Survival Through Staged Palliation: Fate of Infants Supported by Extracorporeal Membrane Oxygenation After the Norwood Operation

Joshua M. Friedland-Little, MD, Ranjit Aiyagari, MD, Sunkyung Yu, MS, Janet E. Donohue, MPH, and Jennifer C. Hirsch-Romano, MD

Division of Pediatric Cardiology, Department of Pediatrics and Communicable Disease, and Section of Pediatric Cardiac Surgery, Department of Cardiac Surgery, University of Michigan, Ann Arbor, Michigan

Background. Infants supported by extracorporeal membrane oxygenation (ECMO) after a Norwood operation face in-hospital mortality rates of 60% to 70%. There are limited data on completion of staged palliation for the subset of patients who survive to hospital discharge.

Methods. We performed a retrospective case-control study of 64 sequential patients at a single institution supported by ECMO after a Norwood operation. Primary endpoints were survival to hospital discharge, stage II palliation, and stage III palliation. Predictors of non-survival to each endpoint were identified with logistic regression. Survival was compared with a 3:1 era-matched group of control patients who underwent a Norwood operation but did not require ECMO.

Results. Survival to hospital discharge, stage II palliation, and stage III palliation was 43.8%, 35.9%, and 25.4%, respectively for ECMO cases. Factors independently associated with non-survival to hospital discharge included female gender, ECMO 7 days or greater, and need for renal replacement therapy on ECMO. Non-Caucasian race and ECMO 7 days or greater were independently associated with non-survival to stage II, while non-Caucasian race, lower birth weight, and ECMO 7 days or greater were independently associated with non-survival to stage III. Extracorporeal membrane oxygenation was associated with decreased survival at each endpoint. Patients who survived ECMO had increased interstage mortality between hospital discharge and stage II palliation.

Conclusions. Extracorporeal membrane oxygenation after a Norwood operation can be life-saving but ultimate survival through staged palliation remains suboptimal. The elevated mortality risk for patients supported by ECMO persists after hospital discharge. Both socioeconomic factors and ECMO-related morbidity may contribute to midterm mortality.

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Palliation of hypoplastic left heart syndrome and variants continues to involve significant morbidity and mortality. Most large centers currently report in-hospital mortality rates from 10% to 20% after the Norwood operation [1, 2]. Extracorporeal membrane oxygenation (ECMO) is utilized postoperatively in approximately 10% of patients undergoing a Norwood operation [3, 4]. A recent review of the Extracorporeal Life Support Organization registry described 31% survival to hospital discharge for all infants in the registry requiring ECMO after stage I palliation of hypoplastic left heart syndrome between 2000 and 2009 [5]. Ravishankar and colleagues [4] reported 38.8% survival to hospital discharge in a single center series from a high volume cardiac center. The data on longer term outcomes and staged palliation for this patient population are limited. A case series by Debrunner and colleagues [6] described midterm outcomes for 32 patients at a single institution over a 14-year period who required ECMO after a Norwood operation, with 50.0%, 24.6%, and 13.2% survival at 30 days, 1 year, and 3 years, respectively. Only 4 of the 32 patients requiring ECMO in this series survived to Fontan completion. Given the limited data on post-discharge survival outcomes for this high-risk patient population, we aimed to evaluate survival to staged palliation of patients who required ECMO support after a Norwood operation over a 10-year period at a single high volume surgical center, and to determine risk factors for non-survival in this population compared with an era-matched control population.

Patients and Methods

Surgical and ECMO techniques

Shunt type was dependent on surgeon preference throughout the study period. Chest versus neck cannulation for ECMO was also dependent on surgeon preference. In most cases chest cannulation was utilized for those patients who had not yet undergone sternal closure, while neck cannulation was utilized for patients cannulated after sternal closure.

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Address correspondence to Dr Friedland-Little, University of Michigan Congenital Heart Center, C.S. Mott Children's Hospital, 1540 E Hospital Dr, Ann Arbor, MI 48109-4204; e-mail: jmfriedl@med.umich.edu.

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Data analysis

We performed a retrospective chart review of all patients supported by ECMO after a Norwood operation at the University of Michigan over a 10-year period, from January 1, 2001 to December 31, 2010. After approval from the University of Michigan Institutional Review Board, the internal ECMO registry was reviewed and all patients who received ECMO support during the same hospitalization in which they underwent a Norwood-type operation (identified as Damus-Kaye-Stansel anastomosis and systemic-to-pulmonary artery shunt, ± arch reconstruction) were identified. Patients who underwent a hybrid Norwood procedure and patients requiring ECMO preoperatively were excluded from analysis. In order to assess the impact of ECMO on survival, the University of Michigan Congenital Heart Surgery database was queried to identify 3:1 era-matched (± 6 months of surgical date) control patients who received a Norwood-type operation but did not receive ECMO support. Control group size was determined by a power analysis demonstrating that 3:1 matching would provide greater than 80% power to detect an odds ratio of at least 2.5 at the 0.05 significance level. Electronic charts were reviewed, and demographic and clinical data were collected.

Primary endpoints were survival to hospital discharge, stage II palliation, and stage III palliation. Preoperative, intraoperative, and postoperative data were collected, as presented in Tables 1, 2, and 3, respectively. Data are presented as frequency with percentage for categoric variables and median with range, or mean ± standard deviation (SD), as appropriate, for continuous variables. Unadjusted odds ratios (OR), adjusted odds ratios (AOR), and their 95% confidence intervals (CI) were estimated using logistic regression to evaluate associations between possible risk factors and the risk of non-survival to hospital discharge, stage II palliation, and stage III palliation. Given limitations in sample size, risk factor analysis was performed for all ECMO patients, not only hospital survivors. Variables found to be significantly associated with non-survival at any endpoint in the univariate analyses (ie, p value less than 0.1) were investigated further by building multivariable models with a backward elimination method. Improvements in the model fit were evaluated by the model χ^2 statistics. Survival to each endpoint and interstage survival were computed by the Kaplan-Meier method and compared between ECMO patients and non-ECMO controls using the log-rank test. In each curve, subjects were censored after reaching the relevant endpoint; ie, hospital discharge, stage II palliation, or stage III palliation. Hazard ratios (HR) with 95% CI were also presented. All analyses were performed using SAS Version 9.3 (SAS Institute Inc, Cary, NC), with statistical significance set at a p value less than 0.05 using 2-sided tests.

Table 1. Demographic and Preoperative Clinical Characteristics of Patients Requiring ECMO After a Norwood Operation From 2001 to 2010 (n = 64)

Characteristics	n (%)/Mean ± SD/Median (range)
Female sex	23 (35.9)
Race	
Caucasian	48 (75.0)
African American	10 (15.6)
Other/Unknown	6 (9.4)
Age at stage I surgery, days	6 (1–31)
Birth weight, kg	3.1 ± 0.6
<2.5 kg	10 (15.6)
Prenatal diagnosis	51 (79.7)
Cardiac diagnosis	
MA/AA	18 (28.1)
MS/AA	18 (28.1)
MS/AS	14 (21.9)
MA/AS	1 (1.6)
Unbalanced AVSD	8 (12.5)
DORV/HLV	4 (6.3)
Tricuspid atresia, hypoplastic arch	1 (1.6)
Prematurity (less than 37 weeks)	11 (17.2)
Extracardiac or genetic anomaly	14 (21.9)
Preoperative metabolic acidosis[a]	5 (7.8)
Lactate prior to OR, mmol/L	1.5 (0.6–3.5)
Peak preoperative lactate, mmol/L	3.7 (1.4–8.6)
Blood urea nitrogen (BUN) prior to OR, mg/dL	20 (5–48)
Creatinine (Cr) prior to OR, mg/dL	0.58 ± 0.23
Preoperative intervention on atrial septum	6 (9.4)
Atrioventricular valve regurgitation (preoperative echocardiogram)	
None	20 (31.3)
Trace to mild/mild	35 (54.7)
Mild to moderate/moderate	6 (9.4)
Moderate to severe/severe	3 (4.7)
Systemic ventricular function (preoperative echocardiogram)	
Normal	40 (62.5)
Mildly depressed	16 (25.0)
Mild to moderate/moderately depressed	7 (10.9)
Moderate to severe/severely depressed	1 (1.6)
Aortic size, mm	2.7 (1.3–7.3)
<2.0 mm	16 (25.0)

[a] Defined as pH <7.30 with Pco_2 <45.

Data are presented as n (%) for categoric variables and mean ± SD or median (range) for continuous variables.

AVSD = atrioventricular septal defect; DORV/HLV = double outlet right ventricle/hypoplastic left ventricle; ECMO = extracorporeal membrane oxygenation; MA/AA = mitral atresia/aortic atresia; MA/AS = mitral atresia/aortic stenosis; MS/AA = mitral stenosis/aortic atresia; MS/AS = mitral stenosis/aortic stenosis; OR = operating room.

Results

Of the 425 patients undergoing a Norwood-type operation during the study period, 64 (15.1%) received postoperative ECMO support. Preoperative characteristics are presented in Table 1 while intraoperative data and ECMO data are presented in Table 2.

Forty-four patients (68.8%) survived to decannulation from ECMO, 28 patients (43.8%) survived to hospital