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Mechanical circulatory support and simultaneous heart-kidney transplantation: An outcome analysis

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KEYWORDS:
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BACKGROUND: Single-donor simultaneous heart-kidney transplantation (SHKT) can significantly improve the survival of those with advanced heart failure and advanced renal insufficiency. Data on pre-transplant use of mechanical circulatory support (MCS) devices and outcomes after SHKT are limited and conflicting.

METHODS: Using the United Network for Organ Sharing registry data, we evaluated 749 adults undergoing SHKT after January 1, 2000. Patients were categorized into the following groups according to their type of pre-transplant MCS device: none ($n = 568$), pulsatile-flow left ($n = 28$), continuous-flow left ($n = 68$), temporary ($n = 12$), biventricular ($n = 19$), total artificial heart ($n = 20$), and unknown ($n = 34$). Regression analyses were performed to assess the association between types of MCS and post-transplant outcomes.

RESULTS: Pre-transplant MCS was not associated with in-hospital mortality (univariate odds ratio [OR], 1.57; 95% confidence interval [CI], 0.82–2.97; $p = 0.170$) or post-discharge mortality (univariate hazard ratio, 0.92; 95% CI, 0.58–1.47; $p = 0.733$). Patients supported with pre-transplant temporary MCS devices were more likely to suffer from serious complications (composite of cardiac or non-cardiac surgeries, stroke, any drug-treated infection, and permanent pacemaker; multivariable adjusted OR, 10.0; 95% CI, 2.77–36.0; $p < 0.001$) after SHKT. Pre-transplant MCS did not increase risk of post-transplant dialysis (multivariable adjusted OR, 1.19; 95% CI, 0.81–1.75; $p = 0.375$) or cardiac rejection (univariate OR, 0.71; 95% CI, 0.34–1.51; $p = 0.382$), and did not prolong the length of hospital stay ($\geq$ 4 weeks; multivariable adjusted OR, 1.05; 95% CI, 0.69–1.59; $p = 0.832$). Post-transplant dialysis status was a major determinant of adverse in-hospital (multivariable adjusted OR, 6.17; 95% CI, 3.14–12.1; $p < 0.001$) and post-discharge (multivariable adjusted hazard ratio, 1.56; 95% CI, 1.02–2.39; $p = 0.041$) mortality after SHKT.

CONCLUSIONS: In the current transplant era, survival after SHKT in patients with pre-transplant MCS was equivalent to that of conventional SHKT. Pre-transplant dialysis, and not MCS status, determined the need for post-SHKT dialysis, which in-turn was a major risk factor for in-hospital and long-term mortality.

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A recent report of Organ Procurement and Transplantation Network (OPTN)/United Network for Organ Sharing (UNOS) Thoracic Committee showed that the number of patients listed for and eventually receiving simultaneous heart-kidney transplantation (SHKT) has increased significantly in

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the last decade.[1] This is likely due to our understanding that renal insufficiency (RI) adversely affects survival of those undergoing isolated heart transplantation (HT),[2–4] and that those with RI who undergo kidney transplantation subsequent to HT have better survival than those who do not undergo kidney transplantation.[3] Recent analyses of UNOS registry data similarly demonstrate that SHKT is an effective strategy to improve survival of those listed for HT with concurrent dialysis-dependent or non–dialysis-dependent RI.[2,5,6]

Coinciding with the rising trend of SHKT, the last decade has also witnessed a sharp increase in the use of mechanical circulatory support (MCS) devices, both temporary and durable.[7] Previous studies by Russo et al[8] reported that MCS was associated with poor survival among SHKT recipients; whereas Schaffer et al[2], Yanagida et al,[9] and Ruzza et al[10] reported a non-significant effect of MCS on survival. To determine the effect of MCS on post-SHKT mortality and complications, we evaluated largest SHKT cohort reported to date from the UNOS registry in the current era of solid-organ transplantation.

Our primary objective was to assess the effect of MCS on post-transplant survival. Our secondary objectives were to evaluate the effect of MCS on post-transplant complications, to identify potential predictors of post-transplant mortality, and to analyze the effect of pre-transplant MCS and dialysis status on post-transplant mortality and dialysis requirement.

Method

Patient population and data collection

Retrospective analyses of deidentified data from UNOS were performed after obtaining Institutional Review Board permission. We evaluated 749 adults (age $\geq$ 18 years) who underwent SHKT after January 1, 2000. Follow-up data were available through September 3, 2014. Patients were monitored until death, which was confirmed by using the National Death Index database. Data on various recipient and donor-related demographic characteristics, comorbidities, cardiac hemodynamics, and laboratory parameters at the time of transplantation were examined.

MCS data collection

Patients were categorized into 2 groups based on pre-transplant MCS status (no: 568 [75.8%]; yes: 181 [24.2%]). Those with MCS were further classified into following categories: pulsatile-flow left MCS (28 [15.4%]), continuous-flow left MCS (68 [37.6%]), temporary MCS (12 [6.6%]), biventricular MCS (19 [10.5%]), total artificial heart (TAH; 20 [11%]), and unknown (34 [18.8%]).

Outcomes of interest

The primary outcome of interest was death (in-hospital and post-discharge) after SHKT. Our secondary outcomes of interest were need for post-transplant dialysis, risk of cardiac rejection (treated or not with anti-rejection drugs), index hospital length of stay (categorized as $<$ 4 weeks vs $\geq$ 4 weeks), and other serious complications (a composite of cardiac or non-cardiac surgeries, strokes, drug-treated infections, and need for permanent pacemaker) occurring after SHKT and before hospital discharge. Data on other serious complications were not available for all of the patients, leading us to derive a composite variable incorporating individual outcomes without losing analytic power. Index hospital length of stay was dichotomized at 4 weeks based on 75th percentile distribution cutoff for those who did not die in-hospital. All of these outcome variables were collected as defined by the UNOS registry data definitions.

Statistical analysis

Baseline clinical characteristics were compared in univariate analysis across the categories of MCS status (yes vs no) and sub-categories of MCS. Continuous variables, reported as mean $\pm$ standard deviation, were compared using Student's *t*-test or analysis of variance test, whichever was applicable, and the categoric variables, reported as proportions (%), were compared using the chi-square test or Fisher's exact test, whichever was applicable. After a univariate screen, multivariable logistic regression analyses were performed to assess the effect of MCS on in-hospital mortality post-SHKT. Variables with univariate *p*-values of $<$ 0.15 were entered as candidate independent variables and retained after a forward selection algorithm with an adjusted *p*-value of $<$ 0.05.

For the patients who survived the index hospitalization, a Kaplan-Meier survival curve was generated to graphically illustrate the effect of MCS on survival after the index hospital discharge. Univariate post-discharge survival was assessed using the log-rank test. Multivariate Cox proportional hazard analyses were performed for overall post-discharge survival and included each MCS category in addition to all candidate variables with *p*-values of $<$ 0.15 on univariate log-rank test screening. Separate multivariate Cox-proportional hazards analyses were then performed for each of the various MCS categories.

Our secondary objectives also included analyses to identify potential predictors of post-transplant mortality; separate multivariable regression analyses were performed to identify predictors of in-hospital and post-discharge mortality.

A formal statistical test of interaction was performed to assess for the interplay between pre-transplant dialysis status and MCS on post-transplant survival. To further analyze the effect of pre-transplant MCS and dialysis status on post-transplant mortality, we divided patients into following groups: Group 1, absence of MCS and dialysis (reference category); Group 2, presence of MCS, but absence of dialysis; Group 3, absence of MCS, but presence of dialysis; and Group 4, presence of MCS and dialysis. Kaplan-Meier survival estimates were graphically displayed.

We further assessed for effect of MCS on secondary non-survival outcomes of interest using separate univariate and multivariable logistic regression analyses. The interaction between pre-transplant MCS and dialysis status was formally tested for its effect on post-transplant dialysis status as well. Separate analysis was performed to assess effect of pre-transplant MCS and dialysis groups (as described earlier) on post-transplant dialysis status using multivariable logistic regression analyses. Multivariable analysis was pursued if the pre-specified *p*-value for a particular MCS category was $<$ 0.15; variables adjusted for in the multivariable models were also selected based on their pre-specified *p*-value of $<$ 0.15. To avoid losing patients with missing information on variables of interest, imputations were performed before any analyses using a regression switching (chained equations) approach with predictive mean matching.[8] Given the large sample size and small amount of missing data ($<$ 25%), we performed only 20