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Timing of surgical repair and resource utilisation in infants with complete atrioventricular septal defect

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Abstract

Introduction: Variation exists in the timing of surgery for balanced complete atrioventricular septal defect repair. We sought to explore associations between timing of repair and resource utilisation and clinical outcomes in the first year of life. *Methods:* In this retrospective single-centre cohort study, we included patients who underwent complete atrioventricular septal defect repair between 2005 and 2019. Patients with left or right ventricular outflow tract obstruction and major non-cardiac comorbidities (except trisomy 21) were excluded. The primary outcome was days alive and out of the hospital in the first year of life. *Results:* Included were 79 infants, divided into tertiles based on age at surgery (1st = 46 to 137 days, 2nd = 140 – 176 days, 3rd = 178 – 316 days). There were no significant differences among age tertiles for days alive and out of the hospital in the first year of life by univariable analysis (tertile 1, median 351 days; tertile 2, 348 days; tertile 3, 354 days; p = 0.22). No patients died. Fewer post-operative ICU days were used in the oldest tertile relative to the youngest, but days of mechanical ventilation and hospitalisation were similar. Clinical outcomes after repair and resource utilisation in the first year of life were similar for unplanned cardiac reinterventions, outpatient cardiology clinic visits, and weight-for-age z-score at 1 year. *Conclusions:* Age at complete atrioventricular septal defect repair is not associated with important differences in clinical outcomes or resource utilisation in the first year of life.

Complete atrioventricular septal defect is a relatively common CHD and uniformly warrants surgical repair. Pre-operatively, patients with complete atrioventricular septal defects may develop congestive heart failure and failure to thrive, and common viral illnesses may be poorly tolerated. These problems may lead to increased outpatient visits, cardiac testing, medication use, and hospitalisations.[1] Adverse outcomes in patients who undergo complete atrioventricular septal defect repair beyond one year of age may include severe AV valve regurgitation, increased morbidity from respiratory infections, and failure to thrive in the pre-operative period, as well as the development of irreversible pulmonary hypertension.[2,3] Prior studies have shown that surgical intervention for complete atrioventricular septal defects in infancy rather than early childhood contributed to a decline in post-operative mortality.[3–10] In the current era, complete atrioventricular septal defects are often repaired in mid-infancy, yet the optimal timing remains unknown.

The objective of this study was to determine the association between timing of repair of complete atrioventricular septal defects and resource utilisation and clinical outcomes in the first year of life. We hypothesised that earlier repair would be associated with less resource consumption but similar clinical outcomes.

Material and methods

Study population

This retrospective cohort study was approved by the institutional review board at the participating centres, and the need for informed consent was waived due to the retrospective nature of the study. Patients who had undergone cardiac surgery for a complete balanced atrioventricular septal defect were identified using the Medical University of South Carolina Pediatric Cardiothoracic Surgery internal database. We included patients with balanced complete atrioventricular septal defects repaired prior to 1 year of age between 1 January, 2005 and

30 December, 2019, at the Medical University of South Carolina who received outpatient cardiology care at one of three sites within the Children's Heart Program of South Carolina. For the purposes of this study, we defined a "balanced" complete atrioventricular septal defect as one for which the referring paediatric cardiologist and cardiac surgeon felt that biventricular repair was indicated. As the key exposure variable for this study was the timing of surgical repair and in order to minimise the potential for confounding, we decided to include only patients with relatively uncomplicated complete atrioventricular septal defects. Thus, we excluded those with concomitant outflow tract intervention for tetralogy of Fallot or aortic arch obstruction/coarctation, absent pulmonary valve syndrome, any cardiac surgery prior to complete atrioventricular septal defect repair (e.g., pulmonary artery banding), or greater than moderate pre-operative atrioventricular valve regurgitation. We also excluded those with pre-maturity, chromosomal anomalies (except trisomy 21), and major non-cardiac comorbidities (e.g., duodenal or anal atresia).

Data collection and definitions

Pre-operative characteristics, perioperative data, and early post-operative outcome variables were collected via electronic medical record by investigators at the surgical centre as well as the referring outpatient paediatric cardiology centres. The primary exposure variable was age at surgery. Patients were divided into three groups based on age tertile at surgery. The primary outcome was days alive and out of the hospital in the first year of life. Secondary outcomes were perioperative variables including pre-operative hospitalisation, pre-operative medications, feeding route prior to surgery, weight at surgery, unplanned thoracic interventions (e.g., thoracic duct ligation, diaphragm plication), days of post-operative mechanical ventilation and cardiac ICU stay, unplanned hospital readmission within 30 days, and operative or late mortality. We also assessed clinical outcomes after discharge from the repair hospitalisation including unplanned cardiac interventions and weight-for-age z-score at approximately one year of age. Additional assessments of resource utilisation in the first year of life included the total number of echocardiograms and outpatient cardiology clinic visits before and after surgery. Echocardiograms reported for this study included all inpatient and outpatient transthoracic echocardiograms, including perioperative studies, in the first year of life; transesophageal echocardiograms were excluded.

Statistical analysis

Categorical variables were represented as counts with percentages. Continuous variables were reported as medians with 25^{th} and 75^{th} percentiles unless otherwise specified. Unadjusted comparisons among groups were made using the chi-square, Fisher's exact, Mann–Whitney U, or Kruskal–Wallis tests, as appropriate. Given that the primary outcome was not normally distributed and violated other assumptions necessary for risk adjustment using analysis of variance, a binary variable was created to identify patients in the lowest (worst) quartile of days alive and out of the hospital in the first year of life (340 days or less). Statistical analyses were performed using IBM SPSS Statistics 25 software.

Results

During the study period, 302 patients underwent cardiac surgery for a complete balanced atrioventricular septal defect. Of these, 146 were excluded for concurrent right or left ventricular outflow tract lesions or procedures (e.g., tetralogy of Fallot repair, coarctation repair), 72 were excluded for pre-mature birth, and 8 were excluded for major non-cardiac comorbidities (some patients met more than one exclusion criteria, including other criteria not listed above). The remaining 76 patients met the study criteria and were divided into three groups based on age at surgery. Tertile 1 included patients from 46 to 137 days of age (n = 25), tertile 2 included patients from 140 to 176 days of age (n = 24, and tertile 3 included patients from 178 to 316 days of age (n = 27). The primary reasons for exclusion were unbalanced or non-complete atrioventricular septal defects, pre-maturity, and the presence of non-cardiac comorbidities.

Birth weight and female gender were significantly different across age tertiles, and more patients in tertile 1 were hospitalised pre-operatively. There were no significant differences among age tertiles for prenatal diagnosis, race/ethnicity, gestational age, presence of Trisomy 21 (T21), or repair type (Table 1).

There was no significant difference among age tertiles at surgery for the primary outcome of days alive and out of the hospital in the first year of life by univariate analysis [tertile 1, median 351 days (333, 358); tertile 2, 348 days (340, 356); tertile 3, 354 (348, 357); p = 0.22; Figure 1]. No patients died in the first year of life.

Among the perioperative variables, pre-operative weight was significantly different among age groups, but weight-for-age z-scores were similar, as were pre-operative number of medications and feeding route (Table 2). Fewer post-operative ICU days were utilised in tertile 3 compared to tertile 1, but ICU days were not significantly different when comparing tertile 3 compared to tertile 2 (Table 2). However, days of mechanical ventilation and hospitalisation were similar among groups. There were no significant differences in post-operative complications or feeding route at discharge (Table 2). Clinical outcomes following discharge from the repair hospitalisation in the first year of life were similar in terms of unplanned cardiac reinterventions and weight-for-age z-score at 1 year (Table 2). There were no significant differences among groups in the total number of outpatient cardiology clinic visits in the first year of life. Fewer echocardiograms were performed in tertile 3 compared to tertile 2, but there was no significant difference in the number of echocardiograms between tertile 3 and tertile 1.

Discussion

The objective of this study was to determine the association between timing of repair of complete atrioventricular septal defect and both resource utilisation and clinical outcomes in the first year of life. In contrast to our hypothesis, we found that earlier repair was not associated with differences in the most important measures of resource consumption. As we anticipated, age at surgery was not associated with meaningful differences in clinical outcomes.

Our findings need to be interpreted in the context of prior studies on timing of surgery in this patient population. Atz et al. previously evaluated factors associated with suboptimal outcomes in 120 patients who underwent complete atrioventricular septal defect repair at multiple medical centres. These investigators found that age at surgery less than 2.7 months was associated with increased resource utilisation and adverse outcomes.[11] Similarly, several studies have found that age less than 2.5 – 3.0 months and weight less than 4 kg at the time of surgery are risk factors for increased mortality in this population, which was thought in part to be due to the presence of more fragile left atrioventricular valve tissue in these young infants.[2,10,12] In contrast, other

Table 1. Comparison of baseline characteristics.

Variable	All patients (N = 76)	Tertile 1 (N = 25)	Tertile 2 (N = 24)	Tertile 3 (N = 27)	p-value
Prenatal diagnosis	34 (45%)	12 (48%)	14 (58%)	8 (30%)	0.11
Female sex	48 (63%)	10 (40%)	19 (79%)	19 (70%)	0.01
Race:					0.12
Caucasian	51 (67%)	21 (84%)	16 (67%)	14 (52%)	
Black	21 (28%)	3 (12%)	7 (29%)	11 (41%)	
Other	4 (5%)	1 (4%)	1 (4%)	2 (7%)	
Hispanic ethnicity	1 (1%)	0	0	1 (3%)	1.00
Gestational age (weeks)	38 (37, 39)	38 (37, 39)	39 (38, 39)	38 (37, 39)	0.39
Birth weight (kg)	3.03 (2.70, 3.32)	3.30 (2.89, 3.47)	3.10 (2.83, 3.32)	2.77 (2.60, 3.14)	0.01
Trisomy 21	55 (72%)	16 (64%)	19 (79%)	20 (74%)	0.48
Repair Type:					0.47
Single-Patch	5 (7%)	2 (8%)	0 (0%)	3 (11%)	
Double-Patch	62 (81%)	21 (84%)	21 (84%)	20 (74%)	
Australian	10 (13%)	2 (8%)	4 (16%)	4 (15%)	

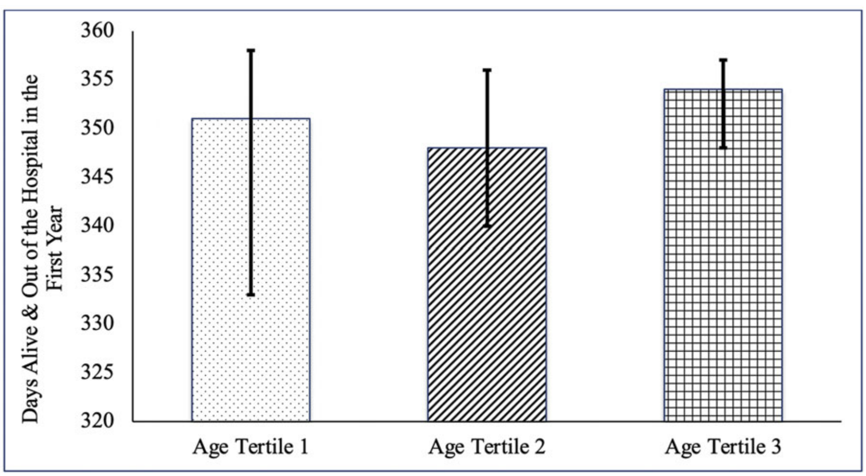

Figure 1. Days alive and out of the hospital in the first year of life among age tertiles (p = 0.22).

single-centre studies have found that operation at less than 3 months of age was not associated with increased mortality.[3,7,8,13] It is possible that we did not find significant differences in resource utilisation among age groups in our study because we only included uncomplicated cases, and the overall outcomes at our centre were quite good (i.e., no mortality and rare cardiac reinterventions in the first year of life for the patients in this study). It should be noted that our study only included one patient who underwent complete atrioventricular septal defect repair at less than 2.7 months of age, and thus, our findings cannot be used to inform decision making for complete atrioventricular septal defect repair in the first 3 months of life. Atz et al. also noted increased length of hospital stay associated with patients with non-cardiac anomalies, which were excluded from our study.[11]

The precise reasons for timing of surgery in the study patients are not easily gleaned from the medical record. Nuances such as judgement of the cardiologist, parental sense of urgency to have the heart “fixed,” and surgical scheduling issues are unknown. Another potential confounder is the relationship between birth weight and perceived optimal weight at the time of surgery. Other things being equal, many cardiac surgeons prefer that patients undergoing elective complete atrioventricular septal defect repair weigh approximately 5 kg at the time of the operation. In our study subjects, there was an inverse relationship between birth weight and age at surgery. It is possible that clinicians were delaying surgery for patients who ultimately ended up in the older age tertiles to allow for more weight gain.

We speculated that patients undergoing surgery at an older age would have more pre-operative problems with failure to thrive. However, the weight-for-age z-scores at surgery and at one year of age did not differ significantly among the three groups. We also anticipated that the patients that underwent surgery at a later age would have a higher resource utilisation due to more pre-operative testing, hospitalisations for intercurrent illnesses, and failure to thrive. However, pre-operative variables such as unplanned hospitalisations, medication use, and nasogastric or gastrostomy tube

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Table 2. Comparison of perioperative outcomes and resource utilisation.

Variable	All patients (N = 76)	Tertile 1 (N = 25)	Tertile 2 (N = 24)	Tertile 3 (N = 27)	p-value
Perioperative outcomes					
Hospitalised pre-operatively	8 (11%)	6 (24%)	1 (4%)	1 (4%)	0.046
≥ 2 medications pre-operatively	20 (27%)	8 (33%)	8 (35%)	4 (15%)	0.20
Weight pre-operatively (kg)	5.1 (4.8, 5.8)	4.9 (4.5, 5.3)[a]	5.0 (4.6, 5.4)[b]	6.0 (5.2, 6.8)	< 0.001
Weight z-score pre-operatively	−2.1 (−2.8, −1.9)	−2.0 (−2.6, −1.8)	−2.4 (−3.2, −2.0)	−2.0 (−2.7, −1.5)	0.10
NG or G tube fed pre-operatively	14 (18%)	8 (32%)	3 (13%)	3 (11%)	0.11
Any of 6 following major post-op complications	3 (4%)	1 (4%)	2 (8%)	0	0.20
Received ECMO	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Received CPR	2 (3%)	0 (0%)	2 (8%)	0 (0%)	
Received dialysis	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Neurologic deficit at d/c	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
Phrenic nerve injury	0 (0%)	0 (0%)	0 (0%)	0 (0%)	
AV block req. perm. PM	1 (1%)	1 (4%)	0 (0%)	0 (0%)	
Unplanned thoracic interventions:					0.10
Pericardial window	7 (9%)	0	3 (13%)	4 (15%)	
Thoracentesis	1 (1%)	0	0	1 (4%)	
Mediastinal exp. for bleed	1 (1%)	0	1 (4%)	0	
Feeds at post-op discharge:					0.30
PO	69 (91%)	22 (88%)	22 (92%)	25 (93%)	
Nasogastric tube	1 (1%)	0 (0%)	1 (4%)	0 (0%)	
PO and gastrostomy tube	1 (1%)	0 (0%)	1 (4%)	0 (0%)	
Gastrostomy tube	5 (7%)	3 (12%)	0 (0%)	2 (7%)	
In-hospital mortality	0 (0%)	0 (0%)	0 (0%)	0 (0%)	–
Unplanned readmit <30 days	6 (8%)	2 (8%)	2 (8%)	2 (7%)	1.00
Days ventilated post-operatively	1 (1, 2)	1 (1, 2)	1 (1, 1)	1 (1, 1)	0.34
ICU days post-operatively	3 (2, 4)	4 (3, 4)[c]	3 (2, 4)[d]	2 (2, 3)	0.03
Days post-op hospitalisation	6 (5, 10)	6 (5, 11)	6 (4, 11)	6 (4, 8)	0.31
RESOURCE UTILISATION					
Days alive & out of hospital in 1st year	352 (341, 357)	351 (333, 358)	348 (340, 356)	354 (348, 357)	0.22
< 341 days (worst 25th %ile) out of the hospital in first year	17 (22%)	7 (28%)	6 (25%)	4 (15%)	0.49
Unplanned cardiac reintervention 1st year	2 (3%)	0 (0%)	2 (8%)*	0 (0%)	0.21
Weight at 1 year of age (kg)	8.3 (7.7, 9.4)	8.4 (7.6, 9.8)	7.9 (7.6, 8.6)	8.7 (8.0, 9.6)	0.12
Weight-for-age z-score at 1 year of age	−1.5 (−2.2, −0.5)	−1.2 (−2.4., −0.3)	−1.9 (−2.2, −1.1)	−1.4 (−1.9, −0.1)	0.37
Number of echos in 1st year#	11 (9, 13)	11 (9, 13)[e]	12 (10, 15)[f]	10 (7, 13)	0.09
Number of total outpatient cardiology clinic visits in first year of life	7 (6, 10)	8 (6, 10)	7 (6, 10)	6 (6, 8)	0.22

CPR = cardiopulmonary resuscitation. D/C = discharge. Echos = echocardiograms. ECMO = extracorporeal membrane oxygenation. Exp. = exploration. G-tube = gastrostomy tube. ICU = intensive care unit. NG = nasogastric. PO = per os. Post-op = postoperatively.
[a]Tertile 1 vs. Tertile 3, p < 0.001.
[b]Tertile 2 vs. Tertile 3, p < 0.001.
[c]Tertile 1 vs. Tertile 3, p = 0.008.
[d]Tertile 2 vs. Tertile 3, p = 0.286.
[e]Tertile 1 vs. Tertile 3, p = 0.185.
[f]Tertile 2 vs. Tertile 3, p = 0.03.
*Both patients underwent mitral valve replacement.
#Includes all inpatient and outpatient echocardiograms, including perioperative studies, in first year of life except transesophageal echocardiograms.

feeding pre-operatively were all found not to be significantly different across the age groups.

With regard to early post-operative outcomes, fewer ICU days were needed after surgery in the oldest age tertile when compared to the youngest tertile, but days of mechanical ventilation and hospitalisation were similar. Post-operative ICU days are known to be an imperfect outcome given that they can be influenced by a number of non-patient factors, such as availability of beds on the step-down unit and nursing staffing. That being said, it is possible that critical care therapies aside from mechanical ventilation were weaned quicker in the older patients and/or clinicians felt more comfortable transferring them out of the ICU earlier. There were no significant differences in post-operative complications or feeding route at discharge. These findings are generally consistent with the previous studies that concluded that surgical intervention in this population can be done safely and effectively at a relatively early age, albeit with some increased length of ICU and hospital stay.[6,7,11,14–16] The lack of important differences in clinical outcomes and resource utilisation outcomes noted in this study was likely influenced by judgement utilised by clinicians practising in the Children's Heart Program of South Carolina. For both pre-operative and post-operative variables, we speculate that patients who were not doing well with medical management were likely referred for surgery sooner, ultimately leading to equivalent outcomes among the age groups.

This study has several limitations. As with all retrospective studies, unmeasured confounding may have influenced outcomes. A more rigorous study design, such as a randomised trial in which eligible patients are assigned an age window for surgery shortly after birth, would certainly provide stronger evidence but is likely not feasible. As all study patients underwent surgery at one centre and were followed in a well-established statewide paediatric cardiology network, the findings may not be generalisable to other paediatric cardiac surgical programmes. The relatively small sample size may have limited our ability to detect differences in certain outcomes. A formal cost analysis was not performed but given the lack of differences in clinical measures of resource utilisation, would likely not add value to the study. Although emergency room visits or hospital days that occurred outside of the three study centres were not captured, given the lack of other tertiary paediatric hospitals in the state of South Carolina, any significant illnesses would have almost certainly resulted in transfer to one of the children's hospitals for which we had access to medical records. Several potential variables of interest, such as discharge and follow-up echocardiogram findings, were not able to be assessed due to the fact that many of the subjects received perioperative care during the paper medical record era, and those charts are difficult to access.

We conclude that for uncomplicated balanced complete atrioventricular septal defect repair during infancy, age at surgery was not associated with important differences in clinical outcomes or resource utilisation in the first year of life. These findings may have been influenced by the judgement of clinicians who determined the timing of surgery for individual patients. The data suggest that in general, infants with uncomplicated balanced complete atrioventricular septal defects may safely undergo surgical repair at 3 to 4 months of age with a neutral effect on most important measures of resource consumption in the first year of life.

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Conflicts of interest. None.

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