-up was 8 months (range 1–33 months). Complete occlusion was shown in all subjects. In one pt paroxysmic complete AV block appeared 5 months after closure and he underwent pace-maker implantation. No other late complications occurred.

Conclusion: In the current era, percutaneous closure of VSD in children can be achieved safely and successfully. The major concern is related to the occurrence of abnormalities of AV conduction.

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MRI-guided balloon angioplasty of aortic coarctation

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Introduction: Balloon angioplasty of coarctation of the aorta (CoA) under MRI guidance would be desirable to visualize detailed morphology and function during intervention without exposure to x-ray and contrast media. This study aimed to assess the feasibility of MRI-guided balloon angioplasty in vivo and to apply this technique to patients (initial results of a clinical study).

Methods: Animal study (swine, n = 4): Angioplasty balloons were inflated with concentrations from 100% to 0.2% of an ion oxide based contrast medium (Resovist, 500 mmol Fe⁺/ml) for susceptibility based catheter visualization and tested for signal contrast between the balloon and the blood pool of the aorta.

Initial Clinical Study: Interventions were performed in four patients with moderate re-CoA. Conventional angiograms were performed first in the catheter laboratory. Then patients were transferred into the MRI scanner and a whole-heart isotropic 3D scan was performed prior to and immediately after the MRI-guided intervention to provide detailed anatomical information. An angioplasty catheter with the shaft filled with 1 ml 90% Resovist was positioned under real-time MRI across the CoA. Pressure gradients were assessed before and after the procedure. Angioplasty was performed by inflating the balloon with 1% Resovist. Afterwards, conventional angiograms and pressure recordings were repeated in the catheter laboratory to reconfirm interventional success.

Results:

Animal Study: Optimal signal contrast of 1150 ± 259 (dimensionless units) between the inflated balloon and aortic blood pool was noted at concentrations of 1% Resovist. At this concentration no distortion due to susceptibility artefacts was present on adjacent anatomy.

Initial Clinical Study: Balloon angioplasty could be well controlled under MRI guidance. There was no significant difference in diameters of the CoA or pressure gradients across the stenosis as assessed with MRI and conventional catheterization. Mean diameter

increased from 7.6 ± 3.3 mm before to 12.4 ± 3.5 mm after intervention and pressure gradients decreased from 36 ± 10 to 13 ± 4 mmHg ($p < 0.05$).

Conclusion: MRI-guided balloon angioplasty of CoA can be performed in the clinical context.

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Radiofrequency catheter ablation of septal hypertrophy in childhood

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Introduction: Hypertrophic cardiomyopathy (HOCM) with asymmetric septal hypertrophy and severe left ventricular outflow obstruction in young children presents a major therapeutic challenge. Surgical myectomy has been the treatment of choice, but carries a risk of permanent AV block necessitating pacemaker implantation. We present our experience with radiofrequency catheter ablation (RFA) of the hypertrophied outlet septum in a 5 year old boy.

Methods: The patient presented with progressive LVOT obstruction and symptoms (tiredness, chest and abdominal pain with exercise), despite maximal beta blocker therapy. The invasive gradient across the LVOT was 70 mmHg. Sequential atrioventricular temporary pacing using varying AV intervals did not influence the invasive gradient. The extent of the septal obstruction was delineated by left ventricular angiography. Transcatheter septal ablation was then performed, using a 7F cooled tip ablation catheter (Sprinkler L, Medtronic) introduced retrogradely via the femoral artery. The bundle and proximal left bundle branch were mapped using the Localisa mapping system, which allowed continuous monitoring of ablation catheter position in relation to the bundle during RF lesion application. A series of lesions was applied, beginning distally, and working towards the aortic valve. Transient junctional rhythm during RF application necessitated constant atrial pacing, to confirm the integrity of AV conduction. Transesophageal monitoring also confirmed echodense lesions in the hypertrophied septum and outflow tract.

Results: The extent of myocardial necrosis was monitored by serial measurement of serum Troponin T and CK-MB, which showed a sharp rise at 6 and 24 hours after the procedure, and normalization 7 days later. At follow-up echocardiography 6 weeks later, the minimal LVOT diameter had increased, and the peak Doppler gradient had decreased to 20 mmHg. The patient was without symptoms.

Conclusions: In young children with septal hypertrophy and severe symptoms, it is possible to alleviate the obstruction and relieve symptoms, while also preserving AV conduction, by targeted transcatheter RF ablation.

P98

Percutaneous transventricular intervention: an unusual but very useful access

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Objective: Interventional targets, when “excluded” by prosthetic valves or Fontan type circulation, may be difficult or impossible to reach through conventional transvenous or transarterial catheterization. We report our experience with direct ventricular puncture.

Patients: Patient 1 (74 yr, high surgical risk, 2 previous sternotomies) with an aortic and mitral prosthetic valve presented with a significant paravalvar leak of the mitral valve at the crux.

Patient 2 (6 yr, 2 previous sternotomies) was referred after a Fontan circuit for double inlet ventricle; the right atrioventricular valve had been attempted to close with a patch at both operations, but a significant patch leak persisted, resulting in Fontan failure.

Methods: General anaesthesia. A – approach: echographic delimitation of ventricular apex; puncture during a short period of apnoea in expiration to avoid pulmonary puncture; placement by Seldinger technique of 6–8 F sheath; B – procedure as required. C – closure of ventricular puncture site: direct suture through small thoracotomy in Pt 1, with Prostar XL (Biomedicon, India) occlusion device in Pt 2. Prolonged echocardiographic monitoring of puncture site for pericardial or pleural effusion.

Results: Easy and immediate access to the ventricle was obtained; the paravalvar leak in Pt 1 could be crossed with a wire under TEE guidance within seconds, in Pt 2 only after opening the closed valve; after balloon sizing of the defect, closure with a 6 and 12 mm muscular VSD Amplatzer occluder respectively. Only a very limited pericardial effusion had developed during the procedure, probably due to multiple post-operative adhesions. However, after removal of the sheath, leakage to the pleura in Pt 1 made obvious that closure of the ventricular puncture site is necessary. Both closure techniques adequately “dried” the puncture site.

Conclusions: In selected patients percutaneous transventricular access is a very valuable technique to reach “inaccessible” targets, thereby avoiding complex and difficult open heart surgery. Haemostasis at puncture site can be controlled with (adapted) transpuncture closing devices or direct suture through mini thoracotomy.

P99

Right to left shunt through interatrial communications in patients with congenital heart disease: results of interventional closure

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Introduction: Interatrial communications are usually closed, to prevent late right heart failure, arrhythmias and pulmonary hypertension, when they induce a right ventricular overload by means of a left to right shunt. No specific reports exist on closure of interatrial communications associated with a right to left shunt in children with congenital heart disease.

Population: From January 2000 to December 2004, 15 patients with a congenital heart disease (median age 13 years, median weight 38 kg) and a right to left shunt through an interatrial communication, underwent percutaneous atrial septal defect (ASD) (n = 6) or patent foramen ovale (PFO) (n = 9) closure. Four patients had repaired tetralogy of Fallot, 6 repaired pulmonary atresia with intact ventricular septum and 5 unrepaired or palliated Ebstein disease. Two patients had had a stroke before ASD or PFO closure.

Methods: All patients underwent an exercise test before and after percutaneous closure of the interatrial communication.

Results: Four patients were desaturated at rest, 8 performed a submaximal test. At exercise oxygen saturation diminished from 94 to 84% (p < 0.05). Closure of interatrial communication lead to immediate increase of oxygen saturation from 94 to 98% (p < 0.05). Three patients had mild and 1 had moderate residual shunt. There were no complications. At a median follow-up of 3 years (range 0.5–5) all but one patient with a Ebstein disease and a residual ASD have a normal oxygen saturation at rest and at exercise. Work capacity increased from 88 to 92% (p < 0.05).

Conclusions: Percutaneous closure of interatrial communications associated with a right to left shunt allows to restore a normal

oxygen saturation at rest, to avoid desaturation at exercise and to improve work capacity.

P100

Transcatheter patch occlusion of atrial lesions using surgical adhesives

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The transcatheter patch has been found effective in the occlusion of several heart defects, avoiding wire related complications; however the application method is somewhat inconvenient, since 24–48 hours are required for patch release. Transcatheter patch occlusion of atrial lesions using surgical adhesive could conceivably accelerate patch release.

Experimental transcatheter patch occlusion using a surgical adhesive was performed in 6 atrial septal defects 10–12 mm in diameter, 3 cases of patent foramen ovale and one case with a combination of patent foramen ovale and left atrial appendage occlusion. The surgical adhesive is a polyethylene glycol in acid solution (A) applied on the inner surface of the waist of the patch. It is activated by an alkaline solution B, inside the body. Heparin (50 u/kg) was used in 5/10 piglets. A single balloon patch was used for all cases. Follow-up was performed, up to 3 weeks.

All patches were released in 15–45 minutes. Effective occlusion was achieved for all lesions. There were no cases of thromboembolism or patch embolization.

There were variable degrees of endothelialization according to the length of implantation.

In conclusion experimental transcatheter patch occlusion and accelerated patch release in 15–45 minutes, is possible using a surgical adhesive, in a variety of atrial lesions.

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Comparison of heart function in children after surgical or Amplatzer occluder closure of perimembranous ventricular septal defect

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The aim of this study was to examine systolic and diastolic functions of the left ventricle after surgical or invasive treatment of the perimembranous VSD.

Material and Methods: 2003–2004 two groups of patients were examined by use of the transthoracic echocardiography before and after the treatment 3–15 mth (10,36 ± 4,34) and 7–16 mth (11,5 ± 2,77): A (Amplatzer – MembrVSDO) – 11 and S (surgery) – 12 children. There were no differences between the groups according to the body weight (0,1037), height (0,1335), Qp:Qs (0,9279), ØVSD/Ao (0,1335) and follow-up time (0,4865). The following parameters were assessed: left ventricle end-diastolic diameter index, EF, mitral valve E, A, E/A ratio, DCT, IVRT and HR.

Results: The LV size and HR decreased significantly after VSD closure in group A and S. There were no statistically significant differences in diastolic function before and after application MembrVSDO and surgery.

Table. Comparison of systolic and diastolic function and size of left ventricle before and after procedure in group A and S.

Variable	Group A before (N = 11)	Group A after (N = 11)	p-value
	Range	Range	
LVEDDI	1–1,32	0,87–1,06	0,004439*
EF (%)	57–80	70–95	0,048*
MV: E (m/s)	0,8–1,39	0,66–1,37	0,2845
MV: A (m/s)	0,4–1,18	0,41–1,13	0,7221
E/A	0,98–2,25	1,08–2,19	0,8588
DCT (ms)	130–240	110–220	0,1688
IVRT (ms)	40–70	40–65	0,308
HR (min ⁻¹)	62–150	56–119	0,0207*

Variable	Group S before (N = 12)	Group S after (N = 12)	p-value
	Range	Range	
LVEDDI	0,99–1,5	0,93–1,22	0,006*
EF (%)	61–86	59,0–80,0	0,286
MV: E (m/s)	0,78–1,28	0,78–1,14	0,1467
MV: A (m/s)	0,45–1,0	0,37–1,1	0,3881
E/A	1,08–2,0	0,97–2,32	0,6378
DCT (ms)	120–220	110–220	0,224
IVRT (ms)	30–70	30–55	0,12348
HR (min ⁻¹)	80–150	58–120	0,050*

LVEDDI – end-diastolic left ventricle diameter to mean norm for body weight ratio; EF – ejection fraction; E/A – wave velocity ratio; DCT – deceleration time; IVRT – isovolumetric relaxation time; HR – heart rate.

In group A comparing to group S a statistically better improvement of LV EF with (0,0044) the decrease of heart rate was observed (0,0438). No differences between LVEDDI ($p = 0,0688$), MV:E ($p = 0,9279$), A ($p = 0,5253$), E/A ($p = 0,8801$), DCT ($p = 0,4131$), IVRT ($p = 0,0908$) were observed.

Conclusions: In mid-term follow-up systolic function of the left ventricle after MembrVSDO implantation was better than after surgical correction of perimembranous VSD in children.

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Experience with the covered stents in patients with congenital heart diseases

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Introduction: Covered stents (CS) have been recently introduced in clinical practice. There are few reports concerning this new device.

Methods: Between January and December 2004, 5 patients aged between 12 and 29 years were treated by using a CS. Procedure was performed under heavy sedation. A long sheath larger than the one needed for the angioplasty balloon alone was used.

Results: Mean age at procedure was 23 ± 5 years. Covered stents were used for the following indications: severe native aortic coarctation (1 pt), severe aortic re-coarctation (1 pt), aortic recoarctation and aneurysm in a patient treated 5 years earlier with balloon angioplasty, aortic recoarctation and aneurysm in a patient treated one year earlier with bare stent (2 pts), partial dehiscence of an intracardiac Fontan conduit producing a right-to-left shunt and giving severe systemic desaturation (1 pt). A BIB balloon was used in three cases, while a Crystal Balloon was used in two procedures. A 34 mm CS was used in one pt, a 39 mm CS in two subjects, a 45 mm in one patient. Finally, early in our experience, a 5014 Palmaz stent was manually covered with ePTFE. Procedure

was successful in all subjects. Mean fluoroscopy and procedure times were 12 ± 8 and 70 ± 15 min, respectively. In patients with aortic coarctation or recoarctation the median gradient reduced from 30 (range 20–35 mmHg) to 0 mmHg. In patient with partial dehiscence of the Fontan conduit oxygen saturation increased from 82 to 93%. No complication occurred.

At a mean follow-up 3 months (range 1 to 11 months) no complication occurred and result was stable.

Conclusion: CS are devices very useful for the treatment of various congenital heart diseases and in particular in patients with aortic coarctation or re-coarctation and aneurysm.

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Balloon angioplasty versus endovascular stenting for treatment of branch pulmonary artery stenosis

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Objectives: Branch pulmonary artery stenosis may develop after surgery of congenital heart disease or may be primary due to hypoplasia of central pulmonary arteries. Aim of the study was to analyse the results of interventional catheter therapy.

Methods: We reviewed the experience of balloon angioplasty and endovascular stenting for branch pulmonary artery stenosis.

Results: From November 1989 to October 2004, 98 children (male:female = 54:44) underwent 155 interventions for left (93/155) or right (62/155) pulmonary artery stenosis: group 1 were 94 primary balloon angioplasty (BAP) and 16 redilatation after primary BAP; group 2 were 28 primary stenting, 6 redilatation after primary stenting, and 9 secondary stenting after primary BAP with 2 secondary redilatation. The success rate (increase in vessel diameter >50%) was 66.4% (group 1) and 73.8% (group 2) with an increase in vessel diameter of 79.7% after BAP (group 1) vs. 95.6% after stenting (group 2). The rate of restenosis leading to further procedures was higher after primary BAP (group 1: 28.7%) than after primary stenting (group 2: 24.2%). Complications such as aneurysm or dissection was lower after primary stenting (group 2: 6.9%) vs. primary BAP (group 1: 10%). No mortality occurred.

Conclusion: BAP and stenting are safe methods for interventional therapy of branch pulmonary artery stenosis. Stenting seems to be more effective for intermediate-term outcome concerning the rate of success, restenosis or complications, although long-term follow up (>2 years) has to be determined.

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Transcatheter closure of ventricular septal defects in children with Amplatzer Occluders – early and mid-term results

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Interventional closure of ventricular septal defects (VSD) is still a rare alternative to surgery. We report our early and partly mid-term results on 14 pediatric patients who received transcatheter closure with an Amplatzer Occluder in our institute since August 2002.

Patients: 10 patients had a perimembranous (5 with aneurysm) and 4 a muscular VSD – 1 was a residual defect after surgical closure. Patients' age ranged from 3,9 to 14,3 years (mean 8,4 years) and body weight from 15 to 56 kg (mean 28,1 kg). In all cases left ventricle was enlarged or in the upper normal range due to volume overload (Qp 1,0 to 5,2, mean 1,9), 1 patient already had

pulmonary hypertension. 3 patients suffered from trivial aortic regurgitation. Defect size was 4–10 mm (mean 5,5 mm).

Results: Interventional procedure could be performed in all cases under additional transesophageal echocardiography guidance without any complications. We implanted 14 Amplatzer Occluders (4–12 mm, mean 8 mm), in one perimembranous defect the device could not be stabilized due to a floppy membranous septum and a completely missing aortic rim, in a second case the device was explanted after 2 months because of significant residual shunt, both defects were then closed surgically. In 1 patient we even closed additionally an atrial septal defect with an Amplatzer device. During follow-up (1–28 months, mean 9,5 months) no hemolysis or thrombus formation on the occluder occurred. Complete closure rate of the defect immediately in the cath lab was 54%, after 1 week 85% and after 3 months 92%. During the first 14 days after intervention in 5 of 10 patients with perimembranous VSD conduction disturbances occurred (3 × right bundle branch block (RBBB), 2 × left bundle branch block (LBBB)), which were all transient and disappeared after 2 weeks. Only in 1 patient a persisting RBBB newly occurred 3 months after closure.

Conclusion: Transcatheter closure of VSD is in well selected pediatric patients a good therapy option with promising results. Close follow-up in the first year after intervention is mandatory especially to register possible rhythm disorders, which are mainly transient.

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Multicenter experience of transcatheter closure of atrial septal defect with the Amplatzer device in small (<15 kg) children

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Introduction: Although most infants and small children with atrial septal defect (ASD) are asymptomatic, poor growth, recurrent lower respiratory tract infections and heart failure are occasionally reported. Surgical closure of ASD is a low-risk and widely accepted procedure. However, it is associated with morbidity, discomfort, prolonged hospital stay and a thoracotomy or sternotomy scar. Transcatheter closure of secundum ASD is a valuable alternative but its efficacy and safety are incompletely assessed in small children. We report the multicenter experience of secundum ASD transcatheter closure in a pediatric population weighting 15 kg or less.

Methods: Between January 1997 and June 2004, 35 children weighting 15 kg or less underwent percutaneous closure of secundum ASD in 8 pediatric cardiology centers in France. There were 15 male and 20 female. The median age and weight at presentation were 3 years (0 to 6,2 years) and 13 kg (3,6 to 15 kg), respectively.

Results: Thirty patients were treated because of symptomatic left-to-right shunt whereas ASD closure was indicated because of cyanosis due to right-to-left shunt in 5 cases. Extracardiac anomalies were Down syndrome in 3 cases and Adams Oliver syndrome in 1 case. All the procedures were performed under general anesthesia. Transesophageal echocardiography monitoring was used in 33 cases whereas the procedure was performed under transthoracic echocardiography guidance in 2 cases. The median size of the "Amplatzer septal occluder" devices used was 13 mm (4 to 24 mm). One patient underwent emergency surgery 24 hours after the procedure for a previously unrecognized cor triatriatum dexter.

No death or other major complications occurred. One child had a small residual shunt at discharge whereas total occlusion of the ASD was achieved in all the other patients. After a median follow-up of 2 years (0,5 to 5,2 years), there were no complications and all the patients are asymptomatic. Follow-up echocardiography demonstrated no residual shunt in all the cases.

Conclusion: Transcatheter device closure of secundum ASD in small children is safe and effective and can be proposed as an alternative to surgical repair.

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Biocompatibility of atrial septal defect closure devices: is the histopathology of human explants comparable to animal studies?

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Objective: So far, information on biocompatibility of cardiovascular devices is mostly derived from animal experiments. No data exist on the correlation of experimental findings to human tissue reactions. We reviewed literature and discuss our own experience with the CardioSeal/StarFlex device and the Amplatzer ASD occluder both from animal experiments and from human explants.

Materials and Methods: ASD occluders both from animal experiments in sheep (n = 32, implantation time 4 days to 1 year) and after surgical removal from humans (n = 7, implantation time 2 months to 3 years) were processed using a uniform protocol. Devices were fixed in formalin and embedded in methylmethacrylate. Serial sections were obtained by sectioning with a diamond cutter and grinding, thus saving the metal/tissue interface for histological evaluation. Beside standard histology and immunohistochemistry we employed scanning electron microscopy for biocompatibility screening.

Results: Immediately after implantation, thrombotic material was formed within the implant in both types of device. Within 6 months, transformation of thrombus material was completed with ingrowth of fibromuscular cells and connective tissue originating from the implant/atrial septum interface both in animals and in humans. An ongoing inflammatory reaction directed against textile fibres of both implants was seen with development of foreign body giant cells. In addition, lympho-plasmacellular infiltrates occurred without correlation to implantation time or type of implant and were observed equally in both human and animal explants. In contrast to our findings, literature reports describe a decline of inflammatory reactions in animal experiments with observation times of more than 6 months. Surface reactions with initial formation of a fibrin layer and early spreading of endothelial cells at the blood/implant interface were demonstrated in a corresponding time pattern.

Conclusion: Biocompatibility screening in single human tissue specimen of explanted septal occluder revealed results corresponding to findings in animal series. Tissue reactions to ASD closure devices in humans are parallel in various aspects to reactions in experimental sheep.

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Transcatheter treatment for recurrent coarctation of the aorta

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Background: The optimal management of recurrent coarctation of the aorta (ReCoAo) is still controversial.

Methods: From 1990 to 2003 in our Institution 46 patients underwent 50 balloon angioplasty (BA) for ReCoAo. Indications to the transcatheter approach was a delayed Doppler upstroke velocity profile with continuous antegrade flow in the descending aorta after surgery.

In this cohort of patients 18 had a previous surgery for isolated coarctation of the aorta, 5 patients had a previous Norwood stage 1 palliation for Hypoplastic Left Heart Syndrome (HLHS) and the remaining 22 patients had a coarctation of the aorta in association with other cardiac lesions (ventricular septal defects, aortic valve stenosis, mitral valve stenosis, double aortic arch, complete AV canal and D-transposition of the great arteries).

The mean elapsed time from the first operation was 35 months (1–283 months), the mean age at dilation was 42 months (1–417 months) and the mean peak-to-peak systolic gradient across the coarctation during the interventional procedure was 43 mmHg (10–100 mmHg).

Results: Immediate and follow-up results were evaluated. The mean residual peak-to-peak gradient across the coarctation was 17 mmHg. We have experienced only 1 procedural deaths (2%) and 1 major complication (cardiac arrest requiring external cardiopulmonary resuscitation) all of these in the sub-group of patients with HLHS. No surgical relief of aortic obstruction was required. 4 patients (8%) developed ReCoAo requiring one or more BA. At follow-up (range 11–184 months) 81% of the patients had a normal Doppler pattern in the descending aorta while 4% had a mild delayed Doppler upstroke velocity, 4% had an abnormal Doppler pattern and 11% were lost in follow-up.

Conclusion: In our institution BA has become the treatment of choice for ReCoAo, in fact it is safe and effective with extremely low rates of mortality and morbidity.

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Interventional catheterization after univentricular surgical repair

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Introduction: Varied catheter interventions can manage complications after univentricular surgical repair. The objective of this study is to describe and analyze interventional catheterization procedures and their follow-up evaluation.

Methods: We retrospectively report all the interventional catheterization procedures ($n = 20$) we performed to 14 patients after partial ($n = 6$) and total ($n = 14$) atriopulmonary or cavopulmonary connections from 1996 to 2004. The patients all had a functional single ventricle. The last surgical operation occurred 4.1 years (*SD* 2.9) before interventional catheterization. We analyzed the two variables “mean pulmonary arterial pressure” and “aortic oxygen saturation” before and after the catheter intervention with paired Student-tests. Intervention catheter procedures were: fenestration closure ($n = 5$), occlusion of tube or tunnel patch defect ($n = 3$), embolization of veino-venous or aortopulmonary collaterals ($n = 6$), dilatation of pulmonary artery ($n = 5$), atrial septostomy ($n = 1$). Different devices were used. Five patients had 2 or 3 different intervention catheter procedures.

Results: During the procedure all catheter interventions were carried to completion and no significant complication was reported; patients were discharged after 2 to 4 days. Mean aortic oxygen

saturation after the fenestration closure is the only variable which significantly increased from 87% to 93% ($p < 0.001$). For all the different procedures, mean pulmonary arterial pressure remained unchanged. Midterm follow-up reports one case of pulmonary embolism 5 months after occlusion of tube defect with the Amplatzer ASD occluder followed by partial thrombosis of the tube 3 years later. One patient presented complete atrioventricular block 8 months after atrial patch defect occlusion.

Long term follow-up reports one case of mild residual shunt 7 years after fenestration closure with the Sideris Umbrella. Partial cavopulmonary connection was always followed by total cavopulmonary connection within 1 to 4 years.

Three patients still present significant aortopulmonary or venous collaterals; one patient presents a residual hepatic vein to pulmonary venous atrium.

Conclusion: Interventional catheterization after partial or total cavopulmonary connections in univentricular hearts safely manages various postoperative shunts and stenosis. It may qualify patients for total cavopulmonary connection, eliminate cyanosis, reduce the risk of paradoxical embolism and lower postoperative morbidity.

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Transcatheter closure of atrial septal defects without balloon sizing: a pilot study

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Introduction: The Amplatzer atrial septal occluder has gained wide acceptance for closure of secundum atrial septal defects (ASDs). Conventionally, the procedure is performed with the aid of transoesophageal (TOE) or intracardiac echocardiography (ICE) and the device is chosen after balloon sizing of the defect.

Objectives: This study reports our initial experience of closure of ASDs without balloon sizing the defect using the maximum colour Doppler jet width (CDJW) as a guide to device selection.

Methods: Transcatheter ASD closure under TOE guidance was attempted without balloon sizing of the defect in nine patients with median age of 55 years (range, 4–69). The ASD was assessed at 0, 45 and 90° and the maximum colour Doppler jet width was recorded. An Amplatzer atrial septal occluder device was chosen based on the maximum CDJW and taking into consideration the presence or absence and floppiness of the surrounding rims. When the rims were floppy or absent in the aortic position, 4 mm was added to the maximum CDJW and when the rims were well developed and complete, 2 mm was added.

Results: Since June 2004 we have closed nine ASDs with this method. Median defect size on 2D echocardiography was 21 mm (range, 6–28). Median CDJW was 23 mm (range, 7–28). Devices used ranged from 11–32 mm, median of 26 mm. Median procedure time was 30 min (range, 20–64) and median screening time of 7 min (range, 4–12). All devices chosen by the colour jet width method were stable when tested and released without any embolisations. None of the patients had a residual atrial shunt the following day.

Conclusions: Transcatheter ASD closure with the Amplatzer atrial septal occluder without prior balloon sizing is feasible using the maximum colour Doppler jet width. Procedure time, fluoroscopy time and cost are reduced. Importantly, this method reduces the potential for significant device oversizing when balloon inflation overstretches the defect. This may reduce the (small) incidence of device erosion that has been reported recently.

P110**Severe congenital stenosis of aortic valve: results of balloon dilation in infants less than 6 months of age**

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Introduction: Balloon dilation of aortic valve has been shown to be an effective treatment for reducing aortic stenosis in neonates and infants.

Methods: We present the experience of our Center from 1991 to 2004 on 31 consecutive infants less than 6 months of age with cardiac failure caused by severe aortic stenosis who underwent 37 procedures of balloon dilations of aortic valve at a median age of 16 days (range 1–172) and a median weight of 3,3 kg (range 2,8–7,5). We examined mid-term results and determinants of survival in 3 subgroups: Group 1 normal dimension and contractility of left ventricle; Group 2 reduced contractility and dilated left ventricle; Group 3 reduced contractility and small left ventricle. Aortic valve morphology was bicuspid in 14 pts (45%).

The procedure was performed by a percutaneous right axillary approach in 23 pts and the size of the balloon was selected 1 mm less than the measured aortic anulus size; if an adequate relief of the stenosis was not achieved a balloon of the same size of the anulus was used.

Results: The systolic gradient across the valve decreased from a mean of 72 (32 mmHg to 23 ± 13 mmHg (72% reduction)). Aortic incompetence was present in all infants after dilation: mild in 24, moderate in 5, severe in 2. 7 patients died 2–33 days after the dilation and 6 were in the group with small left ventricle. Follow-up data were available in 23 survivors with a mean period of FU of 39 months (range 2–132). 4 infants (16%) developed restenosis 1–5 months after procedure and underwent a second balloon dilation. 1 patient died suddenly at home 8 months after dilation, 2 underwent surgery for subvalvular stenosis and 14 (58%) are in good conditions without therapy.

	Pts	Age (days)	Grad (mmHg)	Deaths
Grp1	14	44	87	0
Grp2	9	16	51	1 (11%)
Grp3	8	4	68	6 (75%)

Conclusions: Balloon dilatation of aortic valve is an effective treatment of severe aortic stenosis with low mortality and good mid-term results in infants with adequate dimensions of left ventricle and mitral valve.

P111**Microsurgical approach to avoid femoral artery thrombosis after balloon dilatation of critical left heart stenoses in premature infants**

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Balloon angioplasty is feasible even in neonates with body weights <2000 g. However, these procedures require special precautions to avoid temperature loss and arterial access is the major problem. An incidence of femoral artery thrombosis up to 62% has been reported (Magee, JACC 1997). Therefore, we decided not only to compress but to suture microsurgically the punctured vessel in very small infants.

In 2004, we performed balloon dilatation in 2 premature infants with body weights <1500 g and severe aortic valve stenosis or isthmic coarctation. In patient A (1400 g), echocardiography revealed a dysplastic aortic valve, a diameter of the aortic ring of 4.5 mm and a Doppler gradient of 100 mmHg. In patient B (1460 g), the Doppler gradient across the coarctation was 110 mmHg, systolic blood pressure was 120 mmHg in the upper and 60 mmHg in the lower extremities. Percutaneous access to the femoral artery was obtained using 23 Butterfly needles, 0.021-inch Nitinol wires, and 4 (A) or 3 French (B) sheaths. The patients were wrapped in cotton, and the catheter laboratory had been warmed up. The peak-to-peak gradient across the aortic valve was 71 mmHg (A) and 65 mmHg across the coarctation (B). Dilatation using a 4Fr 4.5 × 20 mm balloon over a 0.018-inch Nitinol wire and a 3Fr 3 × 20 mm balloon over a 0.014-inch Nitinol wire, respectively, resulted in reduction of the pressure gradient by 65% from 71 to 25 mmHg (A) and by 90% from 65 to 5 mmHg (B). Only minimal aortic regurgitation was found in patient A. In both patients, the sheath was removed by a plastic surgeon in the operation theatre and the artery was sutured under the microscope. Heparin (50 IU/kg body weight) was given when the arterial sheath was inserted and the patient remained on heparin infusion for 24 h.

Balloon angioplasty was performed successfully in both low weight premature infants. Microsurgical closure of the punctured vessel in the operation theatre was scheduled at the outset to reduce the risk for femoral artery thrombosis. Such an interdisciplinary cooperation may help to avoid arterial complications, the major problem of balloon dilatation of critical left heart stenoses in very small infants.

P112**Transcatheter closure of patent ductus arteriosus using Amplatzer duct occluder: a two years clinical experience**

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Transcatheter closure of patent ductus arteriosus (PDA) has become therapeutic of choice in many pediatric cardiac centers with excellent results. It has been performed world wide since over the last decade.

We report our early clinical experience in using Amplatzer duct occluder for closure of PDA.

Patients and Methods: From January 2002 to December 2004, 71 pts were diagnosed of PDA confirmed by echocardiography. The age ranged from 4–157 months (med age 55.6 month) and the weight of 5–33 kg (med weight 14 kg) and consist of 13 pts boys and 58 pts girls.

Results: Type of PDA according to criteria of Krichenco were A1 (47), A2 (15), A3 (5), B3 (1), C (2) and E (1). The diameter of PDA was 1.2–9.8 mm (med 3.7 mm) with flow ratio of 1.6–7.3 (med 2.0). The device size implanted ranged from 4–14 mm (med 6.0).

Immediately results were complete closure occur in 52 pts (73.2%), small residual shunts in 7 pts (9.8%) and smoky esidual shunts in 12 pts (16.9%). Follow up was performed after 24 hours, 1 month and 3 month by echocardiography. After 3 months, 70 pts from 71 (98.5%) and only 1 pt had small insignificant shunt.

Conclusion: Transcatheter closure of PDA using Amplatzer duct occluder is safe with high efficacy to close PDA. However, a long-term follow up is required to monitor the late results.

P113**Transcatheter closure of perimembranous ventricular septal defects using the Amplatzer perimembranous ventricular septal defect occluder in infants and children: further experience and intermediate-term follow-up**

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Introduction: There are very few reports in the literature of transcatheter closure of perimembranous ventricular septal defects (PMVSDs) using the Amplatzer PMVSD occluder with encouraging initial results. In this report, we present further experience and intermediate-term outcome in 39 patients with PMVSDs who underwent transcatheter closure with the Amplatzer PMVSD occluder.

Methods: Over a period of 32 months 39 patients aged 4 months to 14 years, with PMVSDs underwent transcatheter closure using the Amplatzer PMVSD occluder.

Results: The device was deployed successfully in 37/39 patients. Complete occlusion of the communication at follow-up occurred in 36/39 patients (92.3%). The main complications were device embolization into the descending aorta and transient complete heart block in 3 and 1 patient, respectively. In 2/3 patients with device embolization transcatheter removal of the device was successful and the defect was closed using other occluder. In 1 patient with embolization and an associated large and long septal aneurysm the device was removed through a femoral artery cut-down and the defect was surgically closed. No device failure or other complications were observed during a mean follow-up of 15 months (range 1 to 32 months).

Conclusions: The Amplatzer PMVSD occluder is an efficient device that can be safely used in selected patients with PMVSDs. Further studies and long-term follow-up are required before this technique enters routine clinical practice.

P114**Combined transcatheter and surgical management of a complex case of interrupted aortic arch**

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Introduction: Postoperative course after neonatal aortic arch reconstruction with circulatory arrest remains difficult especially with single ventricle physiology. Neurological morbidity is not negligible. Neonatal stenting of the ductus arteriosus (DA) is currently performed in some heart diseases such as HLHS.

Methods and Results: A 3.2kg baby-boy was born full term after prenatal diagnosis of double inlet left ventricle with truncus arteriosus type II and suspicion of interrupted aortic arch (IAA). Fetal karyotyping was normal and FISH analysis didn't show 22q11 microdeletion. Postnatally, IAA type C was confirmed by echocardiography by constriction between the right innominate artery (RAI) and the left carotid artery at ductal closure. Prostaglandins were started. To avoid prolonged circulatory arrest, per-operative stenting of the DA and branch pulmonary artery (PA) banding was decided. Through a median thoracotomy, a 7F sheath was inserted into the main pulmonary artery. An auto-expendable stent (8mm–2cm) was positioned into the aortic arch between

the RIA and the descending aorta under fluoroscopy. Bilateral branch PA's banding was performed with 3.5mm Goretex[®] shunts (for diameter calibration). The child was kept on prophylactic dosis of low molecular weight heparin and aspirin[®]. At 3 months, follow up heart catheterization showed a large aortic arch without any significant gradient but obstruction of the RIA, probably secondary to ductal constriction, as no clot was visualized at subsequent surgery (Figure). At 6 months, the child underwent aortic arch reconstruction, including removal of the stent, RIA reimplantation together with a bidirectional superior cavopulmonary anastomosis. Immediate postoperative period was marked by profound cyanosis due to left PA compression and the opening of a large decompressing venous collateral between the SVC and the IVC. The collateral was embolized. Left PA balloon dilation was not efficient and a stent was placed and dilated to 6mm. Postoperative brain ultrasound was normal. The child is now 8.5 months old with normal development, a transcutaneous saturation of 84% and no aortic arch gradient.

Conclusions: Temporary stenting of an IAA is feasible and allows to postpone complex aortic arch repair, including stent removal, after the critical neonatal period.

**P115****Angioplasty and stent implantation in cardiac defects from the axillary and carotid artery in critically ill low birth weight neonates and infants less than one year of age**

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Introduction: Low birth weight infants with critical cardiac defects can be addressed by interventional procedures to stabilize heart function before surgery. Femoral arterial access is often impossible due to low flow and small vessel size. We describe a series of patients that could be palliated by transcatheter intervention with access from the axillary/carotid artery.

Patients and Methods: From 9/98–12/04, 19 transcatheter interventions were performed in 17 patients with congenital heart defects weighing 1.2–4.9 kg (m = 2.9 kg).

Diagnoses: Aortic coarctation (n = 7), interrupted aortic arch (n = 1), HLHS (n = 1), aortic valve stenosis (n = 2), tricuspid

atresia (n = 1), pulmonary atresia (n = 4), TOF (n = 1). Balloon dilatation was performed for aortic valve stenosis (n = 3), aortic coarctation (n = 6). Stents were implanted in the arterial duct (n = 6), AP-shunt (n = 1), aortic coarctation (n = 3).

Arterial access was reasonable from the axillary artery (AA) (n = 17) or from the carotid artery (n = 2) to save the femoral arteries, because of favourable anatomy to enter a stenotic shunt/arterial duct and due to obstructed femoral arteries after prior catheterization procedures. Two patients needed cut down of the axilla, the others were punctured percutaneously. No introducer sheaths larger than 4–5 F were used.

Results: Entering the AA was possible in all. Pressure gradients across aortic coarctation and aortic valve were reduced effectively. Stent implantation was successful in all but one, where the dislodged stent was removed surgically. There was one thrombotic occlusion of the AA, where first lysis was installed and 6 days later an aneurysm was resected in a 1.2 kg baby. Blood transfusion was necessary in 3 patients. There were no other vessel complications. All patients could be stabilized by the intervention besides one, who died despite successful intervention. Most interventions were planned to palliate the patients for later surgery. Re-dilatation/surgery were performed in 10 patients, two died of heart failure because of their heart defect, four did not need further treatment in follow up.

Conclusion: Arterial access from the axillary or carotid artery should be considered in low birth weight infants with critical congenital heart defects to save femoral artery perfusion. Complication rate is low and the procedure is facilitated with respect of the anatomy.

P116

In vitro fabrication of a tissue engineered human cardiovascular patch for future use in cardiovascular surgery

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Objective: One approach to tissue engineering has been the development of in vitro conditions for the fabrication of functional cardiovascular structures intended for implantation. In the experiment, we developed a pulsatile flow system that provides biochemical and biomechanical signals in order to regulate autologous patch-tissue development in vitro.

Methods: We constructed a biodegradable patch scaffold from a porous poly-4-hydroxy-butyrate (P4HB; pore size: 80–150 micron; Tefco Inc., USA). The scaffold was seeded with pediatric aortic cells. The cell-seeded patch constructs were placed in a self-developed bioreactor for 7 days to observe potential tissue formation under dynamic cell culture conditions. As a control, cell-seeded scaffolds were not conditioned in bioreactor system. Following maturation in vitro, the analysis of the tissue engineered constructs included biochemical, morphological and immunohistochemical examination.

Results: Macroscopically, all tissue engineered constructs were covered by cells. After conditioning in the bioreactor, the cells were mostly viable, had grown into the pores and formed tissue on the patch construct. Electron microscopy showed confluent smooth surfaces. Additionally, we demonstrated the capacity to generate collagen and elastin under in vitro pulsatile flow conditions in biochemical examination. Immunohistochemical examination stained positive

for alpha smooth muscle actin, collagen type 1 and fibronectin. There was minor tissue formation in the non-conditioned control samples.

Conclusions: Porous P4HB may be used to fabricate a biodegradable patch scaffold. The cells attached themselves to the polymeric scaffold, and extracellular matrix formation was induced under controlled biomechanical and biodynamic stimuli in a self-developed pulsatile bioreactor system.

P117

5 years of telemedicine

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Telemedicine allows the pediatric cardiologist to diagnose cardiac disorders at a distance and in real time. Since 1998, through a program sponsored by PT Inovação, Portugal, we have diagnosed and followed up 1056 children.

Telemedicine in Paediatric Cardiology is a viable means of diagnosing cardiac disorders, with results that are similar to those obtained in conventional consultations. To those involved, it offers professional gratification, shortens waiting list, provides faster management strategies and improves the quality of life of those requiring it.

During this period, 1761 consultations were done between our Department and the regional district hospitals, with a weekly session per hospital.

The main reason for referral was a cardiac murmur (73%). In 49%, no cardiac defects were found. Of the septal defects (43%), the most frequently diagnosed was the Ventricular Septal Defects (20%). Approximately 10% of the consultations required reevaluation. Only 6 consultations were done as emergencies.

In conclusion, consultations via telemedicine has become a practical and viable way of excluding cardiac pathologies, with results identical to conventional consultations. The overall costs are reduced, namely those related to transport and time off work. The waiting time is also reduced, as is the starting of specific management. A Paediatric Cardiologist, can thus, provide assistance to a considerably larger area and a greater number of patients, as well as providing education at a distance through the sharing of knowledge.

P118

Blood-myocardial contrast optimization in 3D True-FISP cardiac imaging at 1.5 T

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Introduction: True fast imaging with steady precession (True-FISP) techniques are frequently applied for magnetic resonance imaging (MRI) of coronary arteries, intra-cardiac morphology and extra-cardiac vessels. Recently, the T2 magnetization preparation was suggested to enhance the blood-myocardial contrast in 3D True-FISP sequences. The purpose of this study was to assess two steady state preparation schemes in combination with the T2 preparation in order to improve contrast between blood and myocardium. The steady state preparation method of an alpha/2 pulse (alpha is data acquisition RF-pulse flip angle) followed by constant flip angle preparation cycles (CFA) and linear flip angle preparation (LFA)

were compared. Numerical simulations and in-vivo studies were performed.

Methods: A T2 preparation pulse was implemented on a commercial 1.5 T scanner (Siemens Medical Solutions, Erlangen, Germany) in a 3D navigator gated True-FISP sequence (TE/TR = 1.9/3.8 ms, $\alpha = 60\text{--}110^\circ$, $TE_{T2\text{prep}} = 48$ ms, voxel-size = $2 \times 2 \times 2$ mm³). CFA and LFA preparation schemes with twenty preparation cycles were used. The relative blood-myocardial contrast was numerically simulated and tested in-vivo as a function of the number of RF excitations and the flip angle for CFA and LFA

Results: Numerical simulations showed higher blood to myocardium contrast using the CFA preparation compared with LFA preparation (Fig. 1). For example with CFA preparation an increase of the flip angle from 65° to 110° resulted in a relative contrast increase of 1.37, whereas LFA preparation obtained only an increase of 1.11. For flip angles 65° , 90° , and 110° relative contrast ratios between CFA/LFA of 1.25, 1.40 and 1.54 were calculated.

Theoretical results were confirmed in-vivo. Increasing the flip angle from 65° to 110° , the relative contrast in images with CFA increased by 1.42. LFA showed lower increase by 1.15. The relative contrast between CFA/LFA of 1.15, 1.25 and 1.40 were measured for 65° , 90° and 110° flip angles.

Conclusions: The steady state CFA preparation leads to increased relative contrast between blood and myocardium in T2 prepared 3D True-FISP imaging. Contrast ratios (CFA/LFA) increase with larger flip angles. High correlation between numerical and in-vivo data is shown. The CFA preparation may improve imaging results of coronary arteries, intra-cardiac blood pool and extra-cardiac blood vessels.

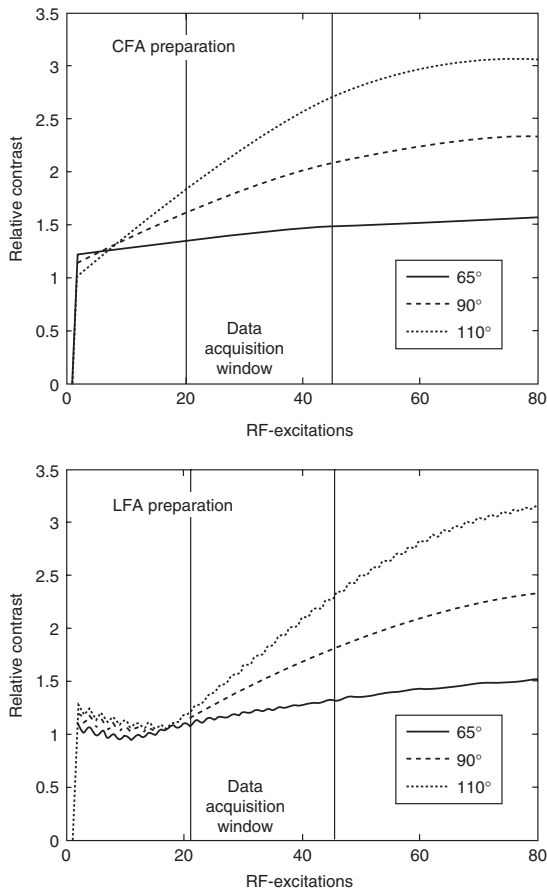


Figure 1. Numerical simulations of the relative contrast between blood and myocardium using True-FISP with CFA and LFA steady state preparation for flip angles of 65° , 90° and 110° .

P119

Non-invasive quantification of stent stenosis using MRI

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Objective: Endovascular stents with MRI-compatible artifact behavior were recently reported. The aim of this study was to determine the accuracy of MRI for quantitative assessment of in-stent stenosis as compared to invasive angiography in MRI-compatible iliac artery stents.

Material and Methods: A total of 8 MRI-compatible custom-made stents (MRI stents) and 8 control stents (Flexx, Bard/Angiomed) were tested in 4 in-vivo experiments (swine).

All stents evaluated were self-expanding nitinol stents (diameter = 8 mm). The MRI stents had weakly paramagnetic wire mesh with a specification designed to minimize susceptibility and radiofrequency shielding. The lumen of 4 control and MRI stents was prepared with a Dacron mesh to create vascular obstruction after implantation. All stents were delivered into the iliac artery using a transcatheter technique and investigated 9 weeks after implantation with MRI (1.5 Tesla) and conventional angiography. MRI was based on (1) contrast medium enhanced MR angiography (MRA) and high resolution inflow gradient echo images (GRE) (pixel dimension = 0.8 mm³). Conventional angiography was performed immediately after MRI. The degree of in-stent stenosis was quantified and the results of both techniques compared using Bland-Altman test. After completion of the experiments the animals were euthanized and the stents inspected post mortem.

Results: Significant in-stent stenosis was observed in the stents prepared with Dacron mesh, whereas no other stents were stenosed. On MRA and GRE there was significant radiofrequency shielding within the lumen of the control stents (signal intensity = 322 ± 45 units) but not in the MRI stents (signal intensity = 1233 ± 122 units) ($p < 0.001$). In turn, in-stent stenosis was revealed with MRA and GRE only in the MRI stents. GRE allowed direct visualization of thrombus and tissue ingrowth at the site of stent stenosis, which could be clearly differentiated from the patent lumen. A mean stent stenosis of $58 \pm 21\%$ was measured with GRE and conventional angiography in the stents with Dacron mesh and of $2 \pm 2\%$ in the other stents. Bland-Altman test showed excellent agreement between measurements by MRI and conventional angiography.

Conclusion: Stenosis within the lumen of nitinol stents can be directly visualized and accurately quantified using MRI.

P120

Simulator for training in multiplane transesophageal echocardiography (TEE). Presentation and preliminary results

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Objectives: TEE requires visual-perceptive (interpretation of the images) and sensorimotor (steering of the probe) skills, both of which cannot be taught adequately by lectures or textbooks. In addition examinations performed by a beginner might pose the patient at risk. New learning media like computer simulators might overcome these problems.

Methods: We have designed a Java-based TEE simulator that addresses these problems.

Results: On a computer screen a side-by-side presentation of a three-dimensional (3D) virtual reality scene on the right side and a two-dimensional echocardiographic (2DE) view on the left side is given. The virtual scene consists of a 3D heart model and an animated TEE probe with scan plane. The 2D view is calculated from real 3DE data sets that are registered with the heart model to achieve spatial and temporal congruency. The displayed 2DE view is defined and controlled by the orientation of the virtual scan plane. Since the 2D views are derived from a 3D echocardiographic data set in real time they are not restricted by pre-recorded views but the beginner can interactively explore the heart by manipulating the virtual TEE probe. A dummy TEE probe with an attached 3D tracking system is inserted into a dummy torso. Through a calibration the spatial relationship between this dummy probe and the dummy torso is the same as the relationship between the virtual TEE probe and the virtual heart on the computer screen. Any manipulations of the dummy TEE probe (moving the probe, angulation of the tip and rotating the scan plane) are transferred to the application showing the 2D views that would be achieved if a "real" patient would be scanned.

Discussion: In pediatric cardiology TEE is performed less often than in adult cardiology. Therefore it is often difficult to accomplish proficiency in a reasonable time. Training on simulators is very realistic, helping the beginner to achieve proficiency faster without posing patients at risk. The virtual scene of our simulator provides additional spatial information that helps beginners in getting a perception of the 3D anatomy of the heart.

Paediatric Cardiac Intensive Care (see also

OP23-10)

P121

N-BNP: a potential useful tool in the management of newborn with right ventricular obstruction

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Objective: In adults, levels of the aminoterminal brain-type natriuretic peptide (N-BNP) have been used as a non-invasive marker of ventricular dysfunction and a prognostic indicator. Although its utility in pediatrics was recently suggested, its value in congenital heart diseases with right ventricular overload is not defined. The purpose of this study was to determine N-BNP plasmatic levels in newborns with critical right ventricular obstruction.

Material and Methods: Seven newborns with critical obstruction of right ventricle (six with critical pulmonary stenosis and one with pulmonary atresia and intact ventricular septum) where enrolled in a prospective study, from January to December of 2004. Clinical data included associated diagnosis, blood arterial pressure, requirement for mechanical ventilation and therapeutic with prostaglandin E1. Echocardiography was performed to evaluate direction of the shunt at patent foramen ovale, tricuspid regurgitation and estimated right ventricular systolic pressure. All newborns underwent therapeutic cardiac catheterization in the first days of life. Before injection of contrast product and therapeutic procedure, blood samples were collected to N-BNP measurement and, simultaneously, right ventricular systolic and end-diastolic pressures assessed. Plasmatic levels of N-BNP were compared with a healthy age-matched group. Correlation coefficient between plasma peptide levels and hemodynamic variables were calculated by linear regression analysis.

Results: All newborns with critical right ventricle obstruction were managed with prostaglandin E1, one needed mechanical ventilation and no one had associated malformations. In echocardiographic assessment all newborn had signs of ventricular overload, as severe tricuspid regurgitation, right-to-left shunting at patent foramen ovale and high estimated right ventricular pressure to mean blood pressure ratio ($>2/3$). We found a significantly high value of N-BNP in all patients (2653 ± 1383 pg/dl). Furthermore, we found a positive and significant correlation between N-BNP level and systolic right ventricular pressure ($r = 0.81$; $p < 0.05$).

Conclusions: We demonstrated that, in newborns, plasmatic N-BNP correlate with the level of right ventricular pressure overload. Since plasmatic N-BNP reflects ventricular stress it could be an additional parameter useful in the evaluation and management of newborns with right ventricular obstruction.

P122

Benefit of autologous blood donation in paediatric cardiac surgery

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Objective: In scheduled open heart surgery preoperative autologous blood donation (ABD) is an effective method to avoid the need of homologous blood transfusion. Although the risks of transfusion-transmitted diseases like acquired immunodeficiency syndrome, hepatitis and graft-versus-host disease have been reduced widely, immunosuppression with increasing risk of postoperative infection and expression of irregular antibodies still remain severe problems.

Patients and Methods: Our institution offers ABD to children >20 kg undergoing elective cardiac surgery. Thirty five patients with a median age of 14 years (range 10 to 18 year) and a median weight of 51 kg (range 26 kg to 92.8 kg) donated blood preoperatively with an average volume of 300 to 900 ml regarding individual conditions.

Results: A wide spectrum of operations (valve replacement 19, valve annuloplasty 5, arterial and cavopulmonary shunts 3, ASD- and VSD-closure 5, CoA repair 3) was performed after autologous blood donation. 16 patients underwent primary surgery, 19 procedures were reoperations. Total operation time was 102 to 534 min (median 256 min). The cardiopulmonary bypass time was 27 to 168 min (median 104.5 min), 3 operations were done without extracorporeal circuit. Only 1 patient needed additional blood transfusion already during the operation. Five more patients received allogenic blood transfusions in the postoperative period.

Conclusion: Thus, homologous blood transfusion was avoided in 83% (29/34) of our paediatric patients after autologous blood donation. Patients benefited from ABD as a safe procedure to prevent complications related to blood transfusions. Therefore, the efforts to advice and undertake ABD should be intensified in the appropriate group of patients.

Psychosocial Issues

P123

Intellectual performance and quality of life in children with a surgically corrected congenital heart defect six to twelve years postoperatively

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Objectives: To investigate the intellectual and cognitive performances of children with surgically corrected congenital heart defects six to twelve years postoperatively and to find pre-, peri-, and/or postoperative predictors for the possible cognitive dysfunctions.

Methods: Six to twelve years postoperatively, 47 children with various congenital heart defects were tested individually with a short form intelligence battery (WISC-III-NL) and a developmental neuropsychological assessment battery (NEPSY). Pre-, peri-, and postoperative variables were taken from the medical files.

Results: Performances on the short form intelligence battery appeared to be within the normal range (M: 100, SD: 15): verbal intelligence (VIQ) (M: 111.8, SD: 17.75), performal intelligence (PIQ) (M: 114.7, SD: 32.94), total intelligence (TIQ) (M: 114, SD: 25.44). However, as opposed to normative data a higher proportion of the heart group (22%) had a PIQ lower than 85. No child had an IQ lower than 70. On the NEPSY-scales the heart group also performed within the normal range (M: 100, SD: 15) on attention and executive functions (M: 109.5, SD: 10.48), memory (M: 99.7, SD: 14.52), language (M: 100.9, SD: 14.48), visuospatial skills (M: 116.7, SD: 16.55) and sensor-motor functions (M: 85.5, SD: 11.43). On the domains memory and sensor-motor functions respectively 17% and 48% of the heart group performed lower than 85 (thus one or more than one standard deviation below the normal performance). Concerning the medical variables we found no significant predictors for intelligence but for the NEPSY-domains memory, visuospatial skills and sensor-motor functions the duration of the extracorporeal circulation explains a high proportion of the variance on the performances on these domains.

Discussion: Six to twelve years postoperatively, we found most of the children with a surgically corrected congenital heart defect to have a normal intelligence and normal neurocognitive functions. A certain group however appears to have difficulties concerning PIQ and memory. Almost 50% of these children show sensor-motor dysfunctions. The duration of the extracorporeal circulation was found to be a significant predictor for the performances on memory, visuospatial skills and sensor-motor functions. The underlying pathophysiological mechanism needs to be further elucidated.

Surgery in Congenital Heart Disease (see

also OP23-11-12)

P124

Outcomes and associated risk factors of aortic valve replacement in 160 children: a competing-risks analysis

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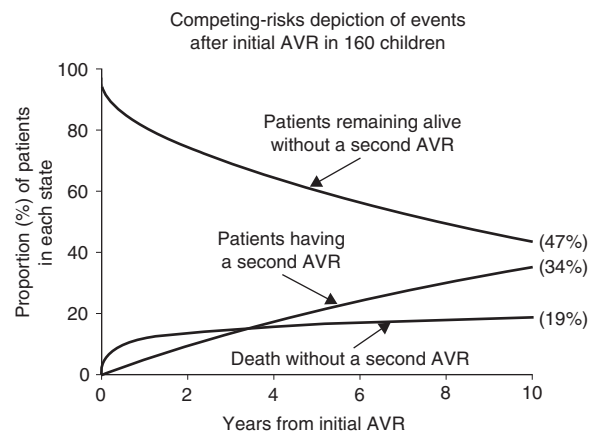
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Introduction: We sought to define patient characteristics, outcomes, and associated risk factors after aortic valve replacement (AVR) in children.

Methods: Clinical records from children undergoing AVR between 1974–2004 at our institution were reviewed. Competing-risks methodology determined the time-related prevalence of three mutually exclusive end-states: death, repeat replacement, and survival without subsequent AVR. Risk factors for death and re-replacement after initial AVR and after a second AVR were also sought. Longitudinal echocardiographic data were analyzed using mixed linear regression models. Underlying aortic valve disease was congenital in 76%, rheumatic 7%, associated with truncus arteriosus 4% or Shone's anomaly 4%, isolated endocarditis 2%, or other in 7%. Primary regurgitation was present in 46%, stenosis in 21%, and both in 33%, with 76% having undergone outflow tract intervention.

Results: 160 children had 198 AVR's, with 33 having more than one. Initial prosthesis type was Bjork–Shiley in 24%, autograft in 18%, homograft in 18%, St. Jude Medical 17%, Hancock 9%, and other types in 14%. Competing-risks analysis predicted that after 10 years from initial AVR, 19% had died without subsequent AVR (steep early and late phase), 34% underwent a second AVR (constant and late phase), and 47% remained alive without replacement, (Figure). Risk factors for death without a second AVR included lower weight ($P < 0.001$), younger age at AVR ($P = 0.04$), performance of aortic root replacement or arch reconstruction together with AVR ($P = 0.03$), and non-autograft use ($P = 0.03$). Incremental risk-factors for a second AVR included earlier year of operation ($P = 0.04$), and implantation of a bioprosthetic or homograft valve ($P = 0.004$). A second competing-risks analysis predicted that after 10 years from the second AVR, 53% underwent repeat replacement, 10% had died without subsequent re-replacement, and 37% remained alive without re-replacement. Regression analysis of repeated echo measurements showed that pulmonary autograft use was associated with slower progression of peak aortic gradient ($P = 0.002$) and smaller left ventricular dimension (LVEDD) ($P = 0.04$).

Conclusions: Mortality and valve re-replacement are common after initial AVR in children especially in younger patients and those with bioprosthetic or homograft valves. Pulmonary autograft use is associated with decreased risk of death, slower gradient progression and smaller LVEDD.



P125

Neonatal aortic commissurotomy for critical aortic stenosis: surgical treatment of a valvular or a myocardial disease?

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Introduction: Critical aortic stenosis is a severe heart disease, burdened by high mortality and reintervention. Determinants of outcome and criteria for surgical or percutaneous treatment have not been determined.

Methods: From January first 1990 to January first 2004, 32 consecutive newborns with critical aortic stenosis (median age and weight 21 days and 3.2 kg) underwent surgical valvotomy by the same surgeon. We evaluated the early and long term results and attempted to identify the predictors of outcome.

Results: Five patients had associated mitral valve dysplasia, 5 aortic coarctation, 13 endocardial fibroelastosis, 9 needed PGE1. Eighteen infants had hypertrophic normokinetic and 14 dilated hypokinetic left ventricle. Six hospital deaths occurred (19%), all in infants with subnormal fractional shortening (FS). Immediately

after surgery FS increased from 30 to 36%. Three patients needed a Ross operation at 1, 4 and 5 years, respectively. There were no late deaths. Low FS, low mean aortic gradient and small aortic annulus were highly correlated with fatal outcome. Small aortic annulus and endocardial fibroelastosis were predictive of early reintervention. At a median follow up of 6 years all children have a normal ventricular function, 2 have a mean aortic gradient higher than 35 mmHg and 4 more than mild aortic incompetence. **Conclusions:** Our data demonstrate that neonatal surgical valvotomy is an optimal therapy for patients with normokinetic left ventricle. On the contrary, a 43% mortality was found in patients with hypokinetic left ventricle. Percutaneous valvotomy could be preferred to surgical valvotomy, at least as a bridge to surgery, in infants with depressed ventricular function.

P126

Independent factors associated with mortality and achievement of complete repair in pulmonary atresia with ventricular septal defect

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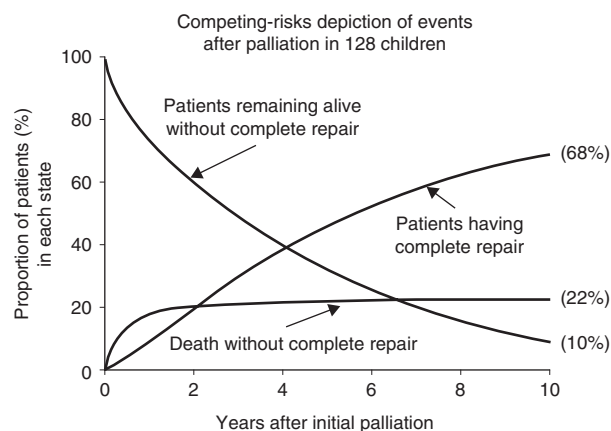
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Background: We sought to describe morphologic characteristics, particularly pulmonary anatomy, and to determine the prevalence of definitive end states and their determinants in children with pulmonary atresia associated with ventricular septal defect (VSD). **Methods:** From 1975–2004, 220 children with pulmonary atresia/VSD underwent 404 operations at our institution. Medical records were reviewed. Echocardiograms and angiograms at presentation and at last follow-up were reviewed blindly to characterize anatomy and bronchopulmonary segment arterial supply. Competing-risks methodology was used to determine the prevalence and associated risk-factors for the time-related events of death, complete repair and reintervention for right ventricular outflow tract (RVOT) or pulmonary artery (PA) obstruction.

Results: The majority (52%) had muscular pulmonary atresia and a single perimembranous VSD (85%). The main PA was present in 62%, and 86% had confluent branch PA's. Major aortopulmonary collaterals (MAPCA's) were present in 31%. No reparative operation was performed in 35 patients; 9 have survived. The presence of MAPCA's was significantly associated with nonoperative management (OR 1.4; $p < 0.001$). Initial operation in the remainder included systemic-PA shunt 57%, complete primary repair 31%, or RVOT reconstruction only in 12%. Overall survival from initial operation was 83%, 74%, and 71% at 1, 5 and 10 years. Incremental risk-factors for death after initial operation (steep early phase) included younger age, earlier birth cohort, fewer bronchopulmonary segments supplied by the true PA's, more unperfused segments, and initial placement of a systemic-PA shunt. Competing-risks analysis for those initially palliated predicted that after 10 years, 68% had achieved complete repair (with associated factors including later birth cohort and more bronchopulmonary segments supplied by the true PA's), 22% had died without complete repair, and 10% remained alive without complete repair. Reoperations were performed in 38 children after complete repair, and catheter reinterventions occurred in 75. A second competing-risks analysis predicted that at 5 years after complete repair, 28% had a second operation, 12% had died without a second operation, and 60% remained alive without subsequent operation.

Conclusions: Outcomes in children with pulmonary atresia/VSD have improved over time. Bronchopulmonary arterial supply is an

important determinant of mortality and achievement of complete repair.



P127

Pulmonary atresia with ventricular septal defect (PA-VSD) and major aorto-pulmonary collateral arteries (MAPCAs): surgical strategy and results

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Introduction: Surgical treatment of pulmonary atresia with ventricular septal defect and MAPCAs is still considered a surgical challenge.

Methods: In order to establish the best strategy of treatment and predictors of outcome we reviewed our institutional experience concerning 47 infants operated by the same surgeon.

Results: Thirty-one patients had confluent (type 3) and 16 absent (type 4) central pulmonary arteries (PAs). The median number of pulmonary segments was 18 in type 3 and 12 in type 4 ($p < 0.05$). The median number of MAPCAs was 2 in type 3 and 3 in type 4. PAs were considered to be adequate when they measured >4 mm. There were 8 deaths (17%): 3 perioperative (1 type 3, 2 type 4) and 5 late (4 type 3, 1 type 4). Complete repair was performed in 24 patients (17 in type 3 and 7 in type 4). One stage complete repair was performed in 3 patients, two-stage repair in 11 and greater than three-stage repair in 10. Twelve patients are waiting for complete repair. Patients expected to attain a complete repair are 75% in group 3 and 56% in group 4. Only 56% of patients with PA-VSD type 3 having had a complete had adequate central PAs; 94% have a right/left ventricular pressure <0.5 and 6% <1 . Among patients with PA-VSD type 4 having had a complete repair, 14% have a right/left ventricular pressure <0.5 , 71% <1 and 14% >1 .

Conclusions: Our data show that the quality of pulmonary vascularisation is the best predictor of complete repair; however, patients without central PAs are expected to have higher RV pressure. The small size of central PAs does not prevent a positive outcome.

P128

Surgical approach to the aortic valve in young patients

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Objective: To report our approach to the diseased aortic valve in young patients.

Material and Methods: From 1/2001 to 10/2004, 66 patients with a median age of 14 years (range: 1 week to 35 years) were operated

on because of aortic stenosis, insufficiency, or both. The valve was reconstructed in 24 pts (using a technique of tricuspidisation of a bicuspid valve in 8 pts) and replaced by a pulmonary autograft (Ross procedure) in 42. A classical mechanical valve or bioprosthesis was not inserted. 15 patients underwent an additional cardiac surgical procedure.

Results: There was no operative death. There were no signs of myocardial infarction. Post-operative complications included the drainage of 1 chronic pericardial hematoma. Two patients underwent re-interventions due to endocarditis and a stenosis of the RVOT conduit. Normalisation of the LV function and morphology occurred in all the patients at 3 months. Patients were not anticoagulated and none sustained a thrombo-embolic event. The repair or replacement has been stable in all the patients with a median follow-up of 25 months (range: 1 month–5.5 years).

Conclusion: Aortic valve reconstruction or replacement with an autograft leads to excellent early results with minimal morbidity. Because of the absence of a residual gradient, it leads to regression of hypertrophy and recovery of the LV function. In the young, active patients, this approach is superior to the implantation of a classical mechanical or biological prosthesis.

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Blood vs crystalloid cardioplegia in pediatric surgery: uptake/release of substrates and amino acids

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Introduction and Objective: We previously reported that blood cardioplegia (CP) preserves LV-function better than crystalloid CP and prevents myocardial lactate release early after cardioplegic arrest (in contrast to crystalloid CP). In this study we expand the metabolic focus to include myocardial substrates and amino acids. It was hypothesized that blood CP maintains a more normal substrate metabolism than crystalloid CP after resumption of coronary blood flow.

Methods: 30 consecutive infants with complete AV-defects were randomly allocated to blood or crystalloid CP. Arterial and coronary sinus blood was sampled after weaning off bypass and during the following hour. Oxygen content, free fatty acids, glucose, lactate and amino acids were analyzed. Myocardial metabolism was estimated by calculating concentration differences between arterial and coronary sinus blood. A positive value indicates myocardial uptake and a negative value indicates myocardial release.

Results: After blood CP a significant uptake of free fatty acids was observed. The uptake matched oxygen uptake. A significant release

of alanine was observed. After crystalloid CP there was a significant uptake of glutamate, leucine, isoleucine ($p = 0.059$) and lysine. A significant release was found for lactate, alanine, and glutamine.

Conclusion: Blood CP maintains a more normal substrate metabolism after resumption of coronary blood flow in pediatric heart surgery with complete AV-defects than crystalloid CP, where uptake of amino acids and lactate release are prominent features.

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Results and short-term outcome after early primary repair of Taussig Bing anomaly

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Purpose: To review the experience with early one-stage repair of Taussig Bing anomaly in a single institution.

Patients and Methods: From 1999 to 2004, 12 consecutive patients (11 neonates, 1 infant), median age at operation 6,0 days (range: 3–124 days) underwent primary one-stage repair of this anomaly. Median weight was 2,8 kg (range 1,8 to 5,8 kg). Six patients had associated critical coarctation, 3 patients had a hypoplastic aortic arch, 1 patient an interrupted aortic arch and in 2 patients the aortic arch was considered to be wide enough. Significant coronary abnormalities were found in 4 cases. Primary repair included: arterial switch operation with VSD closure (N = 12), additionally extended end-to-end anastomosis of the aortic isthmus in 6 patients and aortic arch reconstruction using antegrade cerebral perfusion in 4 patients. Median follow-up: 36 months (2,9–90 months)

Results: There were no early and late deaths. One of the 2 patients who had no initial aortic arch repair needed coarctation repair at 3 months; 1 child needed balloon dilatation of a re-coarctation 12 months after surgery. Re-operation was necessary in 4 more patients: change of an infected VSD patch at 27 days N = 1, patch enlargement of supravulvar pulmonary stenosis (PS) N = 2 at 9 and 19 month respectively, 1 of them needed an additional infundibular resection due to sub-PS; a RV to PA homograft due to significant hypoplasia of the pulmonary trunk was necessary in 1 patient at 1 month. Six patients are free from re-operations. Two of these patients (38, 28 months) developed significant supravulvar PS awaiting patch enlargement in the near future. One patient has sub aortic stenosis (65 mmHg gradient) 6 months after surgery. Moderate delay of neurological development necessitating physical therapy is present in 1 patient. No patient is on long-term medication.

Conclusions: Early primary repair of Taussig Bing anomaly can be achieved with low mortality and morbidity. However, need for re-operation within the first year of life was high. Nevertheless, short-term outcome seems to be good.