ISHLT JOURNAL WATCH
December 2023 | Pediatrics

Samantha Ennis, MBBS
Alfred Health, Melbourne, Australia

Jacob Mathew, MBBS, FRACP | Junior Editor
Ashley Fritz, MD | Senior Editor

ISHLT.ORG

Extracorporeal membrane oxygenation bridge to pediatric lung transplantation: Modern era analysis

Koh W, et al. *Pediatric Transplantation* 10 July 2023 | https://doi.org/10.1111/petr.14570

Study Highlights

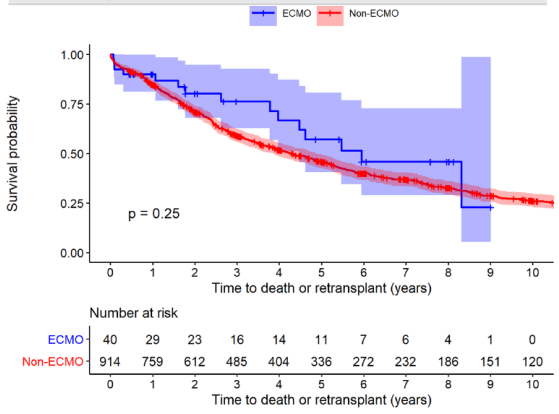
Objective: The use of extracorporeal membrane oxygenation (ECMO) as a bridge to Lung Transplant (LTx)has increased among pediatric patients. To date, survival outcomes remain unclear. The study aim was to investigate the impact of ECMO at time of primary LTx among children (<18 years)

Methods: Retrospective analysis of Pediatric first time LTx recipients transplanted between January 2000 and December 2020 identified in the United Network for Organ Sharing Registry to compare post transplant survival according to ECMO support at time of transplant.

Results: During the study period, 954 children under 18 years of age underwent LTx with 40 patients on ECMO. The most common indication was CF followed by PPH. There was no difference in post-LTx survival between patients receiving ECMO when compared to those that did not.

Conclusions: In this contemporary cohort of children, the use of ECMO at the time of LTx did not negatively impact post-transplant survival.

Variable	Overall, N = 954	ECMO, N = 40	Non-ECMO, N = 914	p-Value
Male recipient	395 (41%)	8 (20%)	387 (42%)	0.01
Male donor	492 (52%)	17 (42%)	475 (52%)	0.30
Race of recipient				
White	697 (73%)	24 (60%)	673 (74%)	0.20
Black	62 (6.5%)	4 (10%)	58 (6.3%)	
Others	195 (20%)	12 (30%)	183 (20%)	
Race of donor				
White	545 (57%)	20 (50%)	525 (57%)	0.30
Black	195 (20%)	12 (30%)	183 (20%)	
Others	214 (22%)	8 (20%)	206 (23%)	
Diabetes	187 (20%)	2 (5.0%)	185 (20%)	0.03
Diagnosis				
PPH	102 (11%)	9 (22%)	93 (10%)	0.03
CF	534 (56%)	9 (22%)	525 (57%)	<0.01
ILD	26 (2.7%)	2 (5.0%)	24 (2.6%)	0.70
ARDS/pneumonia	7 (0.7%)	6 (15%)	1 (0.1%)	<0.01
Others	285 (30%)	14 (35%)	271 (30%)	0.60
Age (year)	13.0 (8.0, 16.0)	13.5 (7.0, 16.2)	13.0 (8.0, 16.0)	0.50
Body mass index[a]	16.7 (14.8, 18.8)	19.2 (15.7, 22.3)	16.7 (14.8, 18.8)	<0.01
Creatinine (mg/dL)[b]	0.4 (0.3, 0.5)	0.3 (0.2, 0.5)	0.4 (0.3, 0.6)	0.20
Ischemic time (hour)[c]	5.5 (4.6, 6.4)	5.5 (5.1, 6.8)	5.5 (4.6, 6.4)	0.20
Bilirubin (mg/dL)[d]	0.3 (0.2, 0.6)	0.6 (0.4, 1.3)	0.3 (0.2, 0.6)	<0.01
Hospital stay (day)[e]	19.0 (13.0, 31.0)	36.0 (26.0, 47.0)	19.0 (13.0, 30.0)	<0.01
Transplant year				
2000–2008	432 (45%)	1 (2.5%)	431 (47%)	<0.01
2009–2010	112 (12%)	1 (2.5%)	111 (12%)	
2011–2020	410 (43%)	38 (95%)	372 (41%)	
LAS scores for age ≥12[f]	37.5 (34.9, 46.0)	88.4 (82.8, 90.4)	37.1 (34.8, 44.0)	<0.01



Reviewer's Comments

- Donor availability for children requiring LTx is scarce, often leading to longer wait list times and increased mortality
- ECMO has emerged as a key strategy to manage waitlist mortality in adults, but efficacy of ECMO as a therapeutic option for pediatric lung transplant patients remains to be fully elucidated.
- The frequency of ECMO utilization as a bridge to transplant reported in this study (4%) is approaching the utilization reported in adult LTx studies.
- This study demonstrates that first time pediatric LTx recipients are not survival disadvantaged by EMCO as a bridge to LTx.

Limitations

- Retrospective study of registry data
- Small sample size of pediatric patients on ECMO at time of LTx
- Salient ECMO data not available in database including ECMO configuration (VA vs VV) and total duration of ECMO support
- Patients undergoing re-transplantation excluded limiting generalizability of the outcomes

ISHLT JOURNAL WATCH
December 2023 | Pediatrics

Alyssa Power, MD, FRCPC, FACC
Hospital for Sick Children, Toronto, ON, Canada

Jacob Mathew, MBBS, FRACP | Junior Editor
Ashley Fritz, MD | Senior Editor

ISHLT.ORG

Pediatric Risk to Orthotopic Heart Transplant (PRO) Score: Insights from United Network for Organ Sharing (UNOS) Waitlist Mortality Findings

Raymundo S, et al. *Pediatr Transplant* July 2023 | https://doi.org/10.1111/petr.14525

Study Highlights

Objective: Pediatric heart transplant (HT) candidates have high risk of waitlist mortality. The study aim was to develop a risk prediction model for waitlist mortality.

Methods: Using the UNOS database, 5,542 children on the waitlist for a single, first time, HT from Jan 2010 to June 2019 were evaluated. A univariate analysis on two-thirds (N = 3,705) derived the factors most associated with waitlist mortality or delisting secondary to deterioration within 1 year. Those with a $p < 0.2$ underwent a multivariate analysis. The resulting factors were used to build a predictive scoring model using Fine-Grey model analysis which was validated on the remaining one-third of patients (N = 1,852).

Results: The Pediatric Risk to OHT (PRO) scoring model incorporates blood type, congenital heart disease (CHD) diagnosis, weight, ventilator support, inotropic support, ECMO status, creatinine level, and region. A higher score indicates an increased mortality risk. The PRO score had a predictive strength of 0.762 as measured by AUC at 1 year.

Conclusion: The PRO score has the potential to better assess mortality for patients awaiting HT.

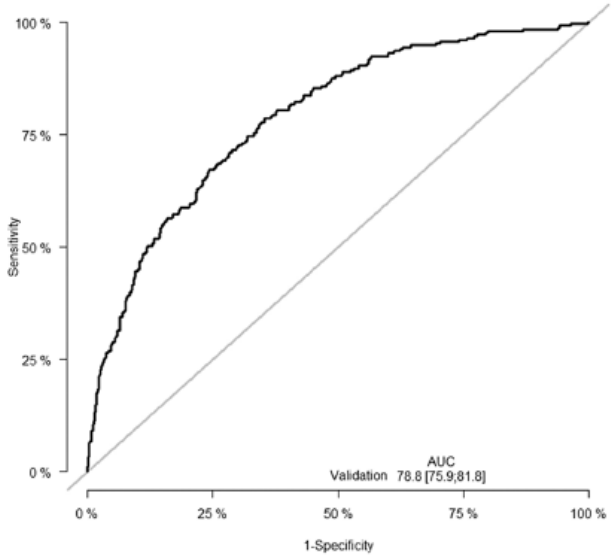


Figure 1: Area under the curve for the validation cohort.

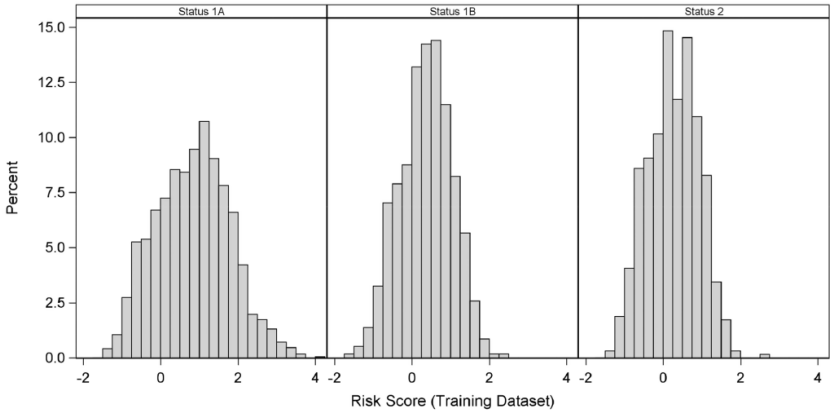


Figure 2: PRO Score distribution within each listing status.

Reviewer's Comments

- The PRO score has the potential to predict pediatric HT waitlist mortality.
- Score distribution varies significantly within each listing status (Figure 2), conveying the patient heterogeneity within individual groups and the poor discrimination of risk offered by the current allocation system.
- Improvements in risk assessment may allow us to optimize the allocation system.
- UNOS region is incorporated as a risk factor in the PRO scoring model. Regional variation in waitlist mortality merits further evaluation, with potential contributing factors including access, offer acceptance ratios, and center volume.

Limitations

- Key factors which may affect waitlist mortality (e.g., specific CHD diagnosis, bilirubin level, estimated GFR, nutritional status, sarcopenia, frailty) are missing due to lack of patient-level clinical data.
- Though blood type is incorporated into the score, the model not account for the fact that patients listed as ABO incompatible candidates may have a similar risk profile to an AB candidate.

ISHLT JOURNAL WATCH
December 2023 | Pediatrics

Madeleine Townsend, MD
Cleveland Clinic Children's, Cleveland, Ohio, USA

Jacob Mathew, MBBS, FRACP | Junior Editor
Ashley Fritz, MD | Senior Editor

ISHLT.ORG

Taking ACTION: A Prognostic Tool for Pediatric Ventricular Assist Device Mortality

Boucek K, *et al. ASAIO* June 2023 | https://doi.org/10.1097/MAT.0000000000001899

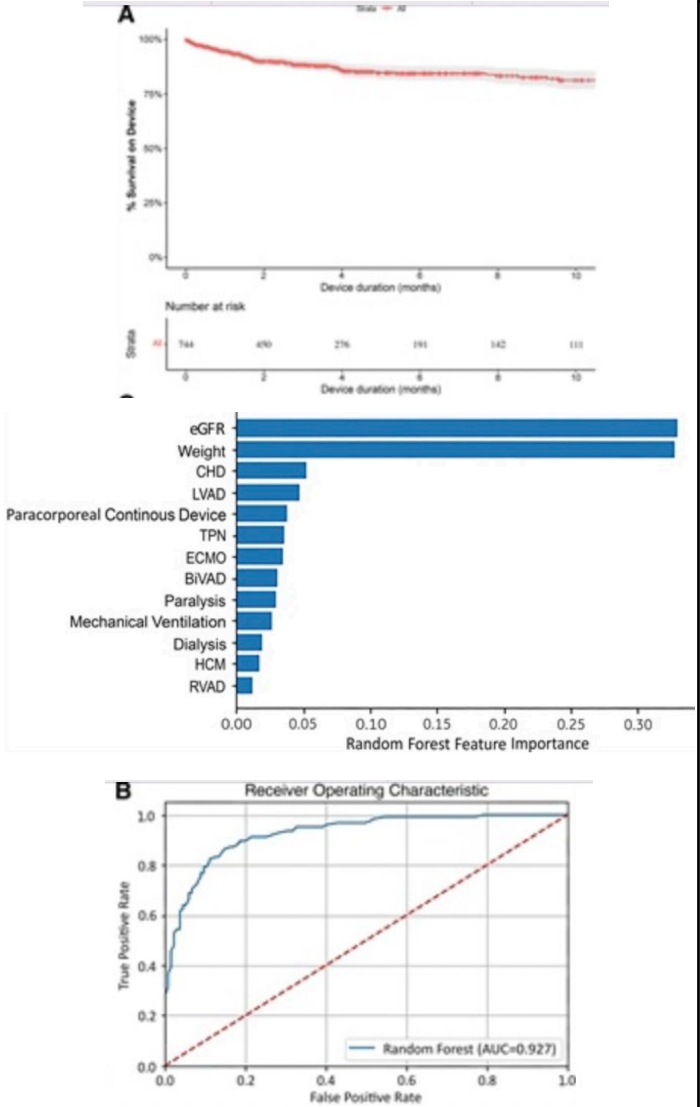
Study Highlights

Objective: Ventricular assist devices (VAD) are increasingly used to bridge children to heart transplant. While INTERMACS guides optimal timing of VAD insertion in adults, a pediatric-specific risk profiling tool does not yet exist. The study aim was to develop a comprehensive VAD risk assessment tool to predict mortality risk for children being considered for VAD support.

Methods: Retrospective analysis of pediatric and adult congenital heart disease (CHD) patients supported on paracorporeal or intracorporeal VAD at ACTION centers from 2018–2021. Univariate and multivariate analyses of patient demographics and pre- and peri-implant characteristics were used to develop a random Forest machine learning model, with mortality as the primary outcome.

Results: During the study period, 744 patients underwent VAD placement, with 94 deaths while on support (12.6%). Small patient size, diagnosis (hypertrophic cardiomyopathy or CHD), end-organ dysfunction, physiologic frailty and device type were important modulators of mortality on VAD.

Conclusions: Identification of modifiable and patient-specific risk factors may improve timing of VAD insertion as well as help prognosticate mortality on support. Next steps include development of a mobile risk calculator for use at bedside.



Reviewer's Comments

- Children with heart failure continue to have the highest waitlist mortality of any age or solid organ despite increased utilization of VAD support.
- ACTION has the largest database of pediatric and ACHD patients on VAD which could support development of a pediatric risk assessment tool to improve survival to heart transplant.
- This model confirmed previously identified risk factors for pediatric VAD mortality (young age/small size, CHD, paracorporeal device) as well as potentially modifiable factors that may be optimizable by timing of VAD insertion or medical management post-VAD.

Limitations

- Retrospective study of registry data with small, heterogenous patient cohort and relatively few events (mortality).
- Risk factors for mortality while on VAD may exist that are not collected in the ACTION registry.
- The machine learning model developed is not readily deployable to the bedside for current evaluation of prospective patients.

ISHLT JOURNAL WATCH
December 2023 | Pediatrics

Julie Wacker, MD
University Hospitals of Geneva, Switzerland

Jacob Mathew, MBBS, FRACP | Junior Editor
Ashley Fritz, MD | Senior Editor

ISHLT.ORG

Monitoring of Hemodynamics With Right Heart Catheterization in Children With Pulmonary Arterial Hypertension

Grynblat J, et al. *J Am Heart Assoc* Mar 2023 | https://doi.org/10.1161/JAHA.122.029085

Study Highlights

Objective: In children with pulmonary arterial hypertension (PAH), right heart catheterization (RHC) is a high-risk diagnostic procedure, but the role of RHC in the follow-up is unclear. This study explores the association between baseline and repeat RHC parameters and any negative outcome (death, transplantation, or need for Potts shunt).

Methods: Retrospective analysis of pediatric PAH patients presenting at a tertiary center between 2000 and 2021 with a baseline RHC and at least one follow-up RHC.

Results: 71 treatment naïve PAH subjects were included. Pulmonary vascular resistance index (PVRi; HR 1.07 per 1 WU•m^2 increase), pulmonary artery compliance index (PACi; HR 0.16 per mL/mm Hg), right atrial pressure (RAP; HR 1.31 per 1mmHg) and stroke volume index (HR 0.95 per L•min^{-1}•m^{-2}) were associated with adverse outcome at baseline RHC. PVRi (HR 1.11 per WU•m^{-2}), PACi (HR 0.11 per mL/mm Hg) and RAP (HR 1.25 per mmHg) were still associated with adverse outcome at repeat RHC. Non-invasive hemodynamic criteria predicted hemodynamic evolution, but 70% of the patients who improved clinically still harboured at least 1 "at risk" hemodynamic parameter based on thresholds defined within this study.

Conclusions: Repeated RHC are helpful to identify children with persistent higher risk after treatment introduction.

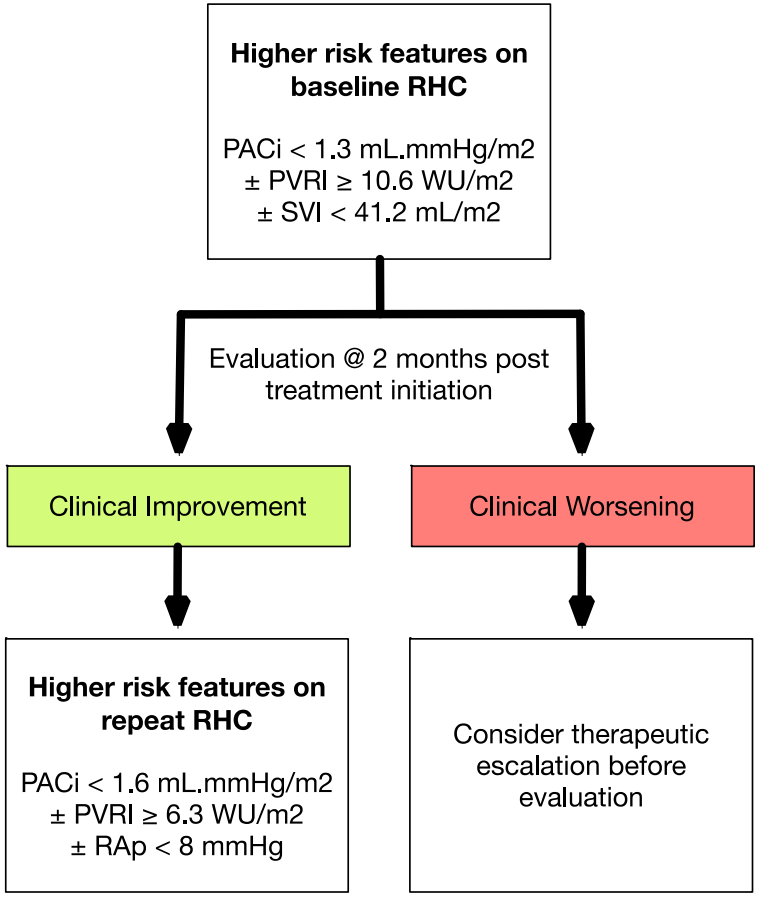


Figure 1: Treatment algorithm proposed by authors based on this study

Reviewer's Comments

- RAP, PACi and PVRi are independent prognosis factors at both baseline and on repeat RHC
- Repeat RHC should remain an essential part of the follow-up in children with PAH, especially in those with clinical improvement based on non-clinical criteria, because a significant proportion of these patients will still have higher risk haemodynamic parameters which predict worse outcome and may benefit from treatment intensification (figure 1)
- Changes in these parameters with treatment may also serve as surrogate endpoints in future studies, as such changes seem to carry prognostic information.

Limitations

- Retrospective and single centre study
- Data collection period spread over a period of 20 years, with changes in therapeutic strategy potentially affecting outcomes
- No attempt at internal or external validation of findings
- It was not possible to evaluate effect of specific PAH therapeutics on hemodynamic parameters
- Further studies needed to validate the use of those hemodynamic parameters as therapeutic targets