

Assessment of Atrioventricular and Ventriculoarterial Coupling Indices in Patients with Hypoplastic Left Heart Syndrome Utilizing Cardiac MRI and Invasive Hemodynamics

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Abstract

Background

Atrioventricular (AV) and ventriculoarterial (VA) coupling indices have demonstrated prognostic value in various cardiac pathologies but have not been studied in hypoplastic left heart syndrome (HLHS). This study assessed known and novel AV and VA coupling indices derived from cardiac MRI (CMR) and invasive hemodynamics for predicting adverse outcomes in HLHS patients with stage II palliation prior to Fontan completion.

Methods

CMR and catheterization data from 45 HLHS patients with stage II palliation undergoing pre-Fontan evaluation (January 2015–October 2025) were retrospectively analyzed. Known AV coupling indices and two novel indices— RA_{SV} -RV coupling index (RA stroke volume indexed/RV end-diastolic volume indexed) and combined RA-RV-Aorta coupling index—were compared between patients with and without adverse outcomes (composite of death, transplantation, heart failure hospitalization, SGLT2 inhibitor initiation, plastic bronchitis, protein-losing enteropathy). Predictive performance was assessed using Firth logistic regression and ROC analysis.

Results

Ten patients (22%) experienced adverse outcomes. Known AV coupling indices did not significantly differ between groups (AUC 0.48–0.69). The RV-Aortic coupling index was significantly lower in the adverse outcomes group (0.17 vs. 0.23, $p = 0.006$; AUC = 0.80). Both novel indices demonstrated superior discrimination: RA_{SV} -RV (0.11 vs. 0.17, $p = 0.002$; AUC = 0.82) and novel RA_{sv} -RV-Aorta (2.13 vs. 3.90, $p = 0.001$; AUC = 0.86). Nested models showed that adding each novel index to RV-Aortic coupling significantly improved model fit ($p = 0.036$ and $p = 0.048$, respectively).

Conclusions

Novel coupling indices designed for single ventricle physiology outperformed known AV coupling indices and provided incremental predictive value beyond RV-Aortic coupling alone for adverse outcomes in HLHS patients with stage II palliation.

1. INTRODUCTION

Hypoplastic left heart syndrome (HLHS) is a form of complex congenital heart disease characterized by varying degrees of hypoplasia of left heart structures that render the left ventricle inadequate to provide

systemic cardiac output. Right ventricular (RV) systolic dysfunction is a known risk factor for morbidity and mortality in patients with HLHS (1–3). Right atrial (RA) function abnormalities have also been associated with increased risk of hospitalization, need for transplant, and death in patients with single ventricle physiology, underscoring the importance of RA function evaluation in this patient population (4–6). While these factors have been examined independently, further exploration of the complex physiologic interactions between RA function, RV function and systemic circulation is needed in patients with HLHS.

Atrioventricular (AV) coupling refers to the interdependence between atrial and ventricular function, that is, the balance and efficiency of ventricular filling. When this process becomes disrupted (i.e. AV uncoupling), a mismatch or loss of coordination occurs between both, which can impair global cardiac performance (7, 8). Ventriculoarterial coupling (VA) looks at the relationship and efficiency between ventricular contractility and arterial resistance and compliance; when this process becomes inefficient (i.e. uncoupling), ventricular contractility is outmatched by arterial load, which can also lead to impaired global cardiac function (9–11). Several AV and VA performance indices have been studied that include RV and/or RA volumetric and strain data. These have been primarily used to evaluate patients with different cardiac pathologies such as cardiomyopathy, repaired tetralogy of Fallot, secondary tricuspid regurgitation, acute heart failure, and patients undergoing cardiac resynchronization therapy. These studies have demonstrated that indices of AV and VA coupling have been predictive of cardiac complications and worsened outcomes in these patient populations (8, 12–19). To our knowledge, there has not been published work exploring the utility of AV and VA performance indices in patients with HLHS.

The primary aims of this study were to assess how right AV and VA coupling indices compared between HLHS patients who did and did not experience adverse outcomes, the utility of existing AV and VA coupling indices in predicting outcomes for HLHS, and how established indices compare to novel indices designed by our group specifically for this patient population. Secondary aims were to compare cardiac MRI (CMR) and invasive hemodynamic data between HLHS patients with and without adverse outcomes.

2. METHODS

2.1 Patient Selection

We retrospectively re-analyzed CMR studies from patients with HLHS and stage II palliation (both Glenn and hemi-Fontan) who had a clinically indicated pre-Fontan CMR and cardiac catheterization at our institution between January 2015 and October 2025. All patients had previously been included in a retrospective study at our institution approved by the Colorado Multiple Institutional Review Board with a waiver of informed consent (6).

2.2 Image Analysis and Cardiac Catheterization Data

Cardiac magnetic resonance imaging studies were performed in 1.5 or 3T scanners (Philips Ingenia, Netherlands). General anesthesia was utilized due to young patient age. Feature tracking strain (RA and RV) was retrospectively performed using Circle Cardiovascular Imaging Software (Calgary, Canada, V 6.2.2). Cine images were obtained using breath-held, balanced steady-state free precession sequences and included a short axis stack (8–10 slices) and 1 horizontal long axis slice (4 chamber) which were contoured to define RV epicardial and endocardial borders (trabeculations excluded). Slice thickness was 5–6 mm, and frame count was 30/cycle. RV volumes were calculated from the short axis stack and RA volumes were calculated from the 4-chamber slice (single plane area-length method). RA appendage, systemic or pulmonary veins were excluded from contours. Feature-tracking RA strain was contoured by tracing the RA endocardium from the AV junction of the lateral/anterior free wall and across the roof of the atrium to reach the other AV valve junction. The feature-tracking module applies algorithmic tracking of myocardium to quantify multidimensional strain metrics. Mesh interface was utilized to visually confirm appropriate RV and RA wall tracking throughout all 30 phases of the cardiac cycle. Strain was calculated as (final length–initial length)/initial length for a given segment. Global RV strains in the longitudinal (GLS), circumferential (GCS) and radial planes (GRS). RA reservoir (RASr), conduit (RAScd) and pump (RASp) strain were recorded. RV, LV and RA volumes indexed to body surface area, as well as vessel flows and ratio of pulmonary to systemic blood flow (Qp:Qs) data was recorded.

Known AV and VA coupling indices were calculated as follows: right atrioventricular coupling index (RACI) = right atrial end diastolic volume (EDV)/ right ventricular end diastolic volume (RVEDV) (8), right atrioventricular coupling (RAVC)_{VOL} = RA maximal volume (RAV)/RV stroke volume (SV) (16), RA_{STIFF} = RA maximal volume indexed (RAVi)/RA longitudinal reservoir strain (RALS) (16), RAVC_{FT} = RALS/RV feature-tracking global longitudinal strain (RVGLS) obtained by CMR feature tracking (16), and RV-Aortic coupling index = [RVGLS/RV systolic pressure (RVSP)]*-1 (19).

Novel coupling indices designed by our group were calculated as follows: Novel RASv-RV Coupling Index = RA stroke volume indexed (RASVi)/RVEDV indexed (RVEDVi). Novel RA-RV-Aorta Coupling Index = (RVGLS/RVSP)*(RASVi/RVEDVi)*100.

Clinically indicated pre-Fontan cardiac catheterization was performed on the same day or within 30 days of the CMR study. We retrospectively collected hemodynamic data from patient charts including mean RA and left atrial pressures, right ventricular end-diastolic pressure, superior vena cava mean pressure, right and left pulmonary arterial pressure, and indexed pulmonary vascular resistance.

2.3 Follow Up

Electronic medical records, including outside records, were reviewed for clinical follow up endpoints. Data collection included the date of the last clinic visit and an adverse clinical outcomes composite of death, heart transplantation, heart failure symptomatology requiring hospital admission or initiation of a SGLT2 inhibitor, and a diagnosis of plastic bronchitis or protein-losing enteropathy. Clinical follow up was expanded from our previous work up to April 2026.

2.4 Statistical Analysis

Continuous variables are reported as median (interquartile range) and categorical variables as counts (percentages), with group comparisons performed using Wilcoxon rank-sum tests and Fisher's exact tests as appropriate. Associations between coupling indices and adverse outcomes were evaluated using Firth penalized logistic regression given the small event rate. Discriminatory performance was assessed using ROC curve analysis and area under the curve (AUC) with bootstrap-derived confidence intervals. Comparisons between AUCs were performed using DeLong's test. Incremental predictive value of novel indices beyond RV–aortic coupling was evaluated using nested logistic regression and likelihood ratio testing. Given the limited number of outcome events, analyses were restricted to parsimonious models to minimize overfitting. A two-sided $p < 0.05$ was considered statistically significant.

3. RESULTS

Forty-five patients with HLHS and stage II palliation who had a pre-Fontan CMR were included in this study. Of these, 44 patients had cardiac catheterization data available, with 33 of them having their hemodynamic study on the same day as the CMR study while 11 patients had it within 30 days. Demographics and clinical characteristics are shown in Table 1.

Table 1
Cohort demographics

Characteristic	N = 45 ¹
Legal sex	
Female	16 (36%)
Male	29 (64%)
HLHS subtype	
MA, AA	15 (33%)
MA, AS, VSD	1 (2%)
MS, AA	16 (36%)
MS, AS	13 (29%)
RV-PA conduit/Sano vs. mBTTs	
Sano/RV-PA conduit	37 (82%)
mBTTs	8 (18%)
Fontan	42 (93%)
Adverse outcome binary	10 (22%)
Age at last visit or event (months)	80 (49, 104)
Age at Fontan (months)	37 (31, 46)

Data are presented as n (%) or median (interquartile range)

AA aortic atresia, AS aortic stenosis, HLHS hypoplastic left heart syndrome, mBTTs modified Blalock-Taussig-Thomas shunt, MA mitral atresia, MS mitral stenosis, PA pulmonary artery, RV right ventricle, TAPVR total anomalous pulmonary venous return, VSD, ventricular septal defect

Of the 45 patients, 10 (22%) experienced the composite adverse outcome and 35 did not. Of the 10 patients with adverse events, 4 underwent heart transplantation, 3 developed heart failure symptomatology, 1 developed plastic bronchitis, 1 developed protein-losing enteropathy, and there was 1 death.

3.1 CMR and Cardiac Catheterization Data

Comparisons between patients with and without adverse outcomes for CMR, catheterization data, and coupling indices are shown in Table 2.

Table 2
Adverse outcome comparisons

Characteristic	Yes N = 10 ¹	No N = 35 ¹	p-value ²
Cardiac MRI Data			
TR Severity			0.3
None/Trivial	6 (60%)	21 (60%)	
Mild	2 (20%)	12 (34%)	
Moderate	2 (20%)	2 (5.7%)	
Age at study (years)	2.73 (1.93, 3.31)	2.87 (2.35, 3.38)	0.5
BSA (m ²)	0.59 (0.45, 0.63)	0.59 (0.55, 0.63)	0.4
HR (bpm)	102 (99, 114)	96 (84, 103)	0.090
RV EDVi (mL/m ²)	152 (121, 161)	123 (104, 143)	0.12
RV ESVi (mL/m ²)	87 (65, 95)	63 (51, 76)	0.029
RV SVi (mL/m ²)	60 (47, 66)	56 (52, 64)	0.8
RV EF (%)	43 (34, 45)	48 (44, 52)	0.002
RV Mass indexed (g/m ²)	40 (38, 52)	39 (35, 44)	0.5
LV EDVi (mL/m ²)	8.1 (2.4, 10.9)	5.5 (3.4, 9.9)	0.6
LV ESVi (mL/m ²)	5.50 (0.90, 8.10)	3.80 (2.70, 5.50)	0.5
Qp:Qs	0.85 (0.77, 1.46)	0.92 (0.79, 1.15)	0.5
AP collateral burden (pulmonary blood flow) (%)	0.59 (0.42, 0.76)	0.45 (0.34, 0.49)	0.045
RV global longitudinal strain (%)	-13.7 (-15.6, -9.6)	-17.8 (-19.8, -15.7)	< 0.001
RV global radial strain (long axis) (%)	20 (14, 24)	31 (24, 36)	< 0.001

Characteristic	Yes N = 10 ¹	No N = 35 ¹	p-value ²
Cardiac MRI Data			
RV global circumferential strain (%)	-12.20 (-13.30, -11.10)	-15.60 (-17.20, -13.70)	0.002
RA reservoir strain (%)	30 (23, 35)	37 (29, 40)	0.041
RA conduit strain (%)	10 (8, 27)	13 (11, 20)	0.4
RA pump strain (%)	15.3 (13.7, 23.1)	17.4 (13.1, 20.9)	> 0.9
Monoplanar 4CV Atrial max. volume indexed (mL/m ²)	38 (37, 64)	53 (41, 66)	0.11
Monoplanar 4CV Atrial min. volume indexed (mL/m ²)	25 (20, 42)	30 (22, 37)	0.7
Monoplanar 4CV Atrial SV indexed (mL/m ²)	17 (12, 21)	22 (16, 30)	0.078
Monoplanar 4CV Atrial EF (%)	34 (30, 46)	44 (37, 52)	0.036
Coupling Indices			
RACI (Right AV coupling index)	0.18 (0.15, 0.27)	0.24 (0.21, 0.27)	0.074
RAVC _{VOL}	0.85 (0.59, 1.00)	0.90 (0.80, 1.07)	0.3
RA _{STIFF}	1.42 (1.05, 2.46)	1.44 (1.13, 2.20)	0.8
RAVC _{FT}	2.27 (1.97, 2.54)	2.09 (1.80, 2.38)	0.2
Novel RAsv-RV coupling index	0.11 (0.08, 0.13)	0.17 (0.14, 0.24)	0.002
RV-Aortic coupling index	0.17 (0.17, 0.19)	0.23 (0.19, 0.26)	0.006
Novel RA-RV-Aorta	2.13 (1.49, 2.63)	3.90 (2.68, 5.29)	0.001

Characteristic	Yes N = 10 ¹	No N = 35 ¹	p-value ²
Cardiac MRI Data			
coupling index			
Invasive Hemodynamic Data			
SVC pressure (mmHg)	12.00 (11.00, 13.00)	9.00 (8.00, 11.00)	0.002
RPA pressure (mmHg)	11.00 (11.00, 12.00)	9.00 (8.00, 10.00)	< 0.001
LPA pressure (mmHg)	11.00 (10.00, 12.00)	9.00 (8.00, 10.00)	0.003
LA mean pressure (mmHg)	6.00 (5.00, 8.00)	4.00 (3.00, 5.00)	0.008
Transpulmonary gradient (mmHg)	4.50 (3.50, 6.50)	5.00 (4.00, 6.00)	> 0.9
RA mean pressure (mmHg)	5.00 (3.00, 7.00)	4.00 (3.00, 5.00)	0.3
RV EDp (mmHg)	7.50 (5.50, 9.00)	7.00 (5.00, 8.00)	0.4
RVSp (mmHg)	80 (76, 80)	80 (72, 88)	> 0.9
Cardiac Index (L/m/m ²)	3.50 (2.78, 4.10)	3.50 (3.00, 4.65)	0.7
Qp:Qs	0.57 (0.47, 0.68)	0.61 (0.55, 0.65)	0.7
PVRi (WU·m ²)	2.38 (1.79, 2.98)	1.91 (1.30, 2.38)	0.2

Data are presented as n (%) or median (interquartile range)

² Fisher's exact test; Wilcoxon rank sum test; Wilcoxon rank sum exact test

4CV 4 chamber view, BSA body surface area, EDp end diastolic pressure, EDVi end diastolic volume indexed, EF ejection fraction, ESVi end systolic volume indexed, PVRi pulmonary vascular resistance indexed, Qp:Qs ratio of pulmonary to systemic blood flow, RVSp right ventricular systolic pressure, SVi stroke volume indexed, TR tricuspid regurgitation

Volumetric analysis by CMR showed no significant difference in right atrial maximum or minimum volume between groups, though atrial ejection fraction was significantly lower in those with adverse outcomes (34% vs. 44%, p = 0.036). The adverse outcomes group had significantly larger indexed RV end-systolic volume (87 ml/m² vs. 63 ml/m², p = 0.029) and lower RV ejection fraction (43% vs. 48%, p =

0.002). RV end-diastolic volume and RV indexed mass were not significantly different between groups. Left ventricular volumes and mass did not differ between the groups.

On CMR strain analysis, patients with adverse outcomes had lower RA reservoir strain (30% vs. 37%, $p = 0.041$). RA conduit and pump strain were not significantly different between groups. All global RV strain magnitudes (longitudinal, radial, and circumferential) were significantly lower in the adverse outcomes group.

Cardiac catheterization data demonstrated higher filling and pulmonary pressures in the adverse outcomes group, including elevated superior vena cava pressure (12mmHg vs. 9mmHg, $p = 0.002$), right and left pulmonary artery pressures (11mmHg vs. 9mmHg for both, $p < 0.001$ and $p = 0.003$, respectively), and mean left atrial pressure (6mmHg vs. 4 mmHg, $p = 0.008$). Other invasive hemodynamic measures, including cardiac index, pulmonary vascular resistance, and transpulmonary gradient, did not differ significantly between groups.

3.2 Coupling Indices

Known AV coupling indices did not show statistically significant differences between groups; however, a trend toward lower RACI was observed in the adverse outcomes group ($p = 0.074$). Known RV-Aortic coupling index was significantly lower in the adverse outcomes group (0.17 vs 0.23, $p = 0.006$). Both novel coupling indices showed marked differences between groups. Novel RAsv-RV coupling index was significantly lower in the adverse outcomes group (0.11 vs 0.17, $p = 0.002$), as was the novel RA-RV-Aortic index (2.13 vs 3.90, $p = 0.001$).

3.3 Predictive value of known and novel coupling indices

On univariable analysis using Firth logistic regression (shown in Table 3), the only known coupling index that was significantly associated with adverse outcomes was the RV-Aortic coupling index ($p = 0.002$).

Table 3
Univariable association of coupling indices with adverse outcomes.

Variable	Odds Ratio	Lower Confidence Interval	Upper Confidence Interval	p-value
RACI	6.32e-05	5.42e-11	5.37	0.099
RAVC _{VOL}	0.89	0.01	1.76	0.781
RA _{STIFF}	1.05	0.56	1.51	0.805
RAVC _{FT}	1.91	0.57	6.68	0.286
Novel RAsv-RV coupling index	2.40e-10	7.76e-20	0.00	0.002
RV-Aortic coupling index	3.76e-13	2.19e-25	9.34e-05	0.002
Novel RA-RV-Aorta coupling index	0.36	0.12	0.73	0.001

Odds ratios with 95% confidence intervals. Statistically significant associations ($p < 0.05$) were observed for the novel RAsv-RV coupling index, the RV-Aortic coupling index, and the novel RA-RV-Aorta coupling index.

The known atrioventricular coupling indices were not statistically significant. In contrast, both novel indices demonstrated strong associations with adverse outcomes, including the RAsv-RV coupling index ($p = 0.0016$) and RA-RV-Aortic coupling index ($p = 0.0012$).

Discriminatory ability differed across indices. Discriminatory ability was assessed using the area under the receiver operating characteristic curve (AUC). AUC values were interpreted as excellent (≥ 0.9), strong (0.8–0.89), moderate (0.7–0.79), weak (0.6–0.69), and no discrimination (≤ 0.5). Strong discrimination was noted for RV-Aortic coupling index (AUC = 0.80), novel RAsv-RV (AUC = 0.82), and novel RA-RV-Aorta (AUC = 0.86) which are shown in Fig. 1.

Again, known AV coupling indices showed limited performance (AUC range 0.48–0.69). Direct comparison of ROC curves using DeLong's test did not show statistically significant difference between the RV-Aortic and novel indices ($p = 0.39$ –0.97).

Nested logistic regression models were then performed, with the addition of each novel coupling index to a base model containing RV-Aortic coupling index resulting in a significant improvement in model fit. Specifically, inclusion of the novel RAsv-RV coupling index resulted in a significant improvement ($\chi^2 =$

4.39, $p = 0.036$), and inclusion of the novel RA-RV-Aorta coupling index similarly improved model fit ($\chi^2 = 3.91$, $p = 0.048$).

4. DISCUSSION

In this study, we evaluated the prognostic utility of known and novel AV and VA coupling indices in HLHS patients with stage II palliation prior to undergoing Fontan completion. The main findings of the study were: 1. Lower RV-aortic coupling index was associated with worsened outcomes post-Fontan. 2. Novel RAsv-RV and RA-RV-Aorta coupling indices outperformed known indices for predicting worsened outcomes. 3. The addition of novel coupling indices significantly improved predictive value compared to known RV-Aortic coupling alone. To our knowledge, this is the first study evaluating these specific indices in patients with HLHS.

Global evaluation of cardiac performance is crucial in patients undergoing staged palliation given its complex interdependence to single ventricle physiology. Assessing AV and VA coupling may offer some insight into these interactions. AV coupling indices have previously shown to be predictive of worse outcomes in patients with biventricular physiology and pathologies such as beta-thalassemia major, dilated cardiomyopathy, and following ST-elevation myocardial infarction (8, 12–14, 16). In the congenital heart disease population, RACI was shown to be the most effective predictor of a high-risk importance score in patients with repaired tetralogy of Fallot (15). In our study, known indices of AV coupling did not perform particularly well as predictive tools, with RACI being the best. We hypothesize these indices did not translate to the HLHS cohort given the distorted atrial geometry following atrial septectomy, variable AV connections (mitral stenosis vs mitral atresia), and simultaneous exposure to systemic and pulmonary venous connections (IVC and pulmonary veins).

Conversely, the known VA coupling index translated well to our HLHS cohort with a significantly lower value in those with adverse outcomes vs. those without. VA coupling has been well studied as RV-pulmonary artery in patients with pulmonary arterial hypertension and identified as an important prognostic factor (20–23). While the anatomy differs greatly, single ventricle physiology in the setting of HLHS similarly exposes the RV to high afterload which in turn leads to a chronic process of maladaptation. As RV systolic dysfunction ensues, reflected as decreased myocardial deformation or strain in our study, while afterload remains elevated, a similar mechanism of uncoupling as pulmonary hypertension appears to occur (i.e. increased strain over systolic arterial pressure ratio)(24). RVGLS indexed to systolic PA pressures to assess RV-PA coupling has been validated against invasive hemodynamics and in our patient population we were able to utilize invasive RVSP to estimate systolic arterial pressures (25).

As part of this study, we sought to derive coupling indices based on single ventricle physiology. In the absence of a sub-pulmonary pump, atrial contribution is the main driver of systemic ventricular filling. However, over time, RA dilation and decreased emptying may ensue as part of the maladaptation process of RV systolic dysfunction (6). This interdependence led us to utilize indexed right atrial stroke

volume (RASVi) as an atrial performance metric in a ratio that would quantify how well it translates to ventricular preload (26, 27). Indexed right ventricular end-diastolic volume (RVEDVi) has been shown to be a strong predictor of death or transplant in Fontan patients and captures a wide array of pathophysiologic causes of ventricular dilation (28). Our study showed the ratio between RASVi and RVEDVi in our novel RASv-RV coupling index is a useful predictor of adverse outcomes and outperforms known AV indices in our specific patient population.

Our study also demonstrated that a combined RA-RV-Aortic coupling index, incorporating the novel RASv-RV coupling index and RV-Aortic coupling index, was the best predictor of adverse outcomes of the indices assessed. This would further emphasize the importance of synchrony throughout the entire forward-flow pathway of single ventricle physiology. In biventricular physiology, the right and left heart operate largely in parallel with the pulmonary vasculature as an intermediary, rendering RA-RV interaction largely decoupled from systemic output. In single ventricle patients, systemic output is entirely reliant on RA contribution to ventricular preload in the absence of a sub-pulmonary pump. As mentioned, RA performance is largely influenced by RV mechanics, which in turn are subject to the abnormal vascular properties of a reconstructed aorta with decreased distensibility and often arch size mismatch (29). The RV therefore faces both abnormal preload and afterload, and our combined RA-RV-aortic index is designed to assess these in unison.

Nested logistic regression models further suggested the benefit of both novel coupling indices, with each showing a significant improvement in model fit when added to a base model containing the known RV-aortic coupling index (the best performing known index in our study). The novel RA–RV–aorta index incorporates both RASv–RV and RV–aortic components; therefore, nested modeling using RV–aortic as a base model evaluates whether the composite index captures additional nonlinear or interaction effects rather than independent additive contributions. Our results show the novel coupling indices provide independent and incremental predictive value over traditional indices alone. As a secondary aim, we assessed CMR and invasive hemodynamic data in patients with and without adverse outcomes. By CMR, worse RVEF, RVESVi, RV strains (longitudinal, radial, and circumferential), and RA reservoir strain were all associated with adverse outcomes which align with previously published work (6, 28, 30). The statistical results of our invasive hemodynamic data were interesting. Despite relatively small differences in PA pressures between the adverse outcomes and no adverse outcomes group (11mmHg vs 9mmHg respectively) this difference was still statistically significant. Elevated mean PA pressure is a well-known risk factor for Fontan failure, though reported at higher values (13 mmHg pre-Fontan and 17 mmHg post-Fontan) (31, 32). We also found that increased SVC and LA pressures were associated with adverse outcomes, while PVRi, RVEDP, and cardiac index did not differ significantly between groups. It is important to note, however, that patients who did not go on to Fontan completion based on pre-operative assessments are not included in these numbers. Overall, our study findings would support the notion of following closely trends in invasive hemodynamics rather than specific values, as well as interpreting these alongside CMR volumetrics in a comprehensive assessment of this patient population.

4.1 Limitations

Our study has several limitations. This is a single-center retrospective study with a relatively small sample size. Specific commercial software was utilized for CMR strain analysis which may introduce bias and reduce generalizability. RA volumes were calculated from a single 4-chamber CMR slice (following the same contours as RA strain); however, no other methods have been studied in our specific patient population whose atrial anatomy is distorted after atrial septectomy. Lastly, a larger cohort would allow for stronger confirmation of our findings.

5. CONCLUSIONS

Lower novel AV and VA coupling indices are observed in HLHS patients with Glenn and hemi-Fontan physiology and adverse outcomes vs. those without adverse outcomes. Previously reported AV coupling indices did not differ between outcome groups in this unique patient population, possibly owing to their unique atrial configuration. Novel indices may provide improved predictive value over traditional VA coupling indices alone. Larger studies will be needed to corroborate our results.

Abbreviations

AV

Atrioventricular

CMR

Cardiac magnetic resonance

EDV

End diastolic volume

GLS

Global longitudinal strain

HLHS

Hypoplastic left heart syndrome

RA

Right atrium

RACI

Right atrioventricular coupling index

RALS

Right atrial longitudinal reservoir strain

RASV

Right atrial stroke volume

RA_{SV}-RV

Right atrial stroke volume-right ventricle RAV, Right atrial maximal volume

RAVC

Right atrioventricular coupling

RV

Right ventricle
RVEDV
Right ventricular end diastolic volume
RVEF
Right ventricular ejection fraction
RVSP
Right ventricular systolic pressure
VA
Ventriculoarterial.

Declarations

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Conflict of Interest Disclosures

(includes financial disclosures): The authors have no conflicts of interest to disclose.

Data statement

Data unavailable to post or share due to research data including confidential information such as patient data.

Author Contribution

A.R., M.M. and C.G. wrote the main manuscript text and tables. M.M. prepared figure 1. All authors reviewed the manuscript.

Data Availability

Data unavailable to post or share due to research data including confidential information such as patient data.

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Figures

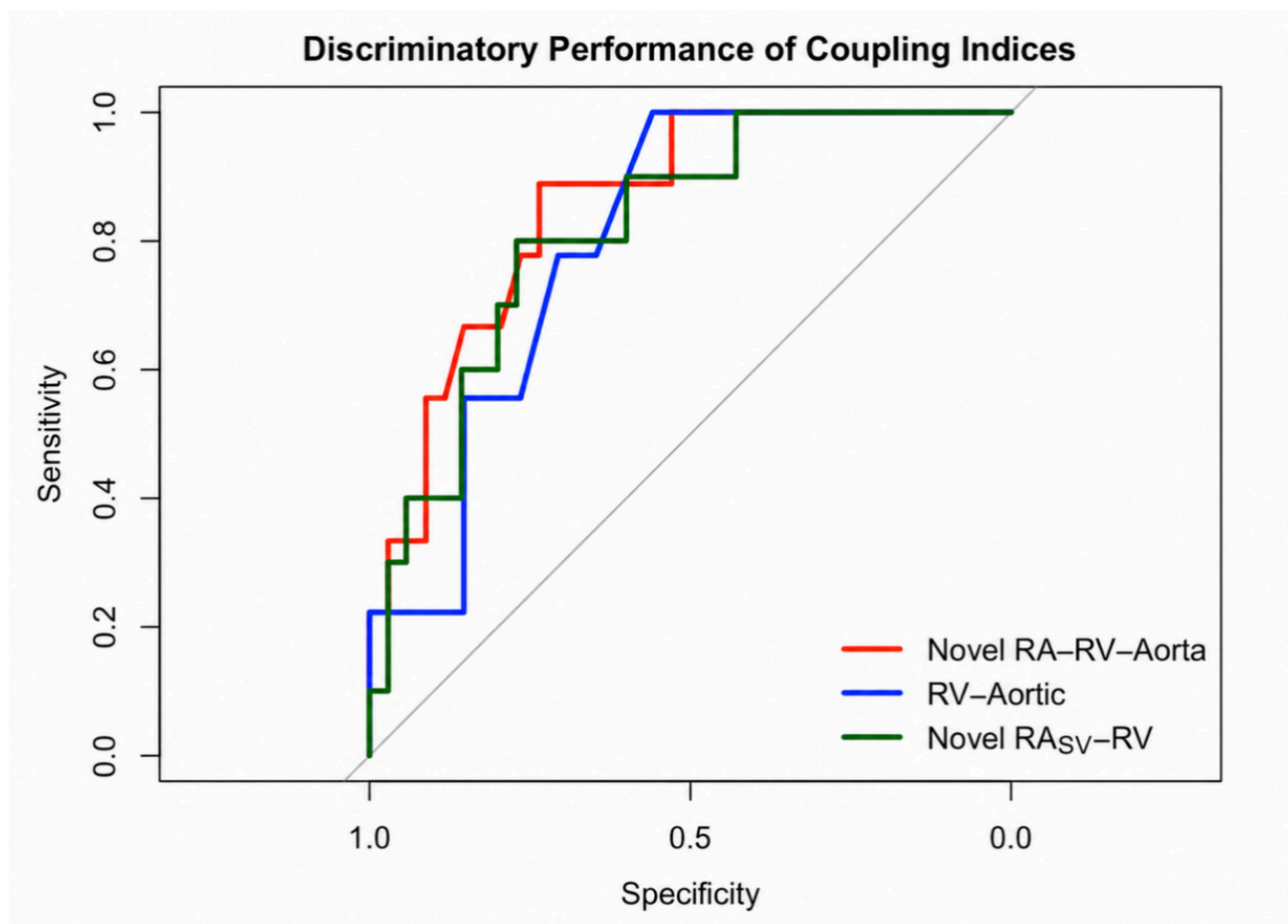


Figure 1

Receiver operating characteristic (ROC) curves demonstrating the discriminatory performance of coupling indices for prediction of adverse outcomes in patients with HLHS. The novel RA–RV–aorta coupling index (red line) demonstrated the highest discrimination (AUC 0.86, 95% CI 0.72–0.96), followed by the novel RAsv–RV index (green line; AUC 0.82, 95% CI 0.68–0.95) and the RV–aortic coupling index (blue line; AUC 0.80, 95% CI 0.66–0.92). The diagonal line represents no discrimination (AUC = 0.5). AUC area under the curve, CI confidence interval.