Interstage mortality after the Norwood procedure: Results of the multicenter Single Ventricle Reconstruction trial

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Objective: For infants with single ventricle malformations undergoing staged repair, interstage mortality is reported at 2% to 20%. The Single Ventricle Reconstruction trial randomized subjects with a single morphologic right ventricle undergoing a Norwood procedure to a modified Blalock–Taussig shunt (MBTS) or a right ventricle-to-pulmonary artery shunt (RVPAS). The aim of this analysis was to explore the associations of interstage mortality and shunt type, and demographic, anatomic, and perioperative factors.

Methods: Participants in the Single Ventricle Reconstruction trial who survived to discharge after the Norwood procedure were included (n = 426). Interstage mortality was defined as death postdischarge after the Norwood procedure and before the stage II procedure. Univariate analysis and multivariable logistic regression were performed adjusting for site.

Results: Overall interstage mortality was 50 of 426 (12%)—13 of 225 (6%) for RVPAS and 37 of 201 (18%) for MBTS (odds ratio [OR] for MBTS, 3.4; $P < .001$). When moderate to severe postoperative atrioventricular valve regurgitation (AVVR) was present, interstage mortality was similar between shunt types. Interstage mortality was independently associated with gestational age less than 37 weeks (OR, 3.9; $P = .008$), Hispanic ethnicity (OR, 2.6; $P = .04$), aortic atresia/mitral atresia (OR, 2.3; $P = .03$), greater number of post-Norwood complications (OR, 1.2; $P = .006$), census block poverty level ($P = .003$), and MBTS in subjects with no or mild postoperative AVVR (OR, 9.7; $P < .001$).

Conclusions: Interstage mortality remains high at 12% and is increased with the MBTS compared with the RVPAS if postoperative AVVR is absent or mild. Preterm delivery, anatomic, and socioeconomic factors are also important. Avoiding preterm delivery when possible and close surveillance after Norwood hospitalization for infants with identified risk factors may reduce interstage mortality. (J Thorac Cardiovasc Surg 2012;144:896-906)

Survivors of the Norwood procedure for hypoplastic left heart syndrome (HLHS) and other single right ventricle anomalies are left with the combination of an inefficient parallel circulation with volume load to the systemic ventricle, potential inferior pumping capability of a systemic right ventricle, and risk of compromise of the systemic to pulmonary artery shunt. These factors expose patients to a heightened risk for circulatory collapse. This inherently fragile physiology persists to the stage II procedure when

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Abbreviations and Acronyms

AVVR = atrioventricular valve regurgitation
BSA = body surface area
CPR = cardiopulmonary resuscitation
DHCA = deep hypothermic circulatory arrest
ECMO = extracorporeal membrane oxygenation
HLHS = hypoplastic left heart syndrome
MBTS = modified Blalock–Taussig shunt
OR = odds ratio
RVEDV = right ventricular end-diastolic volume
RVEF = right ventricular ejection fraction
RVESV = right ventricular end-systolic volume
RVPAS = right ventricle-to-pulmonary artery shunt
SVR = Single Ventricle Reconstruction

the parallel circulation is eliminated through takedown of the systemic to pulmonary artery shunt and creation of a cavopulmonary connection. Mortality postdischarge after the Norwood hospitalization and before the stage II procedure (interstage period) is reported to be 2% to 20%.[1-4]

Specific risks associated with interstage mortality identified in various investigations include a diminutive ascending aorta as seen in aortic atresia, the presence of a restrictive atrial communication, postoperative arch obstruction, obstructed shunt flow, pulmonary artery distortion, and atrioventricular valve regurgitation (AVVR).[5,6] Age at surgery, postoperative arrhythmias, airway complications, feeding difficulties, and noncardiac disease processes such as gastroenteritis or upper respiratory infection also have been implicated.[3,4] Compared with the right ventricle-to-pulmonary artery shunt (RVPAS), higher interstage mortality has been reported for the modified Blalock–Taussig shunt (MBTS).[7,8]

The National Heart, Lung, and Blood Institute–sponsored Pediatric Heart Network Single Ventricle Reconstruction (SVR) trial includes the largest prospective cohort of infants with HLHS or related single right ventricle anomalies with longitudinal follow-up after the Norwood procedure. The primary results of the SVR trial demonstrated improved transplant-free survival at 12 months in those randomized to receive an RVPAS at the Norwood procedure compared with those randomized to the MBTS. Although interstage survival was not specifically reported, the highest incidence of transplant or death occurred between 30 days after the Norwood procedure and the stage II procedure.[9]

The goal of this analysis was to determine anatomic, surgical, and additional patient-related risk factors for interstage mortality postdischarge after the Norwood procedure and before the stage II procedure in this unique cohort. We specifically hypothesized that infants palliated with an MBTS would be at increased risk of interstage death compared with those palliated with an RVPAS.

MATERIALS AND METHODS

The Pediatric Heart Network SVR trial compared outcomes between subjects randomized to RVPAS and subjects randomized to MBTS at the time of the Norwood procedure. Details of the trial design have been reported.[10] The institutional review board or research ethics board at each participating center approved the study protocol, and written informed consent was obtained from parents before trial enrollment.

Study Sample

Subjects randomized in the multicenter SVR trial who survived to discharge from the hospital after the Norwood procedure are included in this analysis. Twenty-two subjects surviving the Norwood procedure, but not discharged before the stage II procedure, were excluded from the primary analysis because of limitations in distinguishing Norwood operative mortality from interstage mortality for subjects with planned inpatient care to stage II procedure. Two subjects whose dates of stage II procedure could not be determined and 2 subjects whose stage II procedures were performed uncharacteristically late (ie, >14 months of age) were excluded from the primary analysis.

Study Design and Measurements

Shunt type was defined for this analysis as the shunt in place at the end of the Norwood procedure. The surgeon had the option to modify the shunt if anatomy was encountered that made the randomized shunt assignment not feasible. Other than random assignment of shunt, all participants were managed according to the standard practices at their clinical centers. A list of all variables that were recorded and analyzed is included in Appendix Table 2. In brief, before the Norwood procedure, a detailed preoperative medical history was recorded, including demographics, patient characteristics, and anatomic diagnosis. Operative variables included shunt type, pharmacologic strategies, perfusion method, and additional cardiac operations. The perfusion method during circulatory support was classified into 1 of 3 categories: deep hypothermic circulatory arrest (DHCA), regional cerebral perfusion with DHCA time of 10 minutes or less, or regional cerebral perfusion with DHCA time greater than 10 minutes. Postoperative data recorded for the Norwood hospitalization included procedures, serious adverse events such as cardiopulmonary resuscitation (CPR) and use of extracorporeal membrane oxygenation (ECMO), number of previously described complications,[11] hospital length of stay, and feeding methods at discharge after the Norwood procedure.

Echocardiograms were obtained before and after the Norwood procedure. The echocardiograms were interpreted centrally at a core laboratory (Medical College of Wisconsin) to assess the degree of AVVR (none/mild vs moderate/severe), to measure right ventricular end-systolic volume (RVESV) and right ventricular end-diastolic volume (RVEDV), and to determine fractional area change and right ventricular ejection fraction (RVEF). The primary measure of right ventricular contractility used in the multivariable model was right ventricular fractional area change, because the other measures of systolic function including RVEF, RVESV, and RVEDV could not be obtained for 23% of the subjects. In the 330 subjects for whom both measurements were available, there was a high degree of correlation ($R = 0.89$) between the RVEF and the right ventricular fractional area change.

A subgroup of subjects consented for evaluation by a geneticist. Genetic evaluations performed for clinical indications were also recorded. Subjects were classified as to whether a specific genetic syndrome was identified and whether "other abnormalities" (ie, not identified with a syndrome) were present.

Socioeconomic status at the time of randomization was assigned using a US census–based score derived from 6 measures based on income, housing, and occupational-related features of the subject's census block tract, as

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