Long-term tricuspid valve function after Norwood operation

Maryam Elmi, BSc,^b Edward J. Hickey, MD,^a William G. Williams, MD,^a Glen Van Arsdell, MD,^a Christopher A. Caldarone, MD,^a and Brian W. McCrindle, MD^b

Objective: Long-term functional outcomes after Norwood palliation are likely to depend on tricuspid valve performance in the systemic role. We therefore aimed to characterize features associated with tricuspid valve intervention.

Methods: All 219 children (1990–2007) who underwent Norwood stage 1 palliation resulting in a systemic right ventricle were investigated. In parametric competing risks analyses, primary end points included surgical tricuspid valve intervention (repair = 27, replacement = 3) and death (N = 105). All 2705 echocardiogram reports were included in time-related analyses of outcome adjusted for repeated measures. Variable selection used bootstrapping.

Results: Approximately 25% of survivors underwent tricuspid valve repair at some point, especially in children with mitral atresia ($P = .04$, 53% reliability), longer myocardial ischemic time during Norwood ($P = .02$, 50%), and moderate/severe tricuspid regurgitation immediately post-Norwood ($P = .006$, 86%). Risk of tricuspid valve intervention was mainly early, but a late risk emerged 10 to 15 years after Norwood. Tricuspid valve intervention was successful in restoring functional natural history to that of the remainder of the cohort. Tricuspid valve intervention did not compromise survival ($82\% \pm 2\%$ 5 years after tricuspid valve intervention), and right ventricular function was not worse in patients requiring tricuspid valve intervention. Repeat tricuspid valve interventions were undertaken in 6 patients (3 repairs, 3 replacements). At latest follow-up, the degree of tricuspid valve regurgitation was not different between those who did and did not receive intervention.

Conclusions: Tricuspid valve surgery is common after single ventricle palliation for hypoplastic left heart syndrome, necessary in up to 25% of survivors. Mitral atresia and lengthy myocardial ischemic times during Norwood surgery are prominent risks. Right ventricular function was preserved by tricuspid repair. However, the emerging late hazard for tricuspid valve intervention may have implications for long-term outcome and should be explored further. (*J Thorac Cardiovasc Surg* 2011;142:1341-7)

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Tricuspid valve (TV) performance in the systemic role is likely to have important implications for survival and functional status after univentricular palliation of hypoplastic left heart syndrome (HLHS). Important tricuspid regurgitation (TR) at the time of diagnosis is a known risk factor for early mortality after stage 1 Norwood palliation.¹ However, important TR after palliative surgery subsequently develops in a proportion of infants with normal TV function pre-Norwood.² Reasons for deteriorating TV function may

include right ventricular (RV) volume loading, RV systolic and diastolic dysfunction, and myocardial ischemic injury during surgical palliation.

The natural and unnatural history of TV function over time have not been clearly delineated in infants with HLHS. We therefore undertook an investigation into our institutional experience with Norwood palliation in children with HLHS since 1990. Data acquisition included all known interventions and all echocardiograms known to have been performed. We aimed to (1) determine the prevalence and time-related risk of TV intervention after diagnosis, (2) characterize the patient-specific factors associated with greater risk of undergoing TV intervention, (3) model the time-related natural and unnatural history of valvular function, and (4) investigate outcomes after TV repair or replacement.

MATERIALS AND METHODS

Study Design and Study Population

We performed a single-center retrospective study of 219 consecutive infants at the Hospital for Sick Children who all underwent a stage 1 Norwood palliation for a diagnosis of aortic atresia or critical aortic stenosis between 1990 and 2007. Patients with all variants of HLHS were included unless they had atrioventricular or ventriculoarterial discordant

From the Division of Cardiovascular Surgery,^a Department of Surgery, and Division of Cardiology,^b Department of Pediatrics, University of Toronto, The Hospital for Sick Children, Toronto, Ontario, Canada.

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Address for reprints: Brian W. McCrindle, MD, The Hospital for Sick Children, 555 University Avenue, Toronto, Ontario, Canada M5G 1X8 (E-mail: brian.mccrindle@sickkids.ca).

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Abbreviations and Acronyms

HLHS	= hypoplastic left heart syndrome
RV	= right ventricular
TR	= tricuspid regurgitation
TV	= tricuspid valve

connections or an interrupted aortic arch. Institutional ethics board approval was obtained, and a waiver of consent was granted because of the study's retrospective nature and because patients were not contacted.

Follow-up and Data Acquisition

Follow-up was undertaken in 2007 via chart review to a median of 5.1 years for survivors (range, 0–15.9 years), providing 749 patient-years of data. All available reports pertaining to surgical interventions, cardiac catheterizations, and autopsies were obtained. To model time-related progression of valvular function (repeated-measures analysis), reports of all echocardiograms were obtained ($N = 2705$) throughout the follow-up period. Variables pertaining to demographics, baseline morphology, operative features at the time of stage 1 Norwood palliation, and echocardiographic dimensions and functional indices were abstracted from reports for subsequent risk-hazard and repeated-measures analyses.

Analysis of Time-Related Events

Separate parametric models of time-related events from the time of diagnosis were generated using multiphase hazard domain techniques.³ For end points other than death, competing risks methodology was used to account for children who died and were therefore no longer at risk of the event occurring. Patients were therefore censored at the last point of follow-up or the time of an alternative mutually exclusive end state occurring (competing risk). Selected patient-specific characteristics (Table E1) were abstracted from reports and used for multivariable risk-hazard analysis using these parametric models. Dimensional variables were standardized and expressed as z scores on the basis of published normative data if available⁴ or otherwise indexed to body surface area. All continuous variables were examined by decile analysis to determine possible transformations to improve linear calibration. Multivariable analysis was undertaken by forward stepwise regression. Missing values were imputed with the mean for that variable. Variables with excessive ($>75\%$) missing values or associated with fewer than 5 events were suppressed during multivariable analysis to reduce the risk of overdetermination. Final selection of variables was guided by bootstrap bagging⁵ ($n = 1000$, threshold for inclusion $P < .1$) to test the robustness of risk factors; those appearing in 50% or more of models or clusters were considered reliable for inclusion.

Analysis of Repeated Measures

Time-related progression of TV regurgitation and RV function were explored by examining serial echocardiographic measurements in linear regression models to produce generalized estimating equations adjusted for repeated measures through autoregressive covariance structure. Patients were censored at the point of intervention. Variable selection was undertaken by backward elimination.

Modulated Renewal Methodology

To compare outcomes of successive interventions, modulated renewal process methodology was used.^{6,7} Patients experiencing a first event are restarted at a new time zero and tracked to the next event, and so forth, for each successive event. The cumulative hazard for all TV interventions ($N = 30$) on the 219 patients was therefore modeled and

stratified by the sequence of interventions to the TV. Stratified plots were generated by creating survival curves for each individual patient. Curves within stratification groups were then aggregated, and the mean was then compared with Kaplan–Meier estimates.

Data are described as frequencies, medians with ranges, or means with standard deviations. Actual time-related outcomes were calculated using Kaplan–Meier principles. Data were entered and analyzed using SAS statistical software, version 9 (SAS Institute, Inc, Cary, NC).

RESULTS

All 219 infants in this investigation were diagnosed with aortic atresia or critical aortic stenosis and underwent Norwood palliation as part of a univentricular strategy. Of the total cohort, 30 TV surgical interventions were performed in 24 children. All 24 primary TV interventions were valvuloplasties. The 6 TV reinterventions were revalvuloplasties ($N = 3$) or mechanical valve replacements ($N = 3$).

Patient-specific features are shown in Table E1. In children who underwent TV intervention, the prevalence of pre-Norwood aortic coarctation was significantly lower ($P = .001$), mitral annular z scores were smaller ($P = .01$), and distribution of birth weights was lower ($P = .004$). Otherwise, features at the time of diagnosis and during Norwood stage 1 were similar between those who did and did not undergo TV surgery.

Time-Related Risk of Undergoing Tricuspid Valve Intervention

The hazard of undergoing TV procedures comprised 2 main periods of risk. An early hazard phase predominated for the initial 5 years after diagnosis and accounted for the large majority of interventions ($>90\%$). A late period of risk appeared to emerge beyond 5 years after diagnosis (Figure 1). However, an important number of children died early during follow-up and therefore were no longer at risk of undergoing TV intervention. Consequently, competing risks methodology more accurately describes the outcomes for the cohort: Ten years after diagnosis, $12\% \pm 3\%$ had undergone TV intervention, $48\% \pm 4\%$ had died without TV intervention, and $41\% \pm 3\%$ remained alive and free from TV intervention (Figure 2, A). Therefore 23% of all survivors had undergone TV intervention within the first 10 years after diagnosis.

Risk Factors for Tricuspid Valve Intervention

Incremental risk factors (at the time of diagnosis) for TV intervention included presence of mitral atresia and longer myocardial ischemia during Norwood operation (Table 1). Of note, indexed TV annular dimensions, TR grade at the time of diagnosis, and other TV morphologic features were not associated with time-related risk of TV intervention in this cohort. In addition, shunt type (Sano vs modified Blalock–Taussig), shunt size, and age at volume unloading (cavopulmonary shunt) were not associated with time-related need for TV intervention.

FIGURE 1. A, Freedom from TV intervention in children with HLHS managed with the Norwood operation ($N = 219$). TV intervention was undertaken in 24 patients (of whom 6 underwent additional reintervention to the TV). B, Hazard function for TV intervention. The hazard for TV intervention comprised 2 main periods of risk. The early hazard phase predominated within the first 5 years, and 75% of all reinterventions were within 1 year of diagnosis. A second later phase appeared to emerge beyond 5 years after diagnosis. During the study period, 92% of TV interventions were attributable to the early hazard component, and 8% were attributable to the late hazard component. Circles represent nonparametric estimates at events; solid lines represent parametric determinants of continuous point estimates; dashed lines and bars enclose 70% confidence intervals. TV, Tricuspid valve.

Incremental risk factors for the competing risk of death without TV intervention included smaller birth weight, earlier operative era, absence of aortic coarctation, and smaller indexed branch pulmonary arteries. At the time of Norwood operation, longer exposure to deep hypothermic circulatory arrest and younger age were additional features contributing to greater risk of death (Table 1).

For any given child, a constellation of aforementioned competing risk factors determines the likelihood of reaching a given end state at a certain point in time. For instance, in a child with a birth weight of 4 kg with mitral atresia who undergoes the Norwood operation on day 7 of life with 100 minutes of myocardial ischemia and 15 minutes of deep

FIGURE 2. A, Competing risks of death and TV intervention. After diagnosis, all children are subject to the mutually exclusive competing risks of (1) undergoing TV intervention ($N = 24$), (2) death without TV intervention ($N = 100$), or (3) remaining alive without reintervention ($N = 95$). Ten years after the index procedure, $12\% \pm 3\%$ had undergone TV intervention, $48\% \pm 4\%$ had died without TV intervention, and $41\% \pm 3\%$ remained alive and free from TV intervention. Therefore, approximately one quarter of survivors had at some point undergone an intervention to the TV. The competing risks plot has then been stratified according to (B) unfavorable features (4-kg infant with mitral atresia undergoing repair with myocardial ischemic time of 100 minutes and deep hypothermic circulatory arrest time of 15 minutes) or (C) favorable features (4-kg infant with patent mitral valve undergoing repair with only 60 minutes of myocardial ischemia and 15 minutes of deep hypothermic circulatory arrest). Lines represent parametric determination of the continuous point estimates of the percentage of patients within each category. TV, Tricuspid valve.

TABLE 1. Incremental risk factors for the competing risks of tricuspid valve intervention or death without tricuspid valve intervention

Variable	PE	P value	% reliability
Risk factors for TV intervention			
Morphologic and demographic risks			
Mitral atresia	+0.92	.04	53
Procedural factors at time of Norwood			
Longer crossclamp duration*	+0.023	.02	50
Immediate post-Norwood factors			
Moderate/severe TR in ICU	+1.32	.006	86
Risk factors for death without TV intervention			
Morphologic and demographic risks			
Smaller birth weight	+0.83	<.0001	57
Earlier operative year	+0.14	<.0001	99
Absence of aortic coarctation	+0.40	.05	62
Smaller branch pulmonary arteries	+0.084	.01	50
Procedural factors at time of Norwood			
Smaller birth weight	+0.84	<.0001	99
Longer DHCA duration	+0.025	.0002	90
Earlier operative year	+0.056	.04	95
Younger age at operation	+0.28	.02	51

DHCA, Deep hypothermic circulatory arrest; ICU, intensive care unit; PE, parameter estimate. Reliability is the bootstrap reliability of the variable's *P* value. *Excluding those in whom TV repair was concomitant with Norwood stage 1.

hypothermic circulatory arrest, the subsequent risk of requiring TV intervention is high: More than half of all survivors will have undergone TV intervention within a few years of diagnosis (Figure 2, B). By contrast, a constellation of features, including birth weight of 4 kg, mitral valve patency, and shorter myocardial ischemic times, confer a low risk of subsequent TV intervention, less than 10% within 10 years of diagnosis, in addition to a low risk of death (Figure 2, C).

All patients received on-table transesophageal or epicardial echocardiography at the time of the Norwood operation. Our strategy throughout the era spanned by this study has been to address moderate or severe TR present at the time of on-table echocardiography. Nevertheless, 21 patients (10%) had TR graded by transthoracic echocardiography on the first formal postoperative investigation in intensive care. In 20 of 21 patients (95%), this hemodynamically significant TR was a new occurrence, having been mild or less pre-Norwood. Moderate/severe TR immediately post-Norwood was itself a strong risk factor for time-related need for subsequent TV intervention (parameter estimate +1.32, $P < .006$, 86% bootstrap resamples).

Timing and Nature of Tricuspid Valve Procedures

All TV interventions were for a primary indication of regurgitation, with or without some degree of RV dysfunction (Table 2). At operation, the anatomic and functional findings were highly variable. Of all 30 TV procedures (primary = 24; secondary = 6), 19 were undertaken

TABLE 2. Surgical details and findings at operation in children who underwent tricuspid valve surgical intervention

Variable	First TV repair N = 24		
	Missing variables	No.	% or range
Repair	0	24	—
Replacement	0	0	—
Indications			
Moderate regurgitation	1	14	61
Severe regurgitation	1	5	22
Leaflet prolapse	1	3	13
Heart failure	1	2	9
Right ventricular dysfunction	1	14	61
Area of incompetency on inspection			
Unspecified	13	4	36
Posterior leaflet	13	2	18
Anterior leaflet	13	3	27
Septal leaflet	13	1	9
Septal-anterior commissure	13	1	9
Morphologic abnormalities on inspection			
Cleft (anterior leaflet)	13	4	36
Septation (septal leaflet)	13	1	9
Triangular leaflet	13	2	18
Accessory leaflet	13	1	9
Surgical details			
Concomitant: Norwood stage 1	0	2	8
Concomitant: cavopulmonary shunt	0	12	50
Concomitant: Fontan completion	0	3	13
Concomitant: pulmonary artery augmentation	0	2	8
Bypass time (min), median	6	113	50–205
Aortic crossclamp time (min), median	7	45	16–142
PA commissure closure	10	3	21
PS commissure closure	10	4	29
AS commissure closure	10	8	57
Unspecified commissure closure	10	3	21
Annuloplasty	10	5	36
Cleft closure	10	2	14
Leaflet augmentation	10	1	7

AS, Anterior-septal; PA, posterior-anterior; PS, posterior-septal. Frequencies are expressed as a proportion of nonmissing values.

concomitant with Norwood stage 1, bidirectional cavopulmonary shunt, or Fontan procedure (Table 2). Therefore, for 11 patients in this series, TV intervention was the primary procedure outside the typical univentricular surgical paradigm. The need for intervention specifically for TV abnormalities would be of particular interest to families and physicians alike (Figure E1). However, the only reliable risk factor for TV as an isolated procedure was the presence of mitral atresia ($P = .0007$).

Functional Results of Tricuspid Valve Intervention

Children who underwent TV interventions were distinguished preoperatively by higher grades of TR. Moreover, the severity of their TR had gradually increased over time

($P < .0001$). Tricuspid valvuloplasty then resulted in a significant immediate improvement in echocardiographic grade of functional regurgitation ($P = .0003$, Figures 3, A, and E2, A). Thereafter, the severity of their TR remained stable, or even tended to decline over the course of follow-up ($P = .08$, Figure 3, A).

FIGURE 3. A, Parametric regression estimates of the time-related change in echocardiographic grade of TR. Patients who underwent TV intervention were characterized by having a higher preoperative grade of regurgitation that worsened significantly over time (parameter estimate +0.19, $P < .0001$). However, after intervention, the grade of regurgitation was improved and showed no significant time-related deterioration in regurgitation thereafter. In fact, grade of regurgitation tended to improve over time after intervention ($P = .08$), thereby more closely approximating those patients who did not undergo TV intervention. Time has been entered as the log-transformation to improve model fit. Number of nonmissing values for analysis: patients not receiving TV intervention, $N = 1731$; preoperative TV intervention, $N = 204$; postoperative TV intervention, $N = 190$. B, Modulated renewal analysis of freedom from TV intervention, stratified according to baseline versus after an initial TV intervention. Freedom from TV intervention tended to be worse after already having undergone a prior tricuspid intervention in risk-unadjusted models ($P = .10$). However, in risk-adjusted models freedom from subsequent intervention was not different ($P = .57$). Lines represent parametric determination of continuous point estimates, symbols represent Kaplan–Meier estimates at each event (reintervention); bars enclose 70% confidence intervals. TV, Tricuspid valve.

After univentricular palliation for HLHS, preservation of RV function in the systemic role is of central importance. Immediately after surgical intervention to the TV, RV performance was no different or even slightly worse (Figure E2, B); however, long-term RV performance in children who required TV intervention was identical to those who did not require intervention, with no obvious late deterioration (Figure E2, C).

Tricuspid Valve Reintervention

The time-related risk of reintervention to the TV was examined using modulated renewal methodology. Modulated renewal analyses explore whether undergoing a first TV intervention places a patient at higher risk of undergoing a second TV intervention. Reinterventions were necessary in 6 children (repair = 3; replacement = 3). Although longevity of the TV repair tends to be inferior to that of native valves in risk-unadjusted models ($P = .10$, Figure 3, B), this difference is not significant ($P = .57$) in risk-adjusted models. Furthermore, on univariate analysis, no aspects specific to the initial TV intervention were associated with increased risk of reintervention. Finally, overall survival in children who underwent TV intervention was excellent: $82\% \pm 6\%$ at 5 years (from the point of intervention to the TV).

DISCUSSION

Our data demonstrate that important TV dysfunction is common in infants born with HLHS managed via univentricular palliation: Approximately one quarter of all survivors will have undergone surgical TV procedures within 10 years. In fact, new-onset TR may be seen in as many as 10% of children immediately post-Norwood, and this finding itself indicates high risk of subsequent need for tricuspid intervention. Most TV interventions are undertaken in the early years of childhood. However, several children have required TV repair late after Fontan completion; the possibility of an emerging late hazard for TV dysfunction carries important functional health implications for children with Fontan physiology.

Among surgically managed patients with HLHS, attrition between stages (“interstage death”) and death later in childhood are both significant concerns.^{8–10} Development of significant TR remains an obstacle in improving survival after the Norwood procedure,^{11–14} and likely compromised functional health after the Fontan procedure. Thus, prevention of TV deterioration seems pivotal to improving long-term outcomes for patients with HLHS. By identifying children at risk of developing severe TV dysfunction, perhaps there are preemptive strategies (pharmacologic or interventional) that can be implemented early to optimize tricuspid function and decrease interstage risk. Our study identified factors predictive for undergoing a later TV intervention (Table 1). Perhaps patients with these presenting features should have a lower threshold

for TV repair at the time of Norwood operation, in addition to being more closely followed for tricuspid dysfunction postoperatively. Pharmacologic strategies to limit TR (eg, afterload reduction) might be considered early for high-risk patients.

The early period of risk for TV intervention during infancy is in part determined by the timing of the 3 staged procedures in the Norwood–Fontan pathway. It is intuitively sensible to undertake concomitant TV repair at the time of a necessary surgical stage. As such, in our series, the majority (19/30) of TV repairs were undertaken as a concomitant staged operation. Incorporating the TV repair as part of an alternate procedure does not render it inconsequential but instead indicates that the child already exhibits significant functional handicaps with regard to a (right) univentricular circulation, even early on. How or whether this will affect survival and functional performance beyond the follow-up of this investigation is of considerable importance. Although no other institution has investigated the time-related risk for TV intervention, some investigators have reported mean ages for TV repairs consistent with our proposed early hazard phase.^{15,16} This implies that particular attention must be given to the TV early in the surgical paradigm, perhaps in the peri-Norwood period as a preventative measure.

More than one third of TV interventions (11/30) were undertaken outside the typical univentricular surgical paradigm. This subset of children are especially important because they presumably reflect TV dysfunction that mandated isolated tricuspid intervention on the grounds of severity or late onset. It is interesting that the most important and reliable determinant of TV intervention outside the usual univentricular operative paradigm was the presence of mitral atresia. In mitral atresia (similar to most cases of aortic atresia), left ventricular flow is completely absent. All systemic cardiac output must necessarily be generated via the RV (by contrast, in univentricular repair of critical aortic stenosis, a small proportion of systemic cardiac output will be via the left heart). When left ventricular flow is zero, presumably the right cardiac structures are therefore operating under maximum hemodynamic stress.

A small, but important, number of children underwent TV repair well beyond completion of Fontan physiology. The principal concern is that tricuspid dysfunction may be a consequence of a failing systemic RV, perhaps due to annular dilatation. Thereafter, TR will further exacerbate ventricular failure in a detrimental positive feedback loop. Tricuspid repair is frequently necessary in those requiring intervention for RV failure after atrial switch repair of transposition of the great arteries.¹⁷ Likewise, in patients dying of RV failure late after the Senning or Mustard operation, severe TR is invariably present.¹⁸ TV repair or replacement in the context of severe RV dysfunction often does not lead

to ventricular recovery.¹⁸ The importance of preserving late TV and RV performance after univentricular repair of HLHS is probably equally real.

Atresia of the mitral valve seems to be strongly associated with subsequent development of important TV dysfunction requiring intervention. Perhaps more important, mitral atresia was especially associated with TV repair or replacement being undertaken as isolated procedures, outside of the typical univentricular surgical paradigm. How atresia of left-sided structures influences TV performance is not obvious. Echocardiographic studies suggest that forces transmitted from the contracting left ventricle may influence TV annular functional morphology.²

Longer myocardial ischemic time during the Norwood operation was also identified as a risk factor for TV intervention. Correct atrioventricular valve function is known to be dependent on ventricular morphology and coordinated contraction of the wall and papillary muscles. Subendocardial ischemic injury may lead to papillary muscle dysfunction or late remodeling of RV geometry. Alternatively, it is possible that longer myocardial ischemic time is a surrogate for more complex cardiac morphology and an indirect risk factor for valvular regurgitation.

TV features and initial grade of TR at the time of diagnosis were not particularly robust predictors of the need for subsequent tricuspid repair. It is likely these are important, but they may have been overshadowed by other more reliable risks. Detailed echocardiographic indices of tricuspid morphology (annular area, annular area changes, saddle shape, and segmental diameter changes) are known to correlate with regurgitation.² It is therefore likely that such features would also be predictive in patients with HLHS.

Numerous reports have previously examined risk factors for death after univentricular repair of HLHS. The risk factors we describe are consistent with these earlier reports, including lower birth weight, earlier operative era, longer deep hypothermic circulatory arrest time, and compromised pulmonary flow.^{19–21}

It is reassuring that TV interventions were effective at producing a sustained and significantly reduced grade of regurgitation. Furthermore, RV function in those patients who required tricuspid repair paralleled those who did not. Presumably, this is because TR was addressed before any functionally detrimental changes to the RV occurred. The Michigan group²² suggested that success of TV repair is contingent on RV function; the presence of significant RV dysfunction instead results in continued deterioration of TV performance even after intervention. Overall, there is consensus in the literature that TV repair is a useful and effective adjunct to staged surgical palliation in HLHS.^{15,16,22–24} The favorable survival after TV intervention, both in our series and others,^{15,16} seems to corroborate this view.

Limitations

One important limitation of the study is that TV repairs in infancy are frequently incorporated in the staged operations. Therefore, intervals to TV intervention are clustered around the time of cavopulmonary shunt and Fontan operations (and are unlikely to be precise surrogates for the interval to onset of important TR). However, we do not think this influences the conclusions drawn from our investigation. The principal purpose of using multiphase time-related techniques was to scrutinize for a late component. The small number of late TV interventions present in our series is interesting and has potential importance. However, this finding is hampered by the restraints of sample size and duration of follow-up. Larger, multi-institutional research databases are likely to be especially useful to more accurately examine the late functional performance of the systemic RV in HLHS.

CONCLUSIONS

Important TV dysfunction is common late after univentricular repair of HLHS. Approximately one quarter of survivors will have undergone a TV intervention within 10 years. A late risk may be emerging and needs to be explored further because it would have important functional implications. Risk of requiring TV repair seems to be particularly associated with atretic left-sided morphology: aortic or mitral atresia. Certain features at the time of diagnosis may therefore be useful in predicting long-term durability of TV performance. However, when required, TV interventions seem durable and associated with favorable survival.

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FIGURE E1. Freedom from TV intervention outside the staged univentricular sequence of operations (Norwood, partial cavopulmonary shunt, total cavopulmonary shunt). TV intervention as the primary operative procedure was undertaken in 11 children. Ten years after diagnosis, $89\% \pm 2\%$ children remained free from TV intervention as the primary indication for surgery. *Circles* represent nonparametric estimates at events; *solid lines* represent parametric determinants of continuous point estimates; *dashed lines* and *bars* enclose 70% confidence intervals. *TV*, Tricuspid valve.

FIGURE E2. A, Histogram detailing the prevalence of echocardiographic grade of regurgitation immediately before and 24 hours after surgical repair (N = 24). B, Histogram detailing the prevalence of echocardiographic grade of RV dysfunction before and 24 hours after surgical repair (N = 24). C, Parametric regression estimates of the time-related change in echocardiographic grade of right ventricular dysfunction. The slightly higher incidence of postoperative right ventricular dysfunction after tricuspid surgery rapidly improved. Thereafter, right mean right ventricular performance for the cohort remained stable throughout follow-up, with no significant decline. Time has been entered as the log-transformation to improve model fit. Number of nonmissing values for analysis: patients

not receiving TV intervention, N = 1796; preoperative TV intervention, N = 201; postoperative TV intervention, N = 193. TV, Tricuspid valve; RV, right ventricular.

TABLE E1. Patient demographics, baseline morphology, and Norwood features

Variable	No TV intervention N = 195			TV intervention N = 24			P value
	Missing values	Value	% or range	Missing values	Value	% or range	
Death at any stage	0	100	51	0	5	21	.0049
Death without TV intervention	0	95	49	0	0	0	–
TV repair	0	0	0	0	24	100	–
Second TV repair	0	0	0	0	3	13	–
Second TV replacement	0	0	0	0	3	13	–
Birth weight (kg)	69	3.3	1.4–4.4	7	3.7	2.5–4.5	.004
Male	0	130	67	0	16	67	>.99
Aortic atresia	0	83	43	1	14	61	.13
Aortic stenosis	0	112	57	1	10	44	.42
Shone syndrome	5	9	5	1	0	0	.60
Subvalvar stenosis	92	15	15	9	1	7	.69
Atrial septal defect	34	150	93	3	20	95	>.99
Ventricular septal defect	92	58	56	13	4	36	.11
Ventricular septal defect, moderate or large	138	19	33	15	1	11	.26
Atrioventricular septal defect	5	22	12	1	1	4	.48
Left superior vena cava	113	22	27	10	2	14	.51
Double-outlet right ventricle	5	13	7	1	2	9	.67
Anomalous pulmonary venous drainage	5	9	5	1	1	4	>.99
Right aortic arch	119	4	5	9	0	0	>.99
Anomalous coronary arteries	118	4	5	9	0	0	>.99
Coarctation	81	99	87	8	8	50	.001
Transverse aortic arch diameter (mm)	65	4	3–5.5	12	3.7	2–7.5	.72
Aortic annular z score	17	–18	–30 to +0.3	3	–12	–19 to –4	.10
Grade of LV hypoplasia							.89
None	0	1	0.5	0	0	0	–
Mild	0	4	2	0	0	0	–
Moderate	0	8	4	0	1	4	–
Severe	0	182	93	0	23	96	–
Grade of LV dysfunction (patent aortic valve only)							
Endocardial fibroelastosis	5	19	10	5	4	21	.29
Mitral atresia	5	47	25	1	11	48	.03
Mitral stenosis	5	39	21	1	4	17	>.99
Parachute mitral valve	4	11	6	1	0	0	.61
Mitral annular z score	50	–10.9	–20 to –0.8	8	–11	–14 to –6	.01
Grade of RV dysfunction							.95
None	0	156	80%	0	20	83%	–
Mild	0	27	14%	0	3	13%	–
Moderate	0	10	5%	0	1	4%	–
Severe	0	2	1%	0	0	0%	–
RVOT stenosis	1	0	0%	11	0	0%	–
Minimum branch pulmonary artery z score	41	–0.36	–29 to +3.0	6	–1.4	–4.4 to +0.6	
Grade of TV regurgitation							.35
None	0	34	17%	0	7	29%	–
Trivial	0	80	41%	0	12	50%	–
Mild	0	67	34%	0	4	17%	–
Moderate	0	12	6%	0	1	4%	–
Severe	0	2	1%	0	0	0%	–
TV stenosis	49	0	0%	6	0	0%	–
Tricuspid annular z score	55	–0.54	–10 to +6	14	–1.3	–5.2 to +2.4	.41
Median age at time of Norwood (d)	0	6	0–175	0	5	2–33	.28
Median weight at time of Norwood (kg)	0	3.3	1.4–19	0	3.6	2.2–5.2	.94
Type of Norwood operation							
Classic	34	131	81%	3	20	95%	.13

(Continued)

TABLE E1. Continued

Variable	No TV intervention N = 195			TV intervention N = 24			P value
	Missing values	Value	% or range	Missing values	Value	% or range	
Brawn modification	34	26	16%	3	1	5%	.32
Modified BT shunt	22	153	88%	1	21	91%	>.99
Sano RV-PA shunt	22	20	12%	1	2	9%	>.99
Median shunt diameter (mm)	43	3.5	2–5	3	3.5	3–4	.67
Total cardiopulmonary bypass duration (min)	31	121	48–437	3	122	99–165	.62
Total myocardial ischemic duration (min)	32	51	19–127	3	62	20–117	.03
Total circulatory arrest duration (min)	50	43	0–100	3	14	1–70	<.001
Minimum core temperature (°C)	87	17	14–23	19	16	15–22	.82
Systemic oxygen saturations at end of procedure (%)	134	73	50–87	20	76	65–80	.76
Delayed sternal closure	46	92	62%	4	16	80%	.14

BT, Blalock–Taussig; LV, left ventricle; PA, pulmonary artery; RVOT, right ventricular outflow tract. Frequencies are expressed as the proportion of nonmissing values.