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ORIGINAL ARTICLE

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Aortic perfusion score for pulmonary atresia with intact ventricular septum: An antegrade coronary perfusion scoring system that is predictive of need for transplant and mortality

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Abstract

Background: Pulmonary atresia with intact ventricular septum is a unique congenital malformation of the heart in which patients may undergo single-, two- or 1½- ventricle repair. Size of the tricuspid valve annulus, morphology of the right ventricle and presence of ventriculocoronary connections can all impact the selection of appropriate palliative strategy. We developed the aortic perfusion score, a novel scoring system based on anterograde coronary perfusion with the aim of being able to identify patients at risk for death or transplant.

Methods: A retrospective study was conducted. Patients were included if an initial catheterization was done prior to any intervention. Each patient was assigned an aortic perfusion score based on the amount of antegrade perfusion to the four main coronary arteries. Various characteristics, including aortic perfusion score, were compared between those who required transplant or died during follow-up vs those who did not. Receiver operator curve analysis was done to determine a cutoff point predictive of a composite endpoint of death or transplant.

Results: A total of 64 patients were included in the analysis with 10 reaching the composite outcome. An aortic perfusion score of 227.5 predicted the endpoint with a sensitivity of 90% and a specificity of 83%. For each 1-point increase in the APS, the odds of death or transplant decreased by 1.7%.

Conclusion: The aortic perfusion score can be used to predict a composite endpoint of death or transplant and may be helpful in selecting patients that should be listed for transplant.

1 | INTRODUCTION

Pulmonary atresia with intact ventricular septum (PAIVS) is a rare form of congenital heart disease with an incidence of just under 1 in 10 000 live births, accounting for approximately 1.5% of all congenital heart disease.[1–3] What makes PAIVS of special interest is the marked variability in the morphology of the right ventricle and the anatomy of the coronary artery system which has led to the need for multiple management strategies.[4,5] While these management strategies have continued to improve, there are still no established guidelines by which an appropriate strategy may be selected. Patients with PAIVS may undergo a single ventricle repair, one and a half ventricle repair, two ventricle repair or cardiac transplantation, many of which can be achieved through a variety of surgical and interventional techniques.[6,7]

Despite advances in the selection of management strategy, reported mortality remains high. Survival of 60% to 85% has been reported at 1 year, 50% to 81%, at 5 years and 60 to 81% at 10 years, although lower survival was noted largely in patients born in earlier decades.[8–11] A unique feature of PAIVS that is associated with mortality is the presence of ventriculocoronary connections (VCCs) in some of these patients. Generally found in patients with a hypoplastic, hypertensive, unipartite right ventricle these connections can be of varying significance. In some instances, these connections are insignificant and offer minimal supply to the coronary artery from the right ventricle while in others this connections can be large and become aneurysmal leading to interruption in the native coronary system and causing to-

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fro flow in these coronary vessels. The latter of these scenarios can lead to coronary insufficiency and impaired perfusion to parts of the myocardium.

This becomes significant when the decision for decompressing the right ventricle is being made, as some patients will have portions of their myocardium being entirely supplied by blood that is being supplied by VCCs such that decompression of the right ventricle will lead to loss of this flow. Earlier studies of decompression in all children with PAIVS have demonstrated that not all areas of the coronary perfusion are necessary for survival and that patients can still survive despite having areas of unperfused myocardium.[12,13]

The aim of this study was to develop the aortic perfusion score, a novel scoring system to determine what percentage of the named coronary artery distribution is receiving antegrade flow through the aorta. Furthermore, this study set forth to determine the ability of such a score to predict the need for transplant or death in patients with pulmonary atresia with intact ventricular septum.

2 | METHODS

2.1 | Study design

A retrospective chart review was conducted of patients cared for at the Children's Hospital of Wisconsin from January of 2000 through December 2013. Patients with pulmonary atresia with intact ventricular septum were identified. Patients were included if they had a cardiac catheterization prior to any intervention and had a right ventricular and aortic root injection during the cardiac catheterization. Those without a catheterization or those without a catheterization prior to intervention were excluded.

2.2 | Echocardiographic data

Echocardiographic data was collected for each included patient. The preoperative echocardiogram done prior to the cardiac catheterization was used to collect this data. Echocardiographic parameters collected included, but were not limited to, tricuspid valve annulus, tricuspid regurgitation and right ventricular morphology.

2.3 | Cardiac catheterization data

Cardiac catheterization data was collected for included patient. The cardiac catheterization data collected included, but was not limited to presence and significance of ventriculocoronary connections, presence of coronary artery stenosis, presence of coronary artery ostial atresia, percentage of coronary flow dependent on ventriculocoronary connections in each separate coronary, and aortic supply score. Ventriculocoronary connections were graded using the following scale: not present, insignificant ventriculocoronary connections, significant ventriculocoronary connections and ventriculocoronary connection causing major interruption in a major coronary artery.

2.4 | Aortic perfusion score

A scoring system was developed to quantify antegrade coronary perfusion. The score was devised as follows. Each major coronary artery was assigned a max of 100 points: left anterior descending, left circumflex, right and posterior descending coronary artery. Points were assigned based on the amount of the coronary artery that was perfused antegrade from the aortic coronary sinus. Thus, 100 points correlates with 100% of the vessel being perfused antegrade from the aorta while 50 points correlates with 50% of the vessel being perfused antegrade from the aorta. The score of the coronary artery was halved if there was to-fro flow in the coronary artery due to ventriculocoronary corrections. Thus, a coronary artery with 50% antegrade perfusion and to-fro flow due to ventriculocoronary connections would receive a score of 25. In the presence of coronary artery ostial atresia the coronary artery would receive a score of 0.

Catheterizations were reviewed separately by both authors. After scoring had been carried out by both authors separately, scores were then compared by the two authors together. Each cardiac catheterization was reviewed by the authors together and a final score decided upon.

2.5 | Statistical analysis

Patients were separated into two groups based on clinical outcome: one group that did not undergo transplant and did not die during follow-up and another that underwent cardiac transplant or died during follow-up. For the remainder of the manuscript those not reaching the endpoints of interest will be referred to as the control group while those who did reach the endpoints of interest will be referred to as the outcome group. Comparative statistics were conducted using a student *t* test for continuous variables and chi-square analysis for descriptive variables due to normal distribution of the data. Receiver operator curve analysis was then done to determine cutoff points in the aortic perfusion score that were predictive of need for transplant or death.

A *P* value of less than 0.05 was considered statistically significant. All statistical analysis was done utilizing SPSS Version 20.0 (IBM Corporation, Chicago, IL).

3 | RESULTS

3.1 | Patient characteristics

A total of 64 patients were included in the final analysis. Of these patients, 10 (16%) underwent transplant or died during the follow-up period. There was no statistically significant difference in the proportion of male and female patients in each group and no difference statistically significant difference in the age of catheterization. In the control group there were 39% females and in the outcome group there were 30% females. Nearly all patients underwent cardiac catheterization within the first 3 months of life with a mean age of 72 days in the control group and a mean age of 32 days in the outcome group ($P = .460$) (Table 1).

The tricuspid valve annulus *z* score by echocardiography did not differ between the two groups (-2.89 ± 1.41 in the control group vs -4.56 ± 2.52 in the outcome group, $P = .186$). Right ventricular morphology did differ between the two groups with a lesser proportion of

TABLE 1 Patient characteristics

	Neither death nor transplant (n = 54)	Death or transplant (n = 10)	*P* value
Female	21 (39)	3 (30)	.594
Tricuspid valve annulus by echo (mm)	7.93 ± 3.80	6.67 ± 3.50	.361
Tricuspid valve annulus *z* score	−2.89 ± 1.41	−4.56 ± 2.52	.186
Age at initial catheterization (days)	72.34 ± 16.93	31.70 ± 18.39	.460
Right ventricular morphology			.019
Unipartite	6 (11)	1 (10)	
Bipartite	10 (19)	6 (60)	
Tripartite	38 (70)	3 (30)	
Ventriculocoronary connection grade			.002
Not present	33 (61)	1 (10)	
Insignificant VCCs	6 (11)	0 (0)	
Significant VCCs	12 (22)	8 (80)	
Major interruption in major coronary	3 (6)	1 (10)	
Stenosis in major coronary artery	0 (0)	5 (50)	.001
Single origin of coronary artery	0 (0)	2 (20)	.002
Percent of dependent right coronary in those with VCCs to right coronary	93.33 ± 11.55	81.67 ± 27.54	.536
Percent of dependent left anterior descending in those with VCCs to LAD	38.75 ± 13.15	80.00 ± 11.18	.001
Percent of dependent left circumflex coronary artery in those with VCCs to LC	–	91.67 ± 14.43	.032
Percent of dependent posterior descending coronary artery in those with VCCs to PD	83.33 ± 28.87	100.0 ± 15.02	.220
Aortic perfusion score	336.23 ± 91.14	137.80 ± 29.03	<.001
Repair status at most recent follow-up			<.001
Functionally univentricular	20 (37)	0 (0)	
1½ ventricular	7 (13)	1 (10)	
Biventricular	19 (35)	0 (0)	
Transplant	0 (0)	6 (60)	
Shunt	8 (15)	3 (30)	
Mortality	0 (0)	5 (50%)	.002
Age at death (months)	–	13.60 ± 3.61	–
Age at most recent follow-up (years)	5.87 ± 2.20	4.38 ± 1.17	.300

Abbreviations: LAD, left anterior descending; LC, left circumflex; PD, posterior descending; VCC, ventriculocoronary connection.

those in the control group having a bipartite ventricle than those in the outcome group (19% vs 60%, $P = .019$) while a greater proportion of those in the control group had a tripartite right ventricle than those in the outcome group (70% vs 30%, $P = .019$) (Table 1).

Ventriculocoronary connections differed between the control group and the outcome group as well: in the control group 61% did not have any ventriculocoronary connections present compared with 10% in the outcome group; 11% of the control group had insignificant ventriculocoronary connections compared with 0% of those in the outcome group; 22% of those in the control group had significant ventriculocoronary connections compared with 80% in the outcome group and 6% of those in the control group had ventriculocoronary connections causing major interruption in a coronary artery compared with 10% of those in the outcome group ($P = .002$) (Table 1).

None of the patients in the control group had stenosis in a major coronary artery compared with 50% of those in the outcome group ($P = .001$). Single origin of the coronary artery was present in none of the patients in the control group but in 20% of those in the outcome group ($P < .001$) (Table 1)

In those with ventriculocoronary connections present to the right coronary artery, there was a significant amount of the coronary being supplied by the ventriculocoronary connection. For those with ventriculocoronary connections to the right coronary artery, the mean percentage of the right coronary artery supplied by ventriculocoronary connections was 93% in the control group compared with 82% in the outcome group ($P = .536$). For those with ventriculocoronary connections to the left anterior descending coronary artery, the mean percentage of the left anterior descending coronary artery supplied by ventriculocoronary connections was 39% in the control group compared with 80% in the outcome group ($P = .001$). There were no patients in the control group with ventriculocoronary connections present to the left circumflex coronary artery. For those in the outcome group with ventriculocoronary connections present

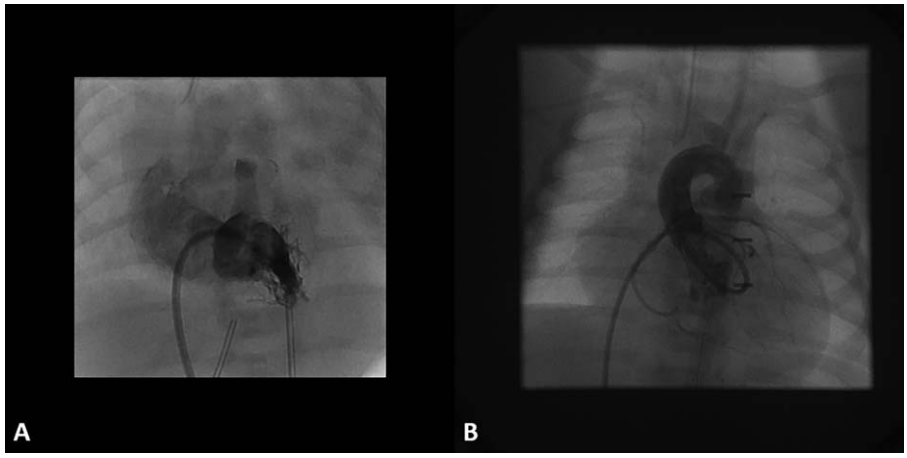

FIGURE 1 (A) Demonstrates a right ventriculogram in the anteroposterior projection from a patient with an aortic perfusion score of 400. Notice that there are no ventriculocoronary connections present. (B) Demonstrates an aortic root injection the in the anteroposterior projection from the same patient with an aortic perfusion score of 400.

to the left circumflex coronary artery the mean percentage of the coronary supplied by these connections was 92% ($P = .032$). For those with ventriculocoronary connections present to the posterior descending coronary artery, the mean percentage of the posterior descending artery supplied by these connections was 83% in the control group compared with 100% in the outcome group ($P = .220$) (Table 1).

The mean aortic perfusion score was 336.23 ± 91.14 in the control group and 137.80 ± 29.03 in those in the outcome group ($P < .001$) (Table 1). Figures 1 and 2 are representative images to demonstrate how scores were assigned. Figure 1A demonstrates an aortic root injection in the anteroposterior projection from a patient with an aortic perfusion score of 400. The left anterior descending, left circumflex, right and posterior descending coronary artery are all filled in their entirety with this injection. Thus, each of these coronary arteries received a score of 100. Neither the aortic root injection nor the right ventricular injection, shown in Figure 1B, demonstrated ventriculocoronary connections, thus there was no to-fro flow within any of the coronary arteries and no points were deducted for such to-fro flow.

Repair status at most recent follow-up differed between the two groups. Those in the control group were more likely to have undergone functionally univentricular palliation (37% vs 0%), were more likely to have undergone $1\frac{1}{2}$ ventricle palliation (13% vs 10%), were more likely to have undergone biventricular palliation (35% vs 0%), were less likely to have undergone transplant (0% vs 60%) and were less likely to have undergone shunt palliation (15% vs 30%) ($P < .001$).

None of the patients in the control group died during the follow-up period compared with 50% of those in the outcome group ($P < .001$). Mean age of death was 13.60 ± 3.61 months. The age at most recent follow-up did not differ between the control and outcome groups (5.87 ± 2.20 vs 4.38 ± 1.17 years, $P < .300$).

Receiver operator curve analysis was conducted to determine the utility of the aortic perfusion score in predicting the composite outcome of transplant or death. An aortic perfusion score of was found to predict the composite outcome with 90% sensitivity and 83% specificity with an area under the curve of 89.4% (Figure 3).

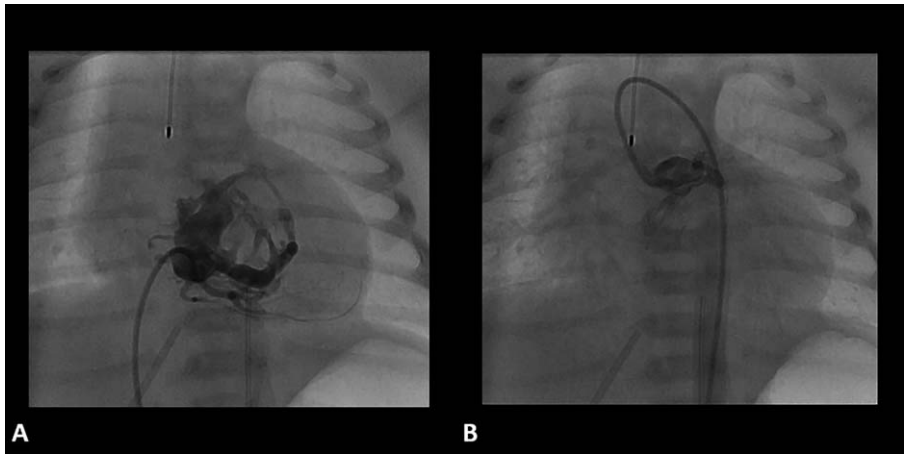

FIGURE 2 (A) Demonstrates a right ventriculogram in the anteroposterior projection from a patient with an aortic perfusion score of 10. Not the large burden of ventriculocoronary connections and the near absence of antegrade perfusion of any of the coronary arteries from the aortic root injection (B).

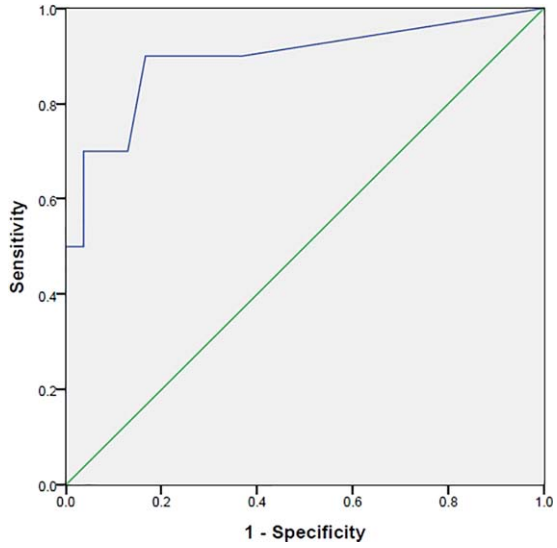

FIGURE 3 Receiver operator curve for aortic perfusion score in predicting need for transplant or death.

4 | DISCUSSION

In this study, 53% of all patients with pulmonary atresia with intact ventricular septum were found to have ventriculocoronary connections. Patients who had underwent heart transplant or experienced death were more likely to have had more significant ventriculocoronary connections with 90% of them having severe ventriculocoronary connections or ventriculocoronary connections leading to interruption in a major coronary artery. Previous studies have demonstrated similar frequency of patients having such ventriculocoronary connections with Freedom and colleagues having reported approximately 40% having such connections.[14] Other studies have noted that there is also a high frequency of other coronary artery anomalies, coronary artery stenosis or coronary artery ostial atresia, in patients with ventriculocoronary connections.[15–18] This finding was also confirmed by our study.

Pulmonary atresia with intact ventricular septum continues to pose a challenge in regards to the best palliation strategy for each individual patient. The Congenital Heart Surgeons Society set forth to study factors that may help decide between a functionally univentricular and biventricular repair strategy and identified initial tricuspid valve *z* score as an important factor in determining the approach that should be used to optimize late aerobic capacity, functional health status and survival.[19] Particular attention was not given to ventriculocoronary connections and their extent in this study.

The aim of this study was to determine what impact ventriculocoronary connections have on the need for transplant and risk of mortality. Using cardiac catheterization data prior to any intervention we were able to successfully determine an aortic perfusion score for all patients included in the study. The aortic perfusion score aimed to quantify the antegrade perfusion in the coronary arteries from the aorta. An aortic perfusion score could be assigned with relative ease when a right ventricular injection and an aortic root injection or selective coronary artery injections were performed. Indeed, this could also be done with good correlation between the two separate pediatric cardiologists.

With a minimum score of 0 representing no antegrade perfusion and all retrograde perfusion and a maximum score of 400 representing only antegrade perfusion of the coronary arteries, we found that an aortic perfusion score of 227.5 was found to predict the composite outcome with adequate sensitivity and specificity.

Few other studies have focused on the long-term implications of ventriculocoronary connections although a study by Dyamenahalli and colleagues reviewed a cohort of 210 patients with pulmonary atresia with intact ventricular septum and found that those with greater severity of coronary anomalies were more likely to develop left ventricular dysfunction.[10] Furthermore, Foker and colleagues reported a small series of patients in which surgical ligation of ventriculocoronary connections was conducted at the time of biventricular repair and noted that ligation of such connections improved myocardial oxygenation, demonstrating the mechanism of myocardial damage secondary to such ventriculocoronary connections.[20] Guleserian and colleagues reviewed the outcomes of a series of patients who had pulmonary atresia with intact ventricular septum they deemed to have right ventricle-dependent coronary circulation who underwent functionally univentricular palliation. They noted that coronary ostial atresia was associated with poor outcomes although an objective quantification of antegrade perfusion was not conducted.[9]

The implications of these findings are relatively straightforward. While one may be able to use the initial tricuspid valve *z* score to determine whether a functionally univentricular or biventricular palliation approach should be undertaken, the aortic perfusion score can predict the outcome of such a score in regards to the need for transplant or death. Patients with a lower *z* score thus are patients that may be better served by primary transplant or initial palliation, such as a shunt, to ensure hemodynamic stability followed by immediate listing for transplant. Such a scoring system has the potential to improve long-term outcomes in patients with pulmonary atresia with intact ventricular septum. Such a scoring system is more objective than simply classifying the coronary circulation as being right ventricle dependent as no discrete definition of right ventricular dependence has been set forth.

This study is not without its limitations. The low number of patients is a limitation to the study although a multicenter effort could help overcome this to further power the findings. If not a multicenter effort then validation of the scoring system by another center would also be valuable. In addition, this is a retrospective study based on chart review which inherently may result in error based on what was documented and how it was documented. A prospective study with a predefined data collection tool could be used in the future to help overcome this. The aortic perfusion score is prone to some subjectivity as well although we found minimal variability between individual scoring. The manuscript itself is limited by the need to demonstrate examples of such scoring using static images rather than cine clips as would be used for scoring.

It would be beneficial for a multicenter effort to be conducted to see if the findings of this study can be replicated. A more accurate cut-off point may also be discerned by such an effort.

5 | CONCLUSION

Quantification of antegrade coronary perfusion in the setting of pulmonary atresia with intact ventricular septum and ventriculocoronary connections may be able to predict patients at risk for transplant or death. Such a scoring system may be helpful in deciding what patients are best served by early transplant.

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CONFLICT OF INTEREST

None of the authors have any financial disclosures or conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

Both authors contributed to the manuscript and provided final approval of the manuscript.

Study design, data collection, APS determination, data analysis and initial drafting of the manuscript: Rohit Loomba

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