Staged ventricular recruitment and biventricular conversion following single-ventricle palliation in unbalanced atrioventricular canal defects

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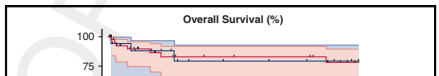
ABSTRACT

Objective: Restoration of biventricular circulation is an alternative management strategy in unbalanced atrioventricular canal defects (uAVCDs), especially in patients with risk factors for single-ventricle palliation (SVP) failure. When ventricular volume is inadequate for biventricular circulation, recruitment procedures may accommodate its growth. In this study, we review our uAVCD experience with biventricular conversion (BIVC) after prior SVP.

Methods: This is a single-institution, retrospective cohort study of uAVCD patients who underwent BIVC after SVP, with staged recruitment (staged) or primary BIVC (direct) between 2003 to 2018. Mortality, unplanned reinterventions, imaging, and catheterization data were analyzed.

Results: Sixty-five patients underwent BIVC from SVP (17 stage 1, 42 bidirectional Glenn, and 6 Fontan). Decision for conversion was based on poor SVP candidacy (n = 43) or 2 adequately sized ventricles (n = 22). Of the 65 patients, 20 patients underwent recruitment before conversion. The staged group had more severe ventricular hypoplasia than the direct group, reflected in prestaging end-diastolic volume *z* scores (−4.0 vs −2.6; $P < .01$), which significantly improved after recruitment (−4.0 to −1.8; $P < .01$). Median follow-up time was 1.0 years. Survival and recatheterizations were similar between both groups (hazard ratio, 0.9; 95% CI, 0.2-3.7; $P = .95$ and hazard ratio, 1.9; 95% CI, 0.9-4.1; $P = .09$), but more reoperations occurred with staged approach (hazard ratio, 3.1; 95% CI, 1.3-7.1; $P = .01$).

Conclusions: Biventricular conversion from SVP is an alternative strategy to manage uAVCD, particularly when risk factors for SVP failure are present. Severe forms of uAVCDs can be converted with staged BIVC with acceptable mortality, albeit increased reinterventions, when primary BIVC is not possible. (JTCVS Open 2022;■:1-14)



Overall survival is similar for staged and primary biventricular conversion in UAVCD.

CENTRAL MESSAGE

Staged and primary biventricular conversion from single-ventricle palliation is an alternative strategy to manage unbalanced atrioventricular canal defects, especially when risk factors are present.

PERSPECTIVE

Severe forms of unbalanced atrioventricular canal defects are often managed with single-ventricle palliation. We demonstrate that biventricular conversion from prior single ventricle palliation can be achieved with acceptable early and late mortality, and that recruitment procedures promotes significant growth of hypoplastic ventricles and allow for successful conversion to biventricular circulation.

See Commentary on page XXX.

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Abbreviations and Acronyms

ASD = atrial septal defect
AV = atrioventricular
CMRI = cardiac magnetic resonance imaging
EDV = end-diastolic volume
mBTTS = modified Blalock-Taussig-Thomas shunt
SVP = single-ventricle palliation
uAVCD = unbalanced atrioventricular canal defect

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Q4 Unbalanced atrioventricular canal defects (uAVCDs) represent 10% to 15% of all patients with complete atrioventricular (AV) canal defects.[1,2] Although the definition of an unbalanced AV canal is actively debated, a general anatomic feature is the presence of varying hypoplasia of the inflow valve and/or ventricle.[3,4] uAVCDs can be further categorized by a left- or right-sided dominance, in reference to the common AV valve positioned predominantly over the left or right ventricle, respectively.[4,5] Based on the severity of AV valve or ventricle hypoplasia, current management includes biventricular repair or, in severe cases, single-ventricle palliation (SVP).[1,6-8]

As widely demonstrated, patients with SVP can develop serious complications later in life such as protein-losing enteropathy, heart failure, and others. Studies report survival outcomes between 60% and 80% at 1 and 5 years.[9] Furthermore, outcomes were reported to worsen with risk factors such as Down syndrome, younger age, or AV valve regurgitation. An alternative strategy for patients with uAVCD is initial SVP followed by subsequent biventricular conversion following somatic growth.[10-13] In circumstances of severe imbalance due to valvular or ventricular hypoplasia, interim ventricular recruitment/staging procedure can be performed to promote inflow into the hypoplastic valve or ventricle, followed by biventricular conversion in patients demonstrating favorable response to recruitment maneuvers.[10,13] The objective of this study was to review outcomes in a tertiary center of patients with uAVCD with prior SVPs who underwent recruitment and subsequent biventricular repair.

METHODS

Study Design

A single-center retrospective review was performed on all patients diagnosed with an uAVCD who had undergone a previous SVP followed by subsequent biventricular conversion at Boston Children's Hospital between January 2003 and December 2018. The hospital institutional review board waived the need for parental consent for patients included in this study and approved this study for publication under protocol No. P00033695 on October 25, 2019.

Patients were separated into 2 groups: staged biventricular conversion: uAVCD with prior SVP who underwent procedures for staged recruitment followed by subsequent biventricular conversion, and primary biventricular conversion: uAVCD with prior SVP who underwent subsequent biventricular conversion without staged recruitment procedures. Patients who are in the process of recruitment were excluded from the current study.

Definitions

An uAVCD was defined as a complete AV septal defect with an AV valve override >60% over either ventricle, the presence of a hypoplastic-/nonapex-forming ventricle, or indexed ventricular volumes with a z score <–2 or 4, and those who were deemed unbalanced and underwent SVP at an outside institution. In determining AV valve override, we measured the area of the common AV valve in diastole, and the left and right AV valve components based on the interventricular septum. SVP was defined as a stage 1 procedure, bidirectional Glenn procedure, or a Fontan procedure. Patients with pulmonary artery banding as sole palliation were not included in this study.

Staging/recruitment procedure was defined as a procedure purposed to redirect or increase blood flow or accommodate growth of the hypoplastic ventricle. Specifically, these comprised a fenestrated atrial septal defect (ASD) creation, septation of AV valve, and/or an aortopulmonary shunt, typically a modified Blalock-Taussig-Thomas Shunt (mBTTS). Techniques for staging/recruitment and biventricular conversion were performed as previously described (Figure E1).[14] In brief, the size of the ASD fenestration is typically 4 mm. AV valve septation at the time of staged ventricular recruitment is typically done by opposing the superior and inferior leaflets in such a way as to close the central portion of the cleft. The atrial patch is then sutured to the confluence of the common leaflets, thus separating the common valve into right and left components. The atrial patch is essentially similar to the atrial patch of the 2-patch repair and is performed without division of the leaflet. The size of the mBTTS depends on the weight and body surface area of the patient, but it has been our institutional preference to use a 3.5- to 4-mm mBTTS. The index surgery was defined as the biventricular conversion procedure. All index and recruitment procedures were done at our tertiary care center, but the initial SVP may have been performed at an outside institution.

Outcomes and Follow-Up

Patient charts were reviewed, and the following data were extracted: patient demographic characteristics, imaging details, prior interventions, operative details, postoperative complications, reinterventions, and mortality. The majority of patients had a cardiac magnetic resonance imaging (CMRI) scan before recruitment and before biventricular conversion. For patients who did not have CMRI data, 3-dimensional echocardiographic data were used to obtain ventricular dimensions from prerecruitment and prebiventricular conversion, to maintain consistency.[15,16] Using the Boston Children's Hospital Heart Center database, z scores were calculated for the corresponding MRI and echocardiographic measurements. Mortality was defined as death or transplant occurring after the biventricular conversion. Reoperations were defined as any unplanned operative procedure that occurred after the index procedure. Likewise, reinterventions were defined as any unplanned catheter-based interventions that occurred after the index procedure. Follow-up was measured from the date of the index procedure. All follow-up was performed at our tertiary care center.

Statistical Analysis

Continuous variables are expressed as median (interquartile range [IQR]). Categorical variables are presented as absolute and relative frequencies. All continuous variables were normally distributed as tested by Shapiro-Wilk test and graphical represented by histograms and Q-Q plots. Variables were analyzed regarding the need or not for recruitment of the ventricle before biventricular conversion. Between-group comparisons were performed using 2-sided t test. Pearson χ^2 test was used for nominal variables. Longitudinal analysis for between-groups comparisons was

performed using 2-way repeated-measures analysis of variance within the framework of fitting mixed-effects linear regression models. To reduce the probability of false-positive results (type I error) due to multiple comparisons, Benjamin and Hochberg false discovery rate was applied to control the familywise error to <0.05. Five-year overall, catheterization-free and reoperation-free survival was estimated following generation of Kaplan-Meier curves. The log-rank test was used to perform comparisons of survival between different groups. Cox proportional hazards univariate models were used to identify the variables that were independently predictive of the outcome of interest. All tests reported are 2-tailed. Statistical analyses were performed with Stata version 15.0 (StataCorp LLC) and GraphPad Prism 8 for MacOS (GraphPad Software).

RESULTS

Baseline Characteristics

A total of 65 patients met our inclusion criteria. Of these, 41 patients had right-dominant uAVCD and 24 had left-dominant uAVCD. The median age at biventricular conversion was 3.5 years (IQR, 1.7-6.1 years). The median end-diastolic volume (EDV) *z* score of the unbalanced ventricle was –3.2. Review of our patient cohort with prior SVP demonstrated that the majority had risk factors for poor SVP candidacy in uAVCDs. Specifically, 54% (35 out of 65) had heterotaxy, 71% (46 out of 65) demonstrated the presence of AV valve regurgitation, 32% (21 out of 65) had pulmonary vein stenosis or partial/total anomalous pulmonary venous return, 9% (6 out of 65) had failing SVP physiology, and 25% (16 out of 65) had trisomy 21. Only 34% (22 out of 65) of patients had no risk factors. Before biventricular conversion, 26% had undergone stage 1/Norwood procedure, 65% had undergone bidirectional Glenn, and 9% had undergone a Fontan procedure. Eighty-five percent of patients (55 out of 65) had their SVP operation at an outside hospital. Baseline patient characteristics are demonstrated in Table 1. The mean left atrial pressure was 7.9 ± 2.3 mm Hg, pulmonary artery pressure was 13.6 ± 3.1 mm Hg, and the mean pulmonary vascular resistance was 2.0 ± 1.1 Woods units (Table 2).

A total of 20 patients underwent staged biventricular conversion and 45 underwent primary biventricular conversion (Figure 1). The average age at the time of biventricular conversion was 4.0 years and 3.4 years for the staged biventricular conversion and primary biventricular conversion, respectively. Staged biventricular conversion patients spent a median of 2.91 years with SVP physiology and 1.1 years with recruitment. Primary biventricular conversion patients spent a median of 3.1 years in SVP. Patients in staged biventricular conversion had a significant difference in the proportion of patients with a severely hypoplastic ventricle, demonstrated by EDV *z* score (–4.0 ± 0.9 vs –2.6 ± 1.4; $P < .01$), when compared with primary biventricular conversion. All 20 patients in the staged biventricular conversion group underwent 1 or more staged recruitment procedure to promote growth of the hypoplastic ventricle and/or AV valve. Recruitment procedures were performed in 35% (7 out of 20) during stage 1, 60% (12 out of 20) during BDG, and 5% (1 out of 20) during Fontan. During recruitment, 75% (15 out of 20) had a fenestrated ASD, 66% (13 out of 20) had an AV valve partitioning, 40% (8/20) had mBTTS placement, and 60% had concurrent procedures (14 out of 20). Preoperative characteristics of patients who underwent staged biventricular conversion are demonstrated in Table E1. When comparing the preoperative imaging and hemodynamics of staged biventricular conversion and primary biventricular conversion, we found the mean left atrial pressures were 7.5 ± 2.1 mm Hg versus 8.1 ± 2.4 mm Hg ($P = .32$), mean pulmonary artery pressures were 12.8 ± 2.5 mm Hg versus 13.8 ± 3.3 mm Hg ($P = .31$), and pulmonary vascular resistances were 2.2 ± 1.5 Woods units vs 1.8 ± 0.8 Woods units ($P = .31$), respectively (Table 2).

TABLE 1. Baseline patient characteristics and baseline patient characteristics of all biventricular conversions (BIVs)

Characteristic	All BIVs (n = 65)	Staged BIV (n = 20)	Primary BIV (n = 45)
Gender*	28:37	9:11	19:26
Dominant ventricle†	41:24	16:4	25:20
Age at BIV conversion (y)	3.5	3.2 (2.2-5.6)	3.7 (1.5-6.9)
Heterotaxy	35 (54)	11 (55)	24 (53)
Pulmonary vein disease	21 (32)	8 (40)	13 (29)
Single papillary muscle	20 (31)	10 (50)	10 (22)
Hypoplastic heart (*z* score <–2)	27 (42)	17 (85)	10 (16)
Trisomy 21	16 (25)	3 (15)	13 (29)
Previous SVP procedure			
Stage 1/Norwood	17 (26)	7 (35)	10 (22)
Bidirectional Glenn	42 (65)	12 (60)	30 (67)
Fontan	6 (9)	1 (5)	5 (11)

Values are presented as n, median (range), or n (%) unless otherwise noted. *BIV*, Biventricular conversion; *SVP*, single-ventricle palliation. *Values are presented as ratio of male to female. †Values are presented as ratio of right to left.

TABLE 2. Preoperative imaging and hemodynamic characteristics

Variable	All BIVs (N = 65)	Staged BIV (n = 20)	Primary BIV (n = 45)	*P* value
Presence of AW regurgitation	46 (71)	12 (60)	34 (76)	.203
Left atrial pressure (mm Hg)	7.9 ± 2.3	7.5 ± 2.1	8.1 ± 12.4	.321
Mean PA pressure (mm Hg)	13.6 ± 3.1	12.8 ± 12.5	13.8 ± 13.3	.308
PVR (Woods Unit)	2.0 ± 1.1	2.2 ± 1.5	1.8 ± 0.8	.311
Right dominant (n = 41)				
AVVI	0.33 ± .08	0.29 ± 1.07	0.36 ± 1.06	<.001
LVEDVi (mL/m^2)	38.9 ± 18.7	27.7 ± 9.64	46.7 ± 9.6	.001
RVEDVi (mL/m^2)	110.1 ± 11.2	97.6 ± 26.5	119.6 ± 26.3	.072
Left dominant (n = 24)				
AVVI	0.63 ± 0.03	0.66 ± 0.02	0.62 ± 0.03	.028
LVEDVi (mL/m^2)	89.1 ± 43.3	133.6 ± 16.2	80.3 ± 28.9	.048
RVEDVi (mL/m^2)	48.4 ± 15.1	36.6 ± 0.8	49.9 ± 15.5	.256
LVEF (%)	55 ± 6	51 ± 6	56 ± 6	.278

Values are presented as n (%) or mean ± SD. *BIV*, Biventricular conversion; *AW*, ■■■; *PA*, pulmonary artery; *PVR*, pulmonary vascular resistance; *AVVI*, ■■■; *LVEDVi*, ■■■; *RVEDVi*, ■■■; *LVEF*, left ventricular ejection fraction. Q12

Comparison of preoperative characteristics between staged biventricular conversion and primary biventricular conversion groups demonstrated similar incidence of heterotaxy (55% vs 53%; $P = .90$), pulmonary venous disease (40% vs 29%; $P = .38$), and trisomy 21 (15% vs 29%; $P = .23$). In both groups, the majority of the uAVCDs were right-dominant defects (80% vs 55%; $P = .50$). No significant differences were found between the 2 groups in regard to single-papillary or closely spaced papillary muscles, left ventricular outflow tract obstruction, AV valve

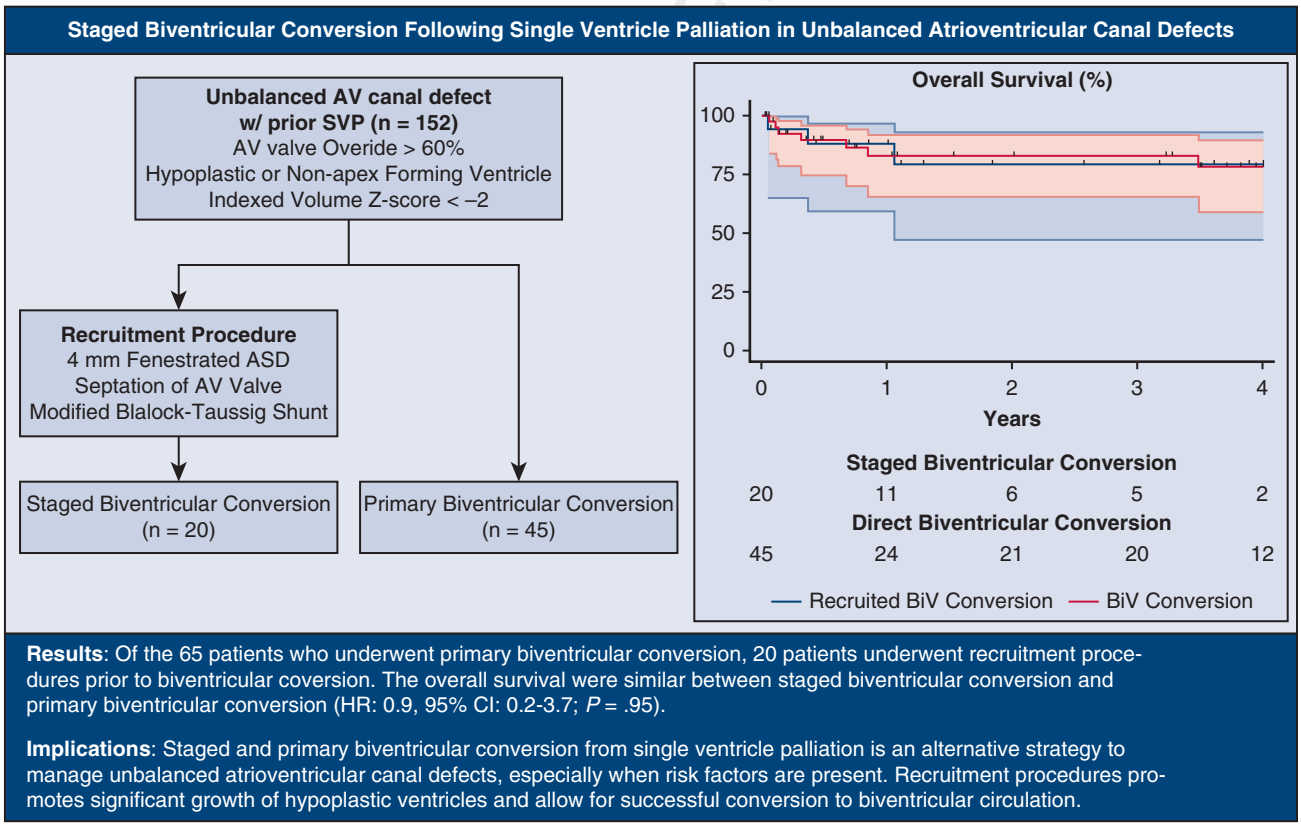

FIGURE 1. Staged and primary biventricular conversion from single-ventricle palliation (*SVP*) is an alternative strategy to manage unbalanced atrioventricular (*AV*) canal defects, particularly in those with high-risk factors for SVP failure, with acceptable early and late mortality. *ASD*, Atrial septal defect; *BIV*, biventricular conversion; *HR*, hazard ratio; *CI*, ■■■. Q15

regurgitation, and nonapex forming unbalanced ventricle ($P = .11$) Baseline patient characteristics based on conversion strategy can be found in Table E1. An AVVI was calculated for patients undergoing staged biventricular conversion and was determined to be 0.29 ± 0.07 and 0.66 ± 0.02 in right-dominant and left-dominant uAVCD, respectively. In direct biventricular conversion, AVVI was calculated to be 0.36 ± 0.06 and 0.62 ± 0.03 for right-dominant and left-dominant patients, respectively (Table 2).

Postoperative Characteristics

Following biventricular conversion, all patients were evaluated and reviewed in terms of early (30 days) and late postoperative outcomes (Table 3). Among all patients, 30-day survival was 95% (62 out of 65), and 1-year survival was 89% (48 out of 54). Median lengths of intensive care unit and hospital stay were 15 and 25 days, respectively. Predischarge echocardiography demonstrated that 23% (15 out of 65) patients developed moderate or more AV valve regurgitation. Left ventricle function was determined to be qualitatively normal in 80% (52 out of 65) patients, whereas 20% (13 out of 65) had mild–moderate or more dysfunction. Comparative analyses of staged versus primary biventricular conversion groups demonstrate no difference between the length of intensive care unit stay (13.5 vs 18.0 days; $P = .40$) and length of total hospital stay (20.0 vs 27.0 days; $P = .46$), respectively. Follow-up time was 1.0 year (IQR, 0.3-2.8 years) and 1.1 years (IQR, 0.2-4.3 years) for staged biventricular conversion and primary biventricular conversion, respectively.

Among all patients, 10 deaths occurred and none of the cohort underwent transplantation. There were 3 deaths among staged biventricular conversion patients, and 7 deaths occurred in patients undergoing primary biventricular conversion (15% vs 16%; $P = .35$). A large portion of the mortalities was due to systolic or diastolic ventricular dysfunction leading to heart failure and multiorgan dysfunction (80%; 8 out of 10 patients), whereas others developed severe AV valve regurgitation and subsequent mortality (20%; 2 out of 10 patients). Of these patients, 1 patient was listed for transplantation. The other 9 patients succumbed to multiorgan failure and were not transplant candidates or died before listing. Characteristics of patients with mortality are described in Table E2. Overall/transplant-free survival between the 2 groups were not statistically different (hazard ratio [HR], 0.9; 95% CI, 0.2-3.7; $P = .95$) (Figure 2, *A*). Reoperations were more frequent in staged biventricular conversion (HR, 3.1; 95% CI, 1.3-7.1; $P = .01$), but no statistical significance was found in catheterized reinterventions (HR, 1.9; 95% CI, 0.9-4.1; $P = .09$) (Figure 2, *B* and *C*).

Subgroup analyses for staged biventricular conversion demonstrate that single papillary muscle in the hypoplastic ventricle was associated with increased reoperation rate (HR, 2.1; 95% CI, 1.1-4.3; $P = .03$) (Table 4). Other preoperative factors were not found to be associated with mortality, reoperation, or recatheterization. For primary biventricular conversion, preoperative AV valve regurgitation was found to be a predictor for both reoperation (HR, 3.2; 95% CI, 1.2-8.6; $P = .02$) and mortality (HR, 8.1; 95% CI, 1.6-41.9; $P = .01$).

Recruitment and Ventricular Growth

Review of CMRI and echocardiographic data from prerecruitment and postrecruitment/prebiventricular conversion demonstrated significant growth of the recruited ventricle following the staged recruitment procedure. EDV of the recruited ventricle was found to be 43.8 mL/m^2 before recruitment and was 61.9 mL/m^2 after recruitment (z score, –4.0 to –1.8; $P < .01$) (Figure 3, *A*). Review of pre- and postbiventricular conversion volumetric data demonstrated a nonsignificant increase EDV of the hypoplastic ventricle (staged biventricular conversion: z score, –1.8 to –1.3; $P = .31$ and primary biventricular conversion: z score, –2.6 to –2.14; $P = .45$) (Figure 3, *B*).

TABLE 3. Postoperative patient characteristics

Variable	Staged BIVC	Primary BIVC	*P* value
Early postoperative complication			
ECMO	0 (0)	6 (13)	.087
Heart block	3 (15)	9 (20)	.835
Follow-up time	1.0 (0.3-2.8)	1.1 (0.2-4.3)	.096
ICU stay	13.5 (5.8-20.5)	18.0 (8.0-25.0)	.396
Hospital stay	20.0 (12.3-37.8)	27.0 (14.0-40.0)	.462
Late postoperative complication			
Death	3 (15)	7 (16)	.350
Reoperation	10 (50)	13 (29)	.147
Catheter-based reintervention	10 (50)	17 (38)	.356

Values are presented as n (%) or median (range). *BIVC*, Biventricular conversion; *ECMO*, extracorporeal membrane oxygenation; *ICU*, intensive care unit.

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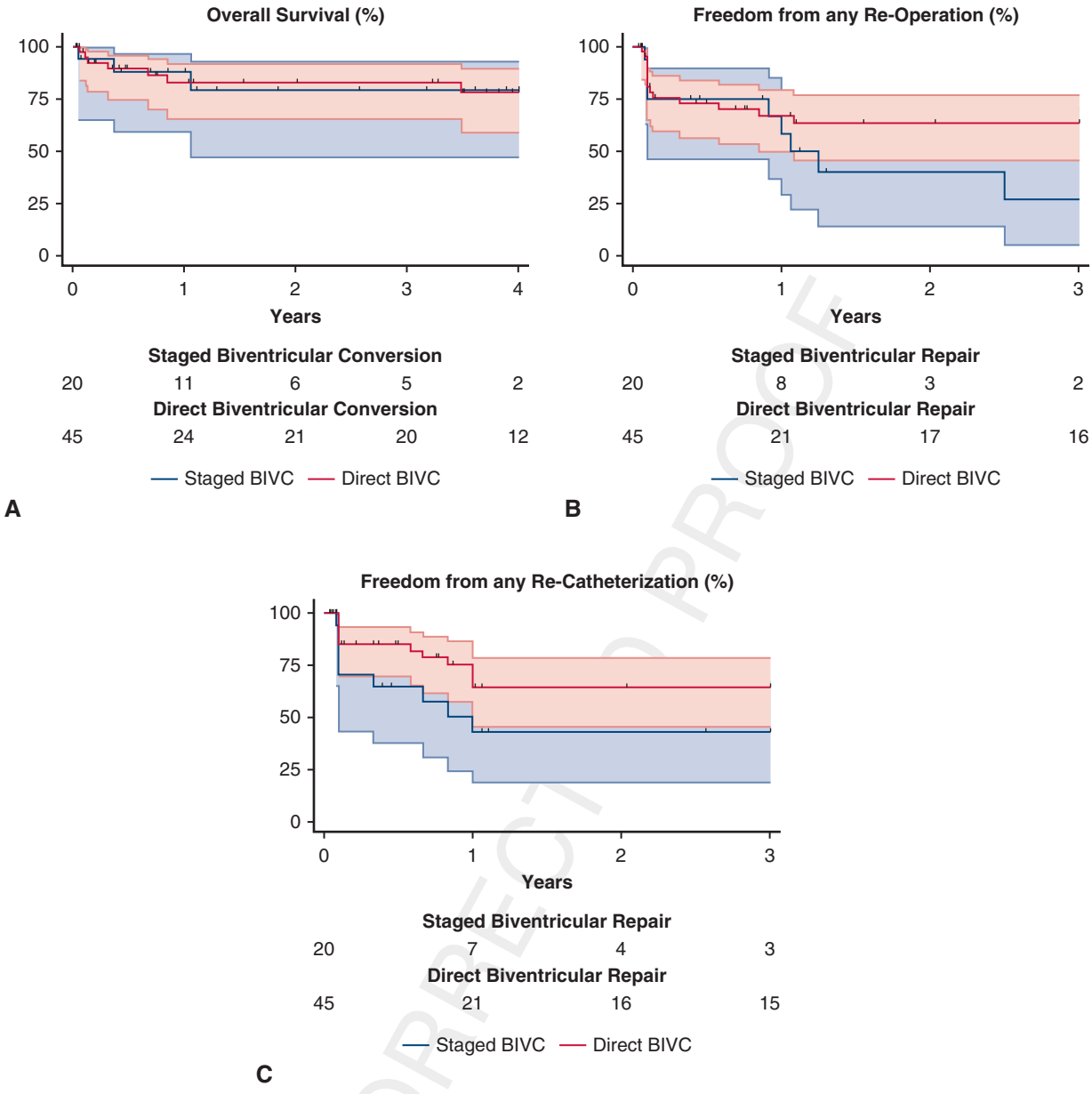

FIGURE 2. A, Overall survival of staged biventricular conversion (*BIVC*) and primary BIVC (hazard ratio [HR], 0.9; 95% CI, 0.2-3.7; $P = .95$). B, Freedom from any reoperation of staged BIVC and primary BIVC (HR, 3.1; 95% CI, 1.3-7.1; $P = .01$). C, Freedom from any recatherization of staged BIVC and primary BIVC (HR, 1.9; 95% CI, 0.9-4.1; $P = .09$).

DISCUSSION

Current management for uAVCDs depends on the severity of imbalance of the AV valve and ventricles. This descriptive study demonstrates a single institutional experience with biventricular conversion following initial SVP for uAVCD, and demonstrates the feasibility of biventricular conversion in a select subset of patients. Many patients undergoing this approach frequently had risk factors for poor outcomes related to SVP. The approach included primary biventricular conversion in patients with favorable ventricular morphology, and staged approach in patients with more significant hypoplasia, with the goal of the staged recruitment being to retain candidacy for biventricular circulation in patients with single-ventricle physiology. The series demonstrates that this approach is feasible in select patients, although mortality and reoperation remain a significant concern in patients with the highest risk.

In this series, biventricular conversion was performed in patients with a hypoplastic, unbalanced ventricle, as demonstrated by a median EDV z score of –3.2. Moreover, most patients presented with 1 or more risk factors for SVP failure, such as heterotaxy; trisomy 21; and, in some cases,

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TABLE 4. Subgroup analysis

Variable	Hazard ratio (95% CI)	*P* value
Mortality		
Staged biventricular conversion		
Trisomy 21	2.1 (0.2-23.2)	.544
Pulmonary venous disease	2.9 (0.3-32.6)	.377
AV valve regurgitation	>10 (0.0->10)	1
Single papillary muscle	0.9 (0.3-3.2)	.888
LVOTO	Cannot estimate	
Heart block	1.1 (0.3-3.9)	.921
Heterotaxy	1.8 (0.2-20.3)	.619
Primary biventricular conversion		
Trisomy 21	0.9 (0.2-4.8)	.936
Pulmonary venous disease	0.7 (0.1-3.7)	.684
AV valve regurgitation	8.1 (1.6-46.9)	.012
Single papillary muscle	1.5 (0.7-3.4)	.312
LVOTO	1.9 (0.2-16.5)	.528
Heart block	1.3 (0.7-2.5)	.371
Heterotaxy	2.5 (0.5-12.9)	.276
Reoperations		
Staged biventricular conversion		
Trisomy 21	0.3 (0.0-2.4)	.261
Pulmonary venous disease	0.7 (0.2-2.6)	.635
AV valve regurgitation	1.2 (0.4-4.4)	.729
Single papillary muscle	2.1 (1.1-4.3)	.033
LVOTO	Cannot estimate	
Heart block	1.7 (0.9-3.3)	.122
Heterotaxy	0.8 (0.3-2.8)	.774
Primary biventricular conversion		
Trisomy 21	0.3 (0.1-1.1)	.071
Pulmonary venous disease	0.5 (0.1-1.6)	.217
AV valve regurgitation	3.2 (1.2-8.6)	.021
Single papillary muscle	1.6 (0.9-2.7)	.118
LVOTO	2.4 (0.7-8.7)	.190
Heart block	1.6 (0.9-2.6)	.069
Heterotaxy	1.3 (0.5-3.7)	.571
Catheter-based reinterventions		
Staged biventricular conversion		
Trisomy 21	1.2 (0.2-5.5)	.856
Pulmonary venous disease	0.7 (0.2-2.6)	.605
AV valve regurgitation	1.0 (0.3-3.6)	.991
Single papillary muscle	2.2 (1.0-4.6)	.048
LVOTO	Cannot estimate	
Heart block	1.7 (0.9-3.4)	.104
Heterotaxy	0.5 (0.1-1.8)	.303
Primary biventricular conversion		
Trisomy 21	0.7 (0.3-1.9)	.509
Pulmonary venous disease	0.8 (0.3-2.0)	.668
AV Valve regurgitation	1.1 (0.4-2.7)	.886
Single papillary muscle	1.1 (0.7-1.9)	.609
LVOTO	1.3 (0.3-5.7)	.715
Heart block	1.2 (0.8-1.8)	.331
Heterotaxy	1.3 (0.6-3.1)	.519

CI, ■ ■ ■; *AV*, atrioventricular; *LVOTO*, left ventricular outflow tract obstruction.

symptoms of failing single-ventricle physiology.[17,18] The presence of left ventricular systolic dysfunction would be a contraindication to biventricular conversion, but none of the patients in this series had this issue. Although hypoplasia of right or left heart structures may be a deterrent for biventricular circulation, previous studies have reported feasibility and success in biventricular repair and conversion in patients with borderline hypoplasia.[10,13] When presented with a patient with uAVCD who had undergone previous SVP, the decision regarding ongoing SVP management versus biventricular conversion should be made based on the risk assessment of each strategy. The majority of patients who underwent biventricular conversion with or without recruitment had undergone a previous bidirectional Glenn procedure (65%), which permitted delay of the conversion to age beyond early infancy.

Previous studies have shown that primary repair of uAVCD carries the highest risk in neonates and young infants.[1,18] In our institution, we have tended to utilize neonatal Norwood operations more liberally in patients with favorable anatomy, with the understanding that staged biventricular conversion is feasible.[19] Still, the decision regarding primary versus staged approach to biventricular conversion requires careful consideration. The staged procedures can be done at the time of BDG, although in this series, the majority of recruitment procedures were performed after the BDG (before Fontan) because they were referred from other institutions. Biventricular conversion is typically performed 12 to 18 months after staged recruitment to allow sufficient time for growth, which has been demonstrated in various pathologies with hypoplastic ventricles.[19] In this present study, comparison of staged and primary biventricular conversion groups demonstrated that the unbalanced ventricle was likely to have greater degree of hypoplasia in those undergoing staged biventricular conversion, demonstrated by a lower ventricular EDV (z score, –4.0 vs –2.6) at initial presentation. This finding reflects our institutional practice of staged recruitment in patients with severely hypoplastic heart structures followed by biventricular conversion in those who demonstrate progressive valvular and ventricular growth.[10,11,13] In patients with severe AV valve hypoplasia and single papillary muscles, a staged approach may be preferred as it allows optimization of the AV valve before biventricular conversion. However, variables such as single papillary muscle or parachute valve, nonapex forming ventricle, heterotaxy, or pulmonary venous disease, were not statistically different between the 2 groups.

Although biventricular conversion by primary or staged approach is feasible, the series demonstrates 15% mortality associated with biventricular conversion. This is clearly

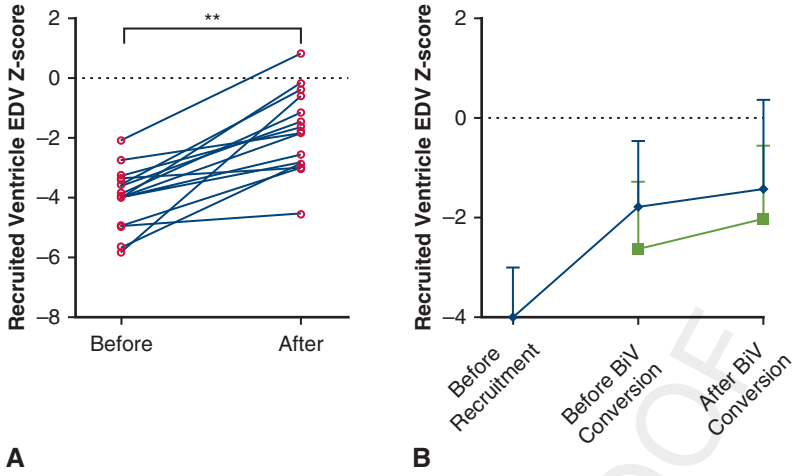

FIGURE 3. A, Prerecruitment (before) and postrecruitment/pre-biventricular conversion (*BIV*) (after) end-diastolic volumes (*EDV*) for the recruited ventricle. B, Recruited ventricle end-diastolic volumes for staged versus primary BIV before recruitment, before BIV, and at discharge.

higher than mortality associated with primary repair of balanced AVCD, but may be similar to mortality in other series of primary repair for uAVCD.[18] This may reflect the advanced levels of preoperative illness, presence of high-risk features, genetic abnormalities, or inadequate circulatory reserve. Given the small number of patients in this study, we were unable to detect clear risk factors for mortality to allow for better patient selection and risk mitigation. Certainly, when considering management of a patient with uAVCD who had undergone SVP, the risk of ongoing SVP should be weighed against the risk of biventricular conversion. The risk of mortality with biventricular conversion should be compared with long-term survival for patients with uAVCD who completed or are undergoing SVP, with literature suggesting survival as low as 60%.[1,18]

The risk of reoperation following biventricular conversion reflects persistent AV valvular dysfunction, which is characteristic of uAVCDs. Certain anatomic features in uAVCDs, including unusual AV cleft, abnormalities of papillary muscle architecture, annular hypoplasia, and leaflets dysplasia can pose significant challenges for repair.[11,13,20] Our data demonstrated 23% had AV valve regurgitation postoperatively. Not surprisingly, reinterventions in both groups were required primarily to address recurrent AV valve regurgitation and, to a lesser extent, outflow tract obstruction. Subgroup analyses demonstrated a greater risk for reoperation in patients with single papillary muscle and in those with preoperative AV valve regurgitation. Presence of a single papillary or parachute valve and preoperative AV valve regurgitation are known to be associated with increased risk of reoperation after primary repair of AVCDs. Improvements in surgical valve repair techniques in patients with severe valve deformities are necessary to reduce the risk of reoperation in this patient population.

The majority of catheter reinterventions were performed to address stenosis of pulmonary artery branches. Because most conversions occurred after a bidirectional Glenn procedure, these reinterventions are likely to result from the manipulation of these branches during SVP or Glenn takedown.

Staged biventricular conversion and primary biventricular conversion have similar early and late postoperative outcomes, but staged conversion is associated with an increased risk of reoperation, especially related to the AV valve. Freedom from recatherization were not statistically significant, although the trend may favor primary biventricular conversion over staged biventricular conversion. However, overall survival for both groups were similar. These outcomes suggest that recruited ventricles are functional and can provide adequate systemic cardiac output, with the acceptable risk of future reintervention, particularly in patient groups who may have unfavorable outcomes in single-ventricle physiology. It also supports an alternative strategy for recruitment in patients with uAVCDs that require optimization before conversion, particularly those who may require additional growth of the hypoplastic ventricle.

The rationale underlying staged recruitment is that fluid forces provide a stimulus for growth of hypoplastic structures.[21,22] Previous studies have demonstrated the ability of hypoplastic heart structures to grow following ventricular recruitment in pediatric populations.[10,22] In patients with uAVCDs, ventricular recruitment consisted of ASD fenestrated closure, AV valve partitioning, and/or additional inflow using a mBTTS in patients with hypoplastic left heart structures. After a median of 1.1 years with staging, staged biventricular conversion patients showed significant growth of the ventricle before conversion. By the end of the recruitment period, the EDV of the staged biventricular

conversion group was similar to that of the primary biventricular conversion group.

Limitations

This study is a retrospective review from a single institution. The biventricular conversion and recruitment strategies are still novel, and this series includes patients in our early experience. The number of staged biventricular conversions in uAVCD continue to be small and do not have a clear comparison group. Another limitation may be that volumetric measurements were extracted from 3-dimensional echocardiograms due to missing CMRI data, in a minority of patients. However, studies demonstrate that measurements taken from either modality are reliable and compare well, even in hypoplastic ventricles.[15,16] Many patients were referred to our center, and thus indications for SVP and preoperative volumetric data were unavailable. A final limitation is that many patients returned to outside institutions for their follow-up visits, leading to decreased numbers of completed follow-up data.

CONCLUSIONS

Patients with uAVCD and severe forms of ventricle hypoplasia continue to experience management challenges and may initially require SVP. Although long-term studies will be required, our study demonstrates that biventricular conversion is an alternative to SVP, with acceptable mortality given the high-risk profile for SVP failure in our patient cohort. Our study also demonstrates that ventricular recruitment provides significant growth of the hypoplastic ventricles and those undergoing staged recruitment before conversion. Conversion to a biventricular circulation is feasible albeit with nontrivial mortality and risk of reintervention.

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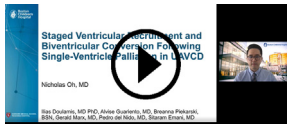

Conflict of Interest Statement

The authors reported no conflicts of interest.

The *Journal* policy requires editors and reviewers to disclose conflicts of interest and to decline handling or reviewing manuscripts for which they may have a conflict of interest. The editors and reviewers of this article have no conflicts of interest.

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Key Words: single ventricle palliation, unbalanced atrioventricular canal defect, biventricular repair

Discussion

Presenter: Dr Nicholas Oh

Dr David Overman *(Minneapolis, Minn)*. That was a very nice presentation, Dr Oh. Congratulations.

Dr Nicholas Oh *(Cleveland, Ohio)*. Thank you, Dr Overman.

Dr Overman. I'll make a couple of comments and then I have a couple of questions for you. Achieving a biventricular end state in any borderline anatomic arrangement can be quite challenging, and any information we can glean regarding early and late outcomes in this group of patients is very welcome. So, thank you. First of all, you chose to group all unbalanced atrioventricular septal defect (AVSD) patients together in your outcomes analysis irrespective of dominance. I would make the observation that right and left dominant unbalanced AVSD are quite different animals, as it were. It's relatively unusual to not achieve a biventricular end state in left-dominant AVSD wherein a one-and-a-half ventricle repair is a surgical strategy option. That's not the case in the right-dominant group wherein competence of the left heart is a more binary phenomenon, viability or not. Second observation I'd make, I would suggest that primary biventricular conversion, as you've defined it, is really a matter of patient selection off the top. That is, it's about properly recognizing an existing anatomic substrate that is consistent with a biventricular end state and properly employing that surgical strategy. In contrast and the third observation I would make is the concept of ventricular growth has been to analyzing the poorly understood and thinly documented clinical phenomenon that aspires to move the needle in borderline situations.

This recruitment strategy, as you've termed it, is the most interesting and impactful data from your cohort. That group numbers 20. They have a very low freedom from reintervention, around 30% at 2 years, and extremely low numbers at risk beyond even 1 year. Thus, I'm afraid we are still left with an uncomfortably small experience regarding such ideas. Those observations made I'd ask you a couple of questions. It appears from your Kaplan-Meier survival group, the early mortality after the primary biventricular conversion—and I think you've said the actual number, but I didn't catch it—is in the neighborhood of 10% or so and survival at one year, roughly 80%. Did you uncover any clues in your research as to what might indicate success or failure in the process of patient selection for primary biventricular conversion?

Dr Oh. So I would say—again, thank you for your comments. They're well received. While I do agree with you in the sense that most of our left-dominant patients may be able to be converted to a biventricular circulation, I do think there is something to be said about some of our patients, at least, in the fact that, at least, they were taken down the single-ventricle palliation route, which I think suggests that maybe they weren't the best biventricular candidates to begin with. I would also say that for our average score for our patients, they are still relatively low. Minus 2 is kind of the average for our primary repair, and minus 3.9 would be for our stage repair. So these are certainly still I would categorize as maybe not the best biventricular repair candidates from the start. In regard to your second question, I believe you asked what characteristics define a good patient for biventricular repair, is that—or conversion, is that correct?

Dr Overman. Yes. Did you uncover in patients that survive versus did not, were there any characteristics or clues as to what, in terms of the patient selection process, might help the surgeons select the proper strategy?

Dr Oh. Well, I think what we found were essentially risk factors or predictors of patients that would not do very well with the biventricular conversion. And in that sense, these are patients with either single papillary muscles or patients who had moderate or greater atrioventricular valve regurgitation. And in these patients, we found that we were having more reoperation rates and is associated with higher mortality.

Dr Overman. Sure. And that makes a lot of sense. My second question is: An important part of the late outcome picture in biventricular repair patients, that is patients in whom a biventricular end state is achieved, is the incidents

and severity of residual disease, and in particular pulmonary hypertension? You did reference analysis of echocardiography and catheterization lab data. Do you have data that you can share with us, echocardiography or catheterization lab, regarding the specific question, that is in the late hemodynamic end state of the biventricular repair group?

Dr Oh. Sure, Dr Overman. So, that's a very good question. So I will say that the average follow-up time for our patients were about 1 year. And in terms of complete follow-up, we had about 55% to 60% in our stage group and about 70% from our primary biventricular conversion group. And I don't have necessarily the catheterization lab data to show whether there was any residual pulmonary hypertensive disease. What I can tell you is that 20% of these patients had moderate to severe atrioventricular valve regurgitation and about 25% from the primary group had atrioventricular valve regurgitation. So, in terms of the qualitative echocardiography findings, I do have those. But the catheterization lab data, because we don't necessarily send these patients to the catheterization lab when we do see them on follow-up, I don't have as clear of picture on that.

Dr Overman. Very good. Thank you for those very clear questions and for a very good presentation, Dr Oh. And thank you to the association for the privilege of discussing your presentation.

Dr Oh. Dr Overman, thank you again. I appreciate your time.

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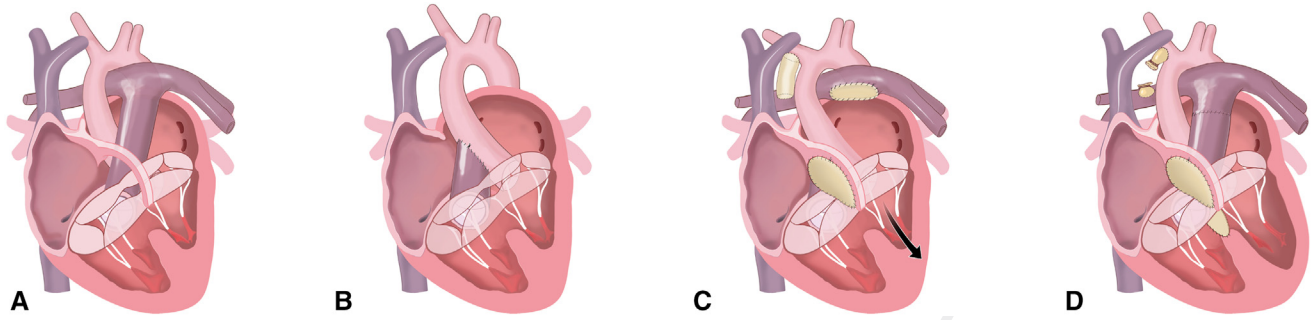

FIGURE E1. Schema of staged biventricular conversion. A, Diagram of an unrepaired unbalanced atrioventricular canal defect. B, Stage 1 procedure is performed. C, Staging procedures such as atrial septation and/or modified Blalock-Taussig-Thomas shunt is performed to promote growth of hypoplastic ventricle during single ventricle palliation state. D, Single ventricle circulation is converted to a biventricular circulation after the ventricle demonstrates adequate growth and function.

TABLE E1. Baseline characteristics of patients undergoing staged biventricular conversion patients and baseline characteristics of patients undergoing staged biventricular conversion

Staged biventricular conversion (n = 20)	Stage I (n = 7)	BDG (n = 12)	Fontan (n = 1)
Gender*	4:3	5:7	0:1
Dominant ventricle†	6:1	9:3	1:0
Heterotaxy	2/7 (29)	9/12 (75)	0/1 (0)
Pulmonary vein disease	1/7 (14)	7/12 (58)	0/1 (0)
Single papillary muscle	3/7 (43)	6/12 (50)	1/1 (100)
Hypoplastic heart (z score <–2)	7/7 (100)	9/12 (75)	1/1 (100)
AW regurgitation	3/7 (43)	8/12 (67)	1/1 (100)
Trisomy 21	2/7 (29)	1/12 (8)	0/1 (0)
4-mm ASD fenestration	5/7 (71)	8/12 (67)	1/1 (100)
AVC septation	4/7 (57)	8/12 (67)	0/1 (0)
Modified Blalock-Taussig shunt	2/7 (29)	6/12 (50)	0/1 (0)
Concurrent recruitment procedures	4/7 (57)	10/12 (83)	0/1 (0)

Values are presented as n/N (%) unless otherwise noted. *BDG*, ■■■; *AW*, ■■■; *ASD*, ■■■; *AVC*, ■■■. *Values are presented as ratio of male to female. †Values are presented as ratio of right to left.

TABLE E2. Characteristics of patient mortality

Procedure	Patient No.	Right dominant	Preoperativc risk factor*	Recruitment details	BIVC details	Postoperative complications	Reintervention	Cause of death
Staged BIVC								
	Patient 1	Yes	Single papillary muscle, AVVR, Trisomy 21	Recruitment after stage KAVV partitioning, fenestrated ASD		Pacemaker, AVVR	Mitral valve replacement	Recurrent left AW regurgitation, progression to multiorgan failure, withdrawal of care
	Patient 2	Yes	Iktcrotaxy, pulmonary venous disease, AWR	Recruitment after BlXi (fenestrated ASD)				Progressive heart failure listed for transplant, placed on ECMO, neurologic injury
	Patient 3	No	Ikterouxy, pulmonary venous disease, AWR	Recruitment after BDG (AW partitioning, fenestrated ASD)		Pacemaker, AVVR	Tricuspid valvuloplasty	Progressive heart failure, progression to multiorgan failure, cardiac arrest
Direct BIVC								
	Patient 1	Yes	Single papillary muscle, AWR		BIVC after Fontan	ECMO, AWR	Stent placement in left main coronary artery	Progressive heart failure, ECMO for cardiac arrest from LV dysfunction, multiorgan failure
	Patient 2	Yes	Single papillary muscle, Trisomy 21		BIVC after stage 1	AVVR	Mitral valve repair, excision of LVOTO, commisuroplasty	Death after discharge, cause of death: heart failure
	Patient 3	Yes	Ikterouxy, pulmonary venous disease		BIVC after stage 1	ECMO, AWR		Death after discharge, cause of death: heart failure
	Patient 4	No	Ikterouxy, AVVR		BIVC after stage 1	ECMO, AWR	Melody† valve placement	Progressive heart failure, progression to multiorgan failure
	Patient 5	No	Ikterouxy. AVVR, Trisomy 21		BIVC after Fontan	Pacemaker, AVVR		Progressive heart failure, death after discharge

(Continued)

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TABLE E2. Continued

Procedure	Patient No.	Right dominant	Preoperativc risk factor*	Recruitment details	BIVC details	Postoperative complications	Reintervention	Cause of death
	Patient 6	Yes	Ikterotaxy. AVVR, pulmonary venous disease		BIVC after BDG	ECMO, AWR	Mitral valve replacement	Recurrent left AW regurgitation, ECMO, neurologic injury, death
	Patient 7	Yes	Ikterouxy. AVVR		BIVC after stage 1	AVVR	Resection of RVOTO	Progressive heart failure, multiorgan failure

BIVC, ■■■; *AVVR*, ■■■; *KAVV*, ■■■; *ASD*, ■■■; *AW*, ■■■; *AWR*, ■■■; *BLXi*, ■■■; *ECMO*, extracorporeal membrane oxygenation; *BDG*, ■■■; *LV*, left ventricle; *LVOTO*, left ventricular outflow tract obstruction; *RVOTO*, right ventricular outflow tract obstruction. *■■■. †Medtronic Inc.

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