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Review

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The effects of percutaneous branch pulmonary artery interventions on exercise capacity, lung perfusion, and right ventricular function in biventricular CHD: a systematic review

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Abstract

Background: Branch pulmonary artery stenosis is common after surgical repair in patients with biventricular CHD and often requires reinterventions. However, (long-term) effects of percutaneous branch pulmonary artery interventions on exercise capacity, right ventricular function, and lung perfusion remain unclear. This review describes the (long-term) effects of percutaneous branch pulmonary artery interventions on exercise capacity, right ventricular function, and lung perfusion following PRISMA guidelines. *Methods:* We performed a systematic search in PubMed, Embase, and Cochrane including studies about right ventricular function, exercise capacity, and lung perfusion after percutaneous branch pulmonary artery interventions. Study selection, data extraction, and quality assessment were performed by two researchers independently. *Results:* In total, 7 eligible studies with low (n = 2) and moderate (n = 5) risk of bias with in total 330 patients reported on right ventricular function (n = 1), exercise capacity (n = 2), and lung perfusion (n = 7). Exercise capacity and lung perfusion seem to improve after a percutaneous intervention for branch pulmonary artery stenosis. No conclusions about right ventricular function or remodelling, differences between balloon and stent angioplasty or specific CHD populations could be made. *Conclusion:* Although pulmonary artery interventions are frequently performed in biventricular CHD, data on relevant outcome parameters such as exercise capacity, lung perfusion, and right ventricular function are largely lacking. An increase in exercise capacity and improvement of lung perfusion to the affected lung has been described in case of mild to more severe pulmonary artery stenosis during relatively short follow-up. However, there is need for future studies to evaluate the effect of pulmonary artery interventions in various CHD populations.

Life expectancy of patients with CHD has significantly increased over the last decades, which shifts the focus to the treatment of long-term morbidity.[1,2] In 20–82% of the patients with biventricular CHD, a reintervention is required during their life.[3–7] Right ventricular outflow tract obstructions are the most common cause for reinterventions of which percutaneous interventions for branch pulmonary artery stenosis account for a significant number.[3,5,6,8,9] Branch pulmonary artery stenosis might result from different underlying mechanisms such as pulmonary coarctation, hypoplastic native pulmonary arteries, stenosis of anastomosis sites, iatrogenic obstruction by previous aortopulmonary shunt, compression of the pulmonary artery branch by an enlarged aorta, or the neo-pulmonary to neo-aortic geometry.[10–12] Research has shown that branch pulmonary artery stenosis is associated with a reduced exercise capacity, lower peak oxygen consumption, and higher minute ventilation during exercise in patients with transposition of the great arteries and tetralogy of fallot.[13,14] This suggests that branch pulmonary artery stenosis has a significant effect on the exercise capacity in these patients. Percutaneous balloon angioplasty and stent implantation in branch pulmonary artery stenosis have been proven safe and effective in patients with CHD.[15–17] However, the (long-term) outcomes on exercise capacity, right ventricular function, and lung perfusion remain fairly unknown. Therefore, the aim of this review was to describe the (long-term) effects of percutaneous branch pulmonary artery interventions on exercise capacity, right ventricular function, and lung perfusion in biventricular CHD.

Methods

Prospective registration

The protocol and search string of this review were constructed by two researchers (RSJ and JPBF). The review was conducted according to the Preferred Reporting Items for Systematic Reviews (PRISMA) guidelines and was registered in PROSPERO International Prospective Register of Systematic Reviews (PROSPERO registration number: CRD42022306617).

Eligibility and exclusion criteria

Studies were included if they reported follow-up data after percutaneous interventions for branch pulmonary artery stenosis in biventricular CHD on at least one of the following outcomes: exercise capacity, right ventricular function, or lung perfusion. All age groups and type of study designs were included. Studies exclusively reporting on branch pulmonary artery stenosis in relation to pathological vessel disease (e.g. Williams or Alagille), single ventricle physiology, a systemic right ventricle, or other locations (right ventricular outflow tract, main pulmonary artery and peripheral pulmonary vessels) were beyond the scope of this review. Other exclusion criteria were studies exclusively reporting on surgical treatment, technical success, safety, efficiency and complications for branch pulmonary artery stenosis, articles that did not include at least one our outcomes of interest, experimental studies, no primary research articles (e.g. reviews, editorials, and commentaries), and articles with no full text available.

Search strategy and data extraction

A systematic search, screening, full-text review, and data extraction for articles from January 1975 to January 10, 2022, on PubMed, Embase, and Cochrane were conducted by two researchers independently (RSJ and JPBF). A date limit was set on 1975 because the arterial switch operation for dextro transposition of the great arteries first has been performed on May 4, 1975. Snowballing and back-referencing were used to ensure maximum article extraction. Deduplication was performed using Endnote (Endnote version 19.3, Clarivate analytics, London, UK), and examination of the titles, abstracts, and the remaining full texts was performed using Rayyan (rayyan.ai). A third author (JMPJB or AvdH) was consulted if initial discussion about discordance of included articles did not resolve disagreement. If the full text was not available, the first and last authors were contacted for the full text. If there was no response or the full text could not be provided, the studies were excluded. The results were presented in a narrative way and a meta-analysis could not be performed due to the heterogeneity of the patients and outcomes from the included articles.

Quality assessment

Risk of bias assessment was performed by two researchers independently (RSJ and JPBF), using the Joanna Briggs Institute critical appraisal tools. The checklist for quasi-experimental studies was used for the studies with a pre and post intervention study design and was based on 7 out of 9 criteria.[18] A detailed description of the quality assessment methods can be found in the supplemental material.

Results

The results were presented in a narrative way due to the heterogeneity of the patients and outcomes from the included articles. The systematic search of PubMed, Embase, and Cochrane up to January 10, 2022, resulted in 4701 hits. After removing the duplicates, 3922 potentially eligible articles remained. After screening title and abstract, 47 articles remained for full-text screening. Of those, 7 articles with in total 330 patients met the inclusion criteria (Fig. 1).[19–25]

Study characteristics

Most studies had a prospective study design (n = 6), while the remaining study was retrospective. Of those studies, 4 were single-centre and 3 were multi-centre. One study exclusively reported on patients with tetralogy of fallot, while the others reported on a heterogeneous group of patients with CHD with tetralogy of fallot as majority of the group. The majority reported on stent angioplasty as intervention for branch pulmonary artery stenosis. All interventions were percutaneous except for the study from Fogelman et al, in which 4 out of 42 patients received a stent during additional surgery (hybrid procedures).[21] In most cases, the intervention was performed in the left pulmonary artery. 5 out of 7 studies specified the number of patients who underwent left pulmonary artery interventions (97 out of 160 [60%]). The remaining studies from Shaffer et al. and Sutton et al. did not distinguish between the pulmonary arteries. 3 out of 7 studies reported exclusively on interventions for unilateral branch pulmonary artery stenosis and the remaining reported on both unilateral and bilateral branch pulmonary artery stenosis. Follow-up duration differed, ranging from almost directly after the intervention to more than a decade after the intervention. The articles included reported on right ventricular function (n = 1), exercise capacity (n = 2), and lung perfusion (n = 7), which were assessed with a wide variety of parameters (Table 1).

Indications for pulmonary artery interventions

Indications for pulmonary artery interventions are listed in Table 2. The studies from Hiremath et al. and Spadoni et al. described specific indications for pulmonary artery interventions while others used more general indications. Pre-interventional haemodynamic data (right ventricle pressures, gradients over stenosis, and blood flow distribution) differed between the studies ranging from mild to more severe pulmonary artery stenosis. Except for right ventricle pressures in the study from Hiremath et al. all pre-interventional haemodynamic data improved post-intervention, even in case of mild pulmonary artery stenosis (Table 2).

Right ventricular function

One study reported on right ventricular function measured using echocardiography and MRI (table S1).[24] The included study used a variety of parameters to assess right ventricular function and follow-up duration varied up to 2 years post intervention. At baseline, the majority of the patients in the study from Ing et al. showed normal right ventricular function, which remained unchanged during follow-up (p = not significant).[24] Therefore, the only study showed no clear information about right ventricular function or remodelling after a percutaneous intervention for branch pulmonary artery stenosis.

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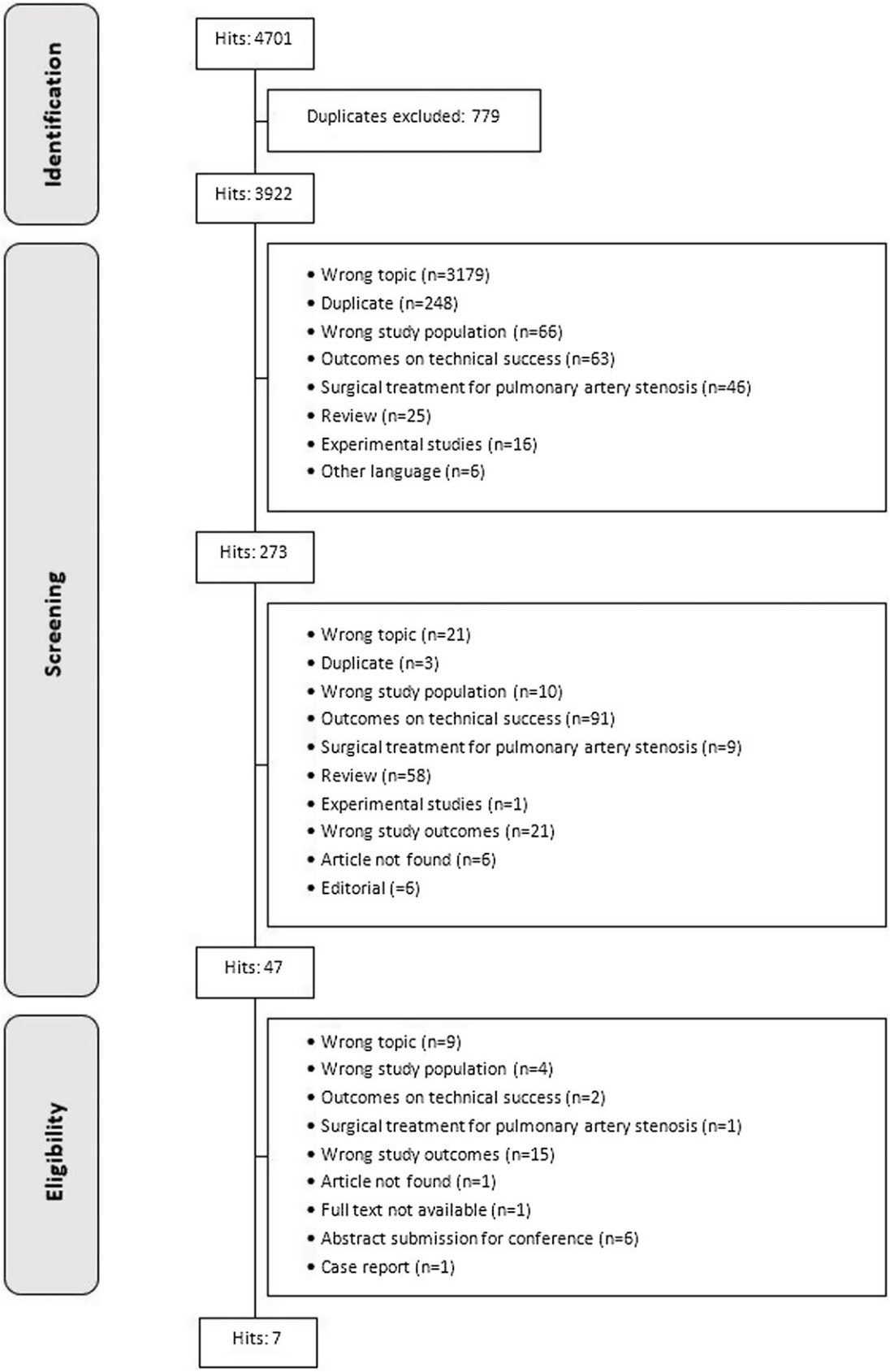

Figure 1. Flowchart.

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Table 1. Baseline characteristics of the included studies.

Study (year)	Design	Centre	Location	Patients	Age (yrs) (mean or median)	Type of intervention	Vessel for intervention	F/u (days, yrs, months) (mean or median)
Fogelman et al. (1995)[21]	Prospective	S	Canada	ToF (n = 12), PA/VSD (n = 11), PA/IVS (n = 4), TA (n = 6), Patent AD (n = 2)*, Tricuspid atresia (n = 2), Other (n = 5)	6.1 ± 4.7	Stent (n = 38), Stent during additional surgery (n = 4)	LPA (n = 22), RPA (n = 15), Bilateral (n = 9)	15M [1,36M]
Hiremath et al. (2019)[19]	Prospective	M	US	d-TGA (n = 3), ToF (n = 8), ALCAPA (n = 1), DORV/PS (n = 2), Ductal origin LPA (n = 1), LPA sling (n = 2), Isolated PAS LPA (n = 1), Alagille[$] (n = 1), PA/IVS (n = 1)	19 [11,66]	Stent (n = 18), Stent during additional surgery (n = 1), Dilatation existing stent (n = 1)	LPA (n = 17), RPA (n = 3)	5.4M [5.9M]
Ing et al. (2014)[24]	Retrospective	M	US	ToF (n = 30), PA/VSD (n = 6), PA/IVS (n = 2), TA (n = 3), d-TGA (n = 2), DORV (n = 2), Isolated PAS (n = 2), Other (n = 11)	10.4 ± 10.3	Stent	LPA (n = 43), RPA (n = 15)	>1Y
Oyen et al. (1995)[22]	Prospective	S	The Netherlands	ToF (n = 7)	15.7 [5,24]**	Stent	LPA (n = 4), RPA (n = 3)	2D-3 M (n = 6), 2Y (n = 1)
Shaffer et al. (1998)[25]	Prospective	M	US	ToF (n = 87), PA (n = 33), d-TGA (n = 10), TA (n = 8), VSD (n = 6), Other (n = 13)	10.5Y [6M-43Y]***	Stent	LPA and/or RPA (n = 136)	19M ± 15M
Spadoni et al. (1999)[23]	Prospective	S	Italy	ToF/PAS (n = 21), ToF/PA (n = 5), ToF/VSD (n = 1), Isolated PAS (n = 2)	12 ± 7	Stent	LPA (n = 11), RPA (n = 3), Bilateral (n = 15)	6M and every year after procedure
Sutton et al. (2008)[20]	Prospective	S	US	ToF/PAS (n = 5), ToF/PA (n = 7), TA (n = 3), d-TGA/VSD/PA (n = 1), DORV/VSD/PS (n = 1)	18.2 ± 11.5	Stent and balloon angioplasty, Dilatation existing stent	RPA/LPA (n = 11), Bilateral (n = 6)	6.3M ± 3.8M

AD = arterial duct; ALPCA = anomalous left coronary artery from pulmonary artery; DORV = double-outlet right ventricle; d-TGA = dextro transposition of the great arteries; F/u= follow-up; IVS = pulmonary atresia with intact ventricular septum; LPA = left pulmonary artery; MD = miscellaneous disorders; PA = pulmonary atresia; PAS = pulmonary artery stenosis; pPS= peripheral pulmonary stenosis; PS = pulmonary stenosis; PVR = pulmonary valve replacement; RPA = right pulmonary artery; TA = truncus arteriosus; ToF= tetralogy of fallot; VSD = ventricular septum defect.

*One patients underwent catheter closure of a patent arterial duct; the other patient had surgical ligation.

**Values are mean (range).

***Values are median (range).

[$]Aligille syndrome without distal pulmonary artery disease.

Table 2. Indications of percutaneous PA interventions.

	Indication	Pre-intervention			Post-intervention		
		RV Psys (mmHg)	Gradient (mmHg)	Blood flow distribution (%)	RV Psys (mmHg)	Gradient (mmHg)	Blood flow distribution (%)
Fogelman et al. (1995)[21]	Failure relief obstruction after BA	48 ± 18	28 ± 21	–	41 ± 14#	7 ± 9*	–
Hiremath et al. (2019)[19]	Minimal 10% deviation of normal pulmonary blood flow (55/45%)	33 (26–72)	11 (1–36)	19.5 (12–21)	34 (25–81)	2 (0–14)*	7 (0–33)#
Ing et al. (2014)[24]	Unilateral PA stenting	44.2 ± 15.5	18.1 ± 10.4	–	41.4 ± 14.3#	5.8 ± 7#	–
Oyen et al. (1995)[22]	PA stenosis	–	33 ± 20.5	–	–	–	–
Shaffer et al. (1998)[25]	PA stenosis that required a stent	–	46 ± 25	–	–	10 ± 12.8*	–
Spadoni et al. (1999)[23]	• PA pressure: systemic pressure>0.5 • Reduction diameter PA to<0.5 from the adjacent normal vessel. • Significant unilateral stenosis: diameter reduction>50%, scientific evidence hypoperfusion and overflow to other lung, lung perfusion affected lung<35% with normal or slightly elevated MPA pressure • Dilatable stenosis with complete waist disappearance during BA but failure to reach 75% of the diameter of the adjacent normal vessel due to immediate elastic recoil.	54 ± 19	36 ± 20	–	42 ± 13#	11 ± 12*	–
Sutton et al. (2008)[20]	Known or suspected residual PA stenoses referred for elective cardiac catheterisation and possible PA angioplasty	–	–	14.2 ± 8.7	–	–	9.4 ± 6.5**

BA = balloon angioplasty; MPA = mean pulmonary artery; PA = pulmonary artery; PI = pulmonary insufficiency; Psys= systolic pressure; RV = right ventricle; ToF= tetralogy of fallot.
*p<0.05 between pre- and post-intervention.
#p<0.01 between pre- and post-intervention.
**p-value unknown.

Exercise capacity

Exercise capacity was assessed in two articles using treadmill and bicycle exercise tests (Table 3).[19,20] The follow-up duration was approximately the same. In both studies, known or suspected residual pulmonary artery stenosis was considered as indication for right heart catheterisation (Table 2). In general, exercise capacity showed improvement after a percutaneous intervention for branch pulmonary artery stenosis. Sutton and Hiremath et al. both showed a significant increase in peak O2 pulse (% predicted), VO2 max (% predicted) and the VE/VCO2 slope (Sutton et al: peak O2 pulse = 87.3 ± 20.1 versus 105 ± 23, VO2max = 66.3 ± 14.4 versus 80.6 ± 12.8, VE/VCO2 slope = 33.4 ± 7.8 versus 28.6 ± 5.4; Hiremath: peak O2 pulse = 82 (51–100) versus 93.5 (53–134), VO2max = 70 (45–96) versus 83 (47–121), and VE/VCO2 slope = 32.5 (26–42) versus 29.3 (20–37), all $p < 0.05$).[19,20] Both studies also showed that successful stenting ≥ 5% improvement in pulmonary blood flow to the stenosed lung (Sutton et al.) and ≥ 20% improvement in pulmonary blood flow to the stenosed lung (Hiremath et al.) significantly improved the exercise capacity, whereas unsuccessful stenting did not. Therefore, both studies that reported on exercise capacity after a percutaneous treatment for branch pulmonary artery stenosis showed a significant improvement.

Lung perfusion

Lung perfusion was reported by seven studies using nuclear lung perfusion scans, MRI, or both (Table 4).[19–25] The follow-up duration varied from shortly after to 2 year after the procedure. All studies included patients with known or suspected pulmonary artery stenosis. Hiremath and Spadoni et al. reported indications based on a number of criteria, while the other studies used the presence of pulmonary artery stenosis in general (Table 2). Overall, the lung perfusion to the affected lung is improved after a percutaneous intervention for branch pulmonary artery stenosis. All studies that assessed mean flow to the affected lung reported improvement, ranging from 20 to 32% before the intervention and 36–47% during follow-up (all $p < 0.05$).[19–25] Fogelman reported, in addition to improved flow after percutaneous treatment for the left pulmonary artery, no significant improvement for the right PA.[21] Sutton and Hiremath et al. both showed significant reduction in blood flow maldistribution measured as the percentage of discrepancy from the normal blood flow distribution (55 right lung/45% left lung).[19,20] Therefore, the majority of the studies show an improvement in lung perfusion after a percutaneous intervention for branch pulmonary artery stenosis.

Quality assessment

Two out of 7 studies were considered low risk of bias and 5 were considered moderate risk of bias. An overview of the quality assessment is given in table S2.

Discussion

This study systematically reviewed literature on (long-term) outcomes for right ventricular function, exercise capacity, and lung perfusion after percutaneous interventions for branch pulmonary artery stenosis in biventricular CHD. In general, lung perfusion and exercise capacity seem to improve after percutaneous treatment for branch pulmonary artery stenosis. No conclusions about right ventricular function or remodelling could be made given that only one study discussed right ventricular function. All results and conclusions discussed in this review should be interpreted with caution because study numbers were low, study populations of the included articles were very heterogeneous, no individual results were reported and conclusions of the articles are based on the group as a whole. This remains a large issue in CHD but cannot be avoided since none of the CHD patients are similar in their anatomy, haemodynamics, and function.

Right ventricular function

A variation of parameters was used to measure right ventricular function with echocardiography and MRI, where MRI is considered the gold standard to assess right ventricular function.[26] The only study reporting on right ventricular function during follow-up showed no clear changes in right ventricular function after a percutaneous intervention for branch pulmonary artery stenosis.[24] However, p-values of echocardiographic right ventricle pressures during follow-up were lacking. In addition, only 17 patients (29%) underwent MRI prior to the intervention and 5 patients (9%) during follow-up. Moreover, right ventricular ejection fraction was already in the normal range in the majority of these limited number of patients, which might explain the lack of a clear improvement after the intervention. Given that only one article reported on right ventricular function without statistical support, it is difficult to discuss any conclusions. This shows the urgency for future research about right ventricular function in the (long-term) follow-up of these patients.

Exercise capacity

Two studies were included for exercise capacity with similarities in parameters that increases the generalisability of the results.[19,20] Both studies showed a significant increase in the exercise capacity despite different study populations (age, type of CHD, severity of pulmonary artery stenosis, and unilateral versus bilateral) and a relatively short follow-up duration. This is supported by other studies, which reported a negative effect of pulmonary artery stenosis on exercise capacity by limiting the pulmonary blood flow.[13,14] Long-term data about exercise capacity after percutaneous interventions for branch pulmonary artery stenosis are limited, but current data suggest that exercise capacity increases, even in case of mild pulmonary artery stenosis. Nevertheless, further research is needed.

Lung perfusion

Lung perfusion was reported by seven studies, which made it the most reported outcome .[19–25] All studies assessed lung perfusion to the affected lung using the gold standard nuclear lung perfusion scans and MRI, which improves the generalisability of the results.[27,28] In general, stent or balloon angioplasty improved lung perfusion and reduced the maldistribution of the pulmonary blood flow, despite differences in study populations and pulmonary artery stenosis severity. This might be explained by the increase in blood vessel diameter and is substantiated by studies that show the effectiveness of interventions for branch pulmonary artery stenosis on dilating the blood vessel.[15–17] Fogelman et al. found no significant improvement for right pulmonary artery flow after the percutaneous intervention, which might be a result of the small sample size (n = 4). Overall, there is a general trend towards improved lung perfusion after a percutaneous intervention in the

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Table 3. Outcomes on exercise capacity.

Study (year)	Patients	F/u duration (mean or median) (yrs or months)	Lost f/u	Method	Outcome	Outcome pre (mean or median)	Outcome post (mean or median)	Outcome f/u (mean or median)	P-value
Hiremath et al. (2019)[19]	d-TGA (n = 3)	5.4M [5.9M]	6	Cycle Treadmill	Exercise time* (min)	9.8 [7.5,13.5]	–	10.67 [7.3, 14]	0.31
	ToF (n = 8)				Peak work*& (W)	127 [60,135]	–	130 [70,196]	0.39
	ALCAPA (n = 1)				Predicted VO2 max* (%)	70 [45,96]	–	83 [47,121]	0.02
	DORV/PS (n = 2)				RER at peak exercise*	1.17 [1.10,1.30]	–	1.11 [0.96,1.37]	0.77
	Ductal origin LPA (n = 1)				Predicted O2 pulse* (%)	82 [51,100]	–	93.5 [53,134]	0.02
					Ve/VCO2 slope*	32.5 [26,42]	–	29.3 [20,37]	0.01
	LPA sling (n = 2)				MRC chronic dyspnea score*	1.5 [0,4]	–	0 [0,3]	0.047
	Isolated PAS LPA (n = 1)				Borg score at peak exercise#*&	17.5 [15,20]	–	15 [9,20]	0.22
	Alagille$ (n = 1)								
	PA/IVS (n = 1)								
Sutton et al. (2008)[20]	ToF/PAS (n = 5)	6.3M ± 3.8M	–	Cycle Treadmill	Successful BAP (n = 9)**				
	ToF/PA (n = 7)				VO2 (ml/[kg min])	28.4 ± 8.3	–	32.5 ± 7.1	<0.05
	TA (n = 3)				VO2 (% predicted)	66.3 ± 14.4	–	80.6 ± 12.8	<0.05
	d-TGA/VSD/PA (n = 1)				VE/VCO2 slope	33.4 ± 7.8	–	28.6 ± 5.4	<0.05
	DORV/VSD/PS (n = 1)				O2 pulse (% predicted)	87.3 ± 20.1	–	105 ± 23	<0.05

AD = arterial duct; ALPCA = anomalous left coronary artery from pulmonary artery; BAP = balloon angioplasty procedure; DORV = double-outlet right ventricle; d–TGA = dextro transposition of the great arteries; F/u= follow–up; IVS = intact ventricular septum; LPA = left pulmonary artery; MD = miscellaneous disorders; Ns= not significant; PA = pulmonary atresia; PAS = pulmonary artery stenosis; pPS= peripheral pulmonary stenosis; PS = pulmonary stenosis; PVR = pulmonary valve replacement ; RPA = right pulmonary artery; TA = truncus arteriosus; ToF= tetralogy of fallot; VSD = ventricular septum defect.

$Aligille syndrome without distal pulmonary artery disease.

#Borg score is a measure of subjective perceived exertion.

&Peak work and Borg score became significant with imputed data (n = 14) (p = 0.03 and $p = 0.02$). Descriptive statistics were similar.

*Values are median (range).

**≥5% improvement in pulmonary blood flow to the stenosed lung.

Table 4. Outcomes on lung perfusion.

Study (year)	Patients	F/u duration (mean or median) (days, yrs or months)	Lost f/u	Method	Outcome	Outcome pre (mean or median)	Outcome post (mean or median)	Outcome f/u (mean or median)	P-value
Fogelman et al. (1995)[21]	ToF (n = 12), PA/VSD (n = 11), PA/IVS (n = 4), TA (n = 6), Patent AD (n = 2)*, Tricuspid atresia (n = 2), Other (n = 5),	5.2M ± 2.6	32	LPS	LPA flow (%), RPA flow (%)	28 ± 13, 32 ± 25	–	40 ± 16, 42 ± 11	<0.05, Ns
Hiremath et al. (2019)[19]	d-TGA (n = 3), ToF (n = 8), ALCAPA (n = 1), DORV/PS (n = 2), Ductal origin LPA (n = 1), LPA sling (n = 2), Isolated PAS LPA (n = 1), Alagille[$] (n = 1), PA/IVS (n = 1),	2.8M	5	LPS or MRI	Maldistribution (percentage point)***, Perfusion to lung with PAS (%)	19.5 [12,31]**, 27 [14,35]**	–	7 [0,33]**, 40.5 [12,56]**	0.003, 0.003
Ing et al. (2014)[24]	ToF (n = 30), PA/VSD (n = 6), PA/IVS (n = 2), TA (n = 3), d-TGA (n = 2), DORV (n = 2), Isolated PAS (n = 2), Other (n = 11),	312.5D [2,1070]**	43	LPS (n = 4), MRI (n = 5), Both (n = 6)	Perfusion to lung with PAS (%)	19.6 ± 9.1	–	35.5 ± 6.1	<0.05
Oyen et al. (1995)[22]	ToF (n = 7)	2D–3M (n = 6), 2Y (n = 1)	–	LPS	Perfusion to lung with PAS (%)	22.7 ± 10.8	38.6 ± 12.3	Unchanged	<0.0001
Shaffer et al. (1998)[25]	ToF (n = 87), PA (n = 33), d-TGA (n = 10), TA (n = 8), VSD (n = 6), Other (n = 13), Congenital branch stenosis (n = 15), Venous stenosis (n = 48),	19M ± 15	94	LPS	Perfusion to lung with unilateral PAS (%)	31 ± 17	46 ± 14	47 ± 17	Pre vs. post: $p < 0.001$,, Post vs. f/u: $p = 0.2$
Spadoni et al. (1999)[23]	ToF/PAS (n = 21), ToF/PA (n = 5), ToF/VSD (n = 1), Isolated PAS (n = 2)	6M, 1Y	–, 3,	LPS	Perfusion to lung with unilateral PAS (%)	22 ± 10	41 ± 12	41 ± 11 (6M)[&], 42 ± 11 (1Y) [&]	<0.001[#]
Sutton et al. (2008)[20]	ToF/PAS (n = 5), ToF/PA (n = 7), TA (n = 3), d–TGA/VSD/PA (n = 1), DORV/VSD/PS (n = 1)	6.3M ± 3.8	–	LPS	Maldistribution (percentage point)***	18.2 ± 8.7,	–	9.9 ± 8	<0.05

AD = arterial duct; ALPCA = anomalous left coronary artery from pulmonary artery; DORV = double-outlet right ventricle; d–TGA = dextro transposition of the great arteries; F/u= follow–up; IVS = intact ventricular septum; LPA = left pulmonary artery; LPS = lung perfusion scans (nuclear); Ns= not significant; MRI = magnetic resonance imaging; PA = pulmonary atresia; PAs= pulmonary arteries; PAS = pulmonary artery stenosis; PS = pulmonary stenosis; RPA = right pulmonary artery; TA = truncus arteriosus; ToF= tetralogy of fallot; VSD = ventricular septum defect.

*One patients underwent catheter closure of a patent arterial duct; the other patient had surgical ligation.

**Values are median (range).

***Maldistribution refers to the percentage point deviation from the normal 55%/45% right/left pulmonary blood flow distribution.

[$]Aligille syndrome without distal pulmonary artery disease.

[&]p–value between lung perfusion post intervention and follow–up (both 6 months and 1 year) not significant ($p > 0.05$).

#p–value between lung perfusion pre intervention and post intervention significant ($p < 0.001$).

branch pulmonary arteries, even in case of less severe pulmonary artery stenosis.

Balloon angioplasty versus stent implantation

The majority of studies performed percutaneous stent placement as treatment for pulmonary artery stenosis.[19,21–25] Sutton et al. were the only study that reported on balloon angioplasty.[20] Even in this study, almost all balloon angioplasty ended in stent placement, and results of balloon angioplasty were not presented separately. Therefore, no comparison can be made between the effects of balloon angioplasty and stent implantation.

Differences in underlying CHD

From the included articles, one exclusively reported on tetralogy of fallot, whereas the others reported on an heterogeneous study population.[22] In all heterogeneous study populations, tetralogy of fallot resembled the majority of the group.[19–21,23–25] The difference in aetiology of pulmonary artery stenosis makes it difficult to generalise the reported results, primarily for tetralogy of fallot, to other CHD such as transposition of the great arteries. In tetralogy of fallot, pulmonary artery stenosis might be caused by pulmonary coarctation, hypoplastic native pulmonary arteries, stenosis of anastomosis sites, or iatrogenic obstruction by previous aorto-pulmonary shunt, whereas in transposition of the great arteries, it is mainly caused by compression of the pulmonary artery branch by an enlarged aorta or the neo-pulmonary to neo-aortic geometry.[10–12] Therefore, balloon angioplasty might be less effective in increasing the branch pulmonary artery diameter in transposition of the great arteries compared to tetralogy of Fallot and percutaneous stent placement might have a more favourable effect.[29] Currently, the data are very limited for transposition of the great arteries, and this review cannot draw any conclusions for this group separately because of the limited number of transposition of the great arteries patients in the included articles (16 out of 330 patients in all studies combined). In addition, no conclusions could be made for other types of biventricular CHD due to low patient numbers.

Limitations

This review has several limitations with the low number of included studies as the most striking one. This small retrieval might partly result from extensive inclusion and exclusion criteria for our specific outcomes of interest in biventricular CHD. As a result, no significant or statistically analysable and practical conclusions can be made from the results. In addition, patient populations of the included articles were very heterogenous, which made it impossible to derive population specific conclusions. Finally, effects between stent and balloon angioplasty could not be compared due to a lack of articles reporting on our outcomes of interest after balloon angioplasty interventions. These limitations show that there is need for larger prospective studies about right ventricular function, exercise capacity, and lung perfusion after pulmonary artery interventions in biventricular CHD. Therefore, we started a multicentre randomised controlled trial about the effects of percutaneous pulmonary artery interventions on exercise capacity and right ventricular function in patients with biventricular CHD in the Netherlands (ClinicalTials.gov ID: NCT05809310).

Conclusion

Although pulmonary artery interventions are frequently performed in biventricular CHD, data on relevant outcome parameters such as exercise capacity, lung perfusion, and right ventricular function are largely lacking. An increase in exercise capacity and improvement of lung perfusion to the affected lung has been described in case of mild to more severe pulmonary artery stenosis during relatively short follow-up. However, there is an urgent need for future studies to evaluate the effect of pulmonary artery interventions in various CHD populations including transposition of the great arteries.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S1047951124000015.

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References

1. Khairy P, Ionescu-Ittu R, Mackie AS, Abrahamowicz M, Pilote L, Marelli AJ. Changing mortality in congenital heart disease. J Am Coll Cardiol 2010; 56: 1149–1157.
2. Stuart AG. Changing lesion demographics of the adult with congenital heart disease: an emerging population with complex needs. Future Cardiol 2012; 8: 305–313.
3. van der Palen RLF, Blom NA, Kuipers IM, et al. Long-term outcome after the arterial switch operation: 43 years of experience. Eur J Cardiothorac Surg 2021; 59: 968–977.
4. Cuypers JA, Menting ME, Konings EE, et al. Unnatural history of tetralogy of Fallot: prospective follow-up of 40 years after surgical correction. Circulation 2014; 130: 1944–1953.
5. Bacha EA, Scheule AM, Zurakowski D, et al. Long-term results after early primary repair of tetralogy of Fallot. J Thorac Cardiovasc Surg 2001; 122: 154–161.
6. Sinzobahamvya N, Boscheinen M, Blaschczok HC, et al. Survival and reintervention after neonatal repair of truncus arteriosus with valved conduit. Eur J Cardiothorac Surg 2008; 34: 732–737.
7. Asagai S, Inai K, Shinohara T, et al. Long-term outcomes after Truncus arteriosus repair: a single-center experience for more than 40 Years. Congenit Heart Dis 2016; 11: 672–677.
8. Santens B, Van De Bruaene A, De Meester P, et al. Outcome of arterial switch operation for transposition of the great arteries. A 35-year follow-up study. Int J Cardiol 2020; 316: 94–100.
9. Khairy P, Clair M, Fernandes SM, et al. Cardiovascular outcomes after the arterial switch operation for D-transposition of the great arteries. Circulation 2013; 127: 331–339.
10. Elzenga NJ, von Suylen RJ, Frohn-Mulder I, Essed CE, Bos E, Quaegebeur JM. Juxtaductal pulmonary artery coarctation. An underestimated cause of branch pulmonary artery stenosis in patients with pulmonary atresia or stenosis and a ventricular septal defect. J Thorac Cardiovasc Surg 1990; 100: 416–424.
11. Trusler GA, Miyamura H, Culham JA, Fowler RS, Freedom RM, Williams WG. Pulmonary artery stenosis following aortopulmonary anastomoses. J Thorac Cardiovasc Surg 1981; 82: 398–404.
12. Morgan CT, Mertens L, Grotenhuis H, Yoo SJ, Seed M, Grosse-Wortmann L. Understanding the mechanism for branch pulmonary artery stenosis

after the arterial switch operation for transposition of the great arteries. Eur Heart J Cardiovasc Imaging 2017; 18: 180–185.
13. Giardini A, Khambadkone S, Taylor A, Derrick G. Effect of abnormal pulmonary flow distribution on ventilatory efficiency and exercise capacity after arterial switch operation for transposition of great arteries. Am J Cardiol 2010; 106: 1023–1028.
14. Rhodes J, Dave A, Pulling MC, et al. Effect of pulmonary artery stenoses on the cardiopulmonary response to exercise following repair of tetralogy of fallot. Am J Cardiol 1998; 81: 1217–1219.
15. Baerlocher L, Kretschmar O, Harpes P, Arbenz U, Berger F, Knirsch W. Stent implantation and balloon angioplasty for treatment of branch pulmonary artery stenosis in children. Clin Res Cardiol 2008; 97: 310–317.
16. Chau AK, Leung MP. Management of branch pulmonary artery stenosis: balloon angioplasty or endovascular stenting. Clin Exp Pharmacol Physiol 1997; 24: 960–962.
17. Ko HK, Kim YH, Yu JJ, et al. Effectiveness and safety of percutaneous transcatheter implantation of pulmonary arterial stent in congenital heart disease. Korean Circ J 2012; 42: 40–45.
18. Tufanaru CMZ, Aromataris E, Campbell J, Hopp L. Chapter 3: systematic reviews of effectiveness. In: Aromataris E, Munn Z (eds). JBI Manual for Evidence Synthesis, JBI, North Adelaide, South Australia; 2020.
19. Hiremath G, Qureshi AM, Prieto LR, et al. Balloon angioplasty and stenting for unilateral branch pulmonary artery stenosis improve exertional performance. JACC Cardiovasc Interv 2019; 12: 289–297.
20. Sutton NJ, Peng L, Lock JE, et al. Effect of pulmonary artery angioplasty on exercise function after repair of tetralogy of Fallot. Am Heart J 2008; 155: 182–186.
21. Fogelman R, Nykanen D, Smallhorn JF, McCrindle BW, Freedom RM, Benson LN. Endovascular stents in the pulmonary circulation. Clinical impact on management and medium-term follow-up. Circulation 1995; 92: 881–885.
22. Oyen WJ, van Oort AM, Tanke RB, van Mill GJ, Aengevaeren WR, Corstens FH. Pulmonary perfusion after endovascular stenting of pulmonary artery stenosis. J Nucl Med 1995; 36: 2006–2008.
23. Spadoni I, Giusti S, Bertolaccini P, Maneschi A, Kraft G, Carminati M. Long-term follow-up of stents implanted to relieve peripheral pulmonary arterial stenosis: hemodynamic findings and results of lung perfusion scanning. Cardiol Young 1999; 9: 585–591.
24. Ing FF, Khan A, Kobayashi D, Hagler DJ, Forbes TJ. Pulmonary artery stents in the recent era: immediate and intermediate follow-up. Catheter Cardiovasc Interv 2014; 84: 1123–1130.
25. Shaffer KM, Mullins CE, Grifka RG, et al. Intravascular stents in congenital heart disease: short- and long-term results from a large single-center experience. J Am Coll Cardiol 1998; 31: 661–667.
26. Pennell DJ. Cardiovascular magnetic resonance: twenty-first century solutions in cardiology. Clin Med (Lond) 2003; 3: 273–278.
27. Dessy H, Hermus JP, van den Heuvel F, Oei HY, Krenning EP, Hess J. Echocardiographic and radionuclide pulmonary blood flow patterns after transcatheter closure of patent ductus arteriosus. Circulation 1996; 94: 126–129.
28. Pruckmayer M, Zacherl S, Salzer-Muhar U, Schlemmer M, Leitha T. Scintigraphic assessment of pulmonary and whole-body blood flow patterns after surgical intervention in congenital heart disease. J Nucl Med 1999; 40: 1477–1483.
29. Formigari R, Santoro G, Guccione P, et al. Treatment of pulmonary artery stenosis after arterial switch operation: stent implantation vs. balloon angioplasty. Catheter Cardiovasc Interv 2000; 50: 207–211.

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