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Extracorporeal membrane oxygenation support and post-heart transplant outcomes among United States adults

Sandip Zalawadiya, MD,[a] Marat Fudim, MD,[b] Geetha Bhat, MD, PhD,[c] William Cotts, MD,[c] and JoAnn Lindenfeld, MD[a]

From the [a]Division of Advanced Heart Failure, Department of Internal Medicine, Vanderbilt University Medical Center, Nashville, Tennessee; [b]Division of Cardiology, Department of Internal Medicine, Duke University Hospital, Durham, North Carolina; and the [c]Division of Advanced Heart Failure, Advocate Christ Medical Center, Chicago, Illinois.

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BACKGROUND: Patients supported with extracorporeal membrane oxygenation (ECMO) are given priority listing status for heart transplant (HT). Data on post-HT outcomes for adults with ECMO support at the time of HT are limited.

METHODS: We analyzed data from the United Network for Organ Registry (UNOS) registry for 157 ECMO-supported adults (age $\geq$ 18 years) undergoing HT after January 1, 2000. Data at the time of HT were examined for their association with post-transplant mortality using multivariable Cox proportional hazard analyses.

RESULTS: Patients (69.4% males; mean age, 46.0 $\pm$ 15.6 years; 15.9% African Americans) were monitored for median of 0.55 years (interquartile range, 0.04–4.5). Seventy patients (44.6%) died during follow-up (survival at 1 year was 57.8%), of which 43 (61.4%) died within 30 days post-HT. For patients surviving the first 30 days after transplant, long-term survival was acceptable (82.3% at 1 year and 76.2% at 5 years). Prevalence of immediate post-HT complications, such as stroke and need for dialysis, were 10.1% and 28.1%, respectively. Post-HT survival did not differ between those who received an allograft before and after January 1, 2009 (univariate hazard ratio, 0.84; 95% confidence interval, 0.51–1.38; $p = 0.48$). Among the predictors identified for 30-day and long-term mortality were recipient history of renal insufficiency (RI; defined as estimated glomerular filtration rate $<$ 45 ml/min/1.73 m^2 or dialysis) and mechanical ventilation (MV; interaction $p < 0.05$); those with both MV and RI had significantly poorer post-transplant survival (29.4% and 12.5% for 30-day and 1-year survival, respectively) compared with those without (78.7% and 71.4% for 30-day and 1-year survival, respectively).

CONCLUSIONS: Post-HT mortality did not change for ECMO-supported adults in the contemporary era, and those with RI and MV had significantly poorer post-transplant survival. A critical review of priority listing status for ECMO-supported patients is warranted for optimal allocation and outcomes of cardiac allografts.

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Despite major advances in the field of end-stage heart failure (HF) management, heart transplantation (HT) remains the most effective long-term treatment.[1] Mechanical circulatory support (MCS) devices, both durable and temporary, are increasingly used to bridge transplant-eligible

Reprint requests: Sandip Zalawadiya, MD, 1215 21st Ave S, MCE 5th Flr, Nashville, TN 37232. Telephone: 615-936-8187. Fax: 615-936-1643.
E-mail address: sandip.zalawadiya@gmail.com

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candidates until a suitable donor organ is obtained.[2] Extracorporeal membrane oxygenation (ECMO) is one such temporary MCS device, and its use has sharply increased in the United States in recent years.[3,4] Improvements in technology, increased clinical experience, relative simplicity of insertion and initiation in emergency situations, relatively low costs, and provision of cardiopulmonary support are some of the advantages accounting for its escalating use.

Current Organ Procurement and Transplantation Network (OPTN) allocation policy is geared towards offering a priority listing status for the highest risk patients, including those on ECMO;[5] however, their waiting list and post-HT survival remain poor compared with those with durable MCS or inotropes.[6,7] Given the limitations of availability of donor organs, it is of utmost importance that we identify higher-risk ECMO patients who may not benefit from direct HT and for whom an alternate management strategy must be sought. Various scoring systems exist to predict mortality on ECMO support among the general population,[8–10] but data on risk factors analysis for post-HT mortality are limited by small, single-center studies.[11–13] Therefore, we initiated this study to evaluate prognostic factors associated with poor post-HT survival among ECMO-supported adults.

Methods

After exempt status approval from the Vanderbilt University Medical Center Institutional Review Board, we analyzed adults (age $\geq$ 18 years) supported by ECMO at the time of HT from the UNOS registry. We analyzed HT occurring after January 1, 2000, with follow up available through September 2015. The analysis excluded patients with prior solid-organ transplants, those undergoing heart-lung transplants, and those with right ventricular MCS alone or unknown types of MCS.

The primary outcome of interest was all-cause post-transplant mortality. We performed univariate Cox proportional hazard analysis of baseline recipient and donor characteristics for their association with 30-days and long-term mortality. Candidate variables with a univariate p-value of <0.15 were analyzed as part of multivariable Cox proportional hazard analyses, and those with multivariable p-value of <0.15 were included in the final model. Because a small number of patients had missing information on variables of interest, 20 imputations were performed using the regression switching (chained equations) approach with predictive mean matching before any regression analyses.[14,15] The analyses were performed using Stata 12 software (StataCorp LP, College Station, TX).

Results

Recent years have seen sharp increase in proportion of patients undergoing direct HT from ECMO support; of the total number of ECMO patients in this study, 35.7% underwent HT before January 2009 compared with 64.3% after January 2009 (Figure 1). Seventy patients died during follow-up, and 43 of the 70 (61.4%) died within 30 days, with graft failure as the major cause of death (30.2%). Survival for the entire sample at 1 year was 57.8%, with a median follow-up of 0.55 years (interquartile range, 0.04–4.5). For patients who survived the first 30 days after

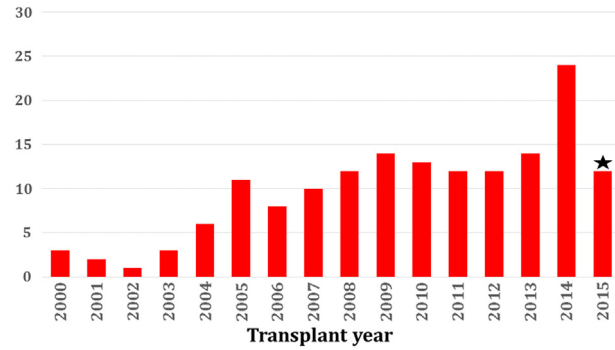

Figure 1 Number of heart transplant recipients with extracorporeal membrane oxygenation support listed at the time of transplantation. ★The number of patients for the year 2015 is limited for transplants until June 2015 and follow-up through September 2015.

transplant, long-term survival was acceptable, at 82.3% at 1 year and 76.2% at 5 years; multiorgan failure (27%) was the major cause of death among these patients. No significant difference in survival was noted between those who received transplants before January 2009 and after January 2009 (univariate hazard ratio [HR], 0.84; 95% confidence interval [CI], 0.51–1.38, $p = 0.486$; Figure 2A). As reported in Table 1, acuity of illness was certainly high for study patients, as reflected by hepatorenal dysfunction, need for mechanical ventilation (MV), intra-aortic balloon pump, MCS, and inotropes. Table 2 reports the results of multivariable analyses outlining potential predictors of post-HT mortality at 30 days and during overall follow-up. Of particular importance were recipient history of MV and renal insufficiency (RI), which was defined as pre-transplant estimated glomerular filtration rate $<$ 45 ml/min/1.73 m^2 or the need for dialysis. We observed the interaction term between RI and MV to be statistically significant ($p < 0.05$ for 30-day and long-term mortality). Those with both MV and RI had a significantly higher risk of post-transplant mortality (29.4% and 12.5% surviving to 30 days and 1 year, respectively) compared with those without MV and RI (78.7% and 71.4% surviving to 30 days and 1 year, respectively; Figure 2B and Appendix Table A, available online at www.jhltonline.org).

Discussion

We used data from this multicenter national registry to report outcomes of ECMO-supported adults at the time of HT. We observed that ECMO-supported adults had a poor 30-day and long-term post-transplant survival, with no improvement in survival in the contemporary era. We also identified the recipient's status of MV and RI to have significant effect on post-transplant survival. Strategy to allocate donor hearts to adults on ECMO support as a priority needs to be critically reviewed, especially for those with both RI and MV given their poor post-transplant survival.

By using simulation analyses to compare various allocation schemes granting status 1A for HT, Colvin et al[6] recently reported ECMO-supported adults had the