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Favorable Outcomes of LVAD as Bridge to Simultaneous Heart-Kidney Transplantation

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Abstract

Background

Chronic kidney disease (CKD) is an established risk factor for incident cardiovascular disease and progression of heart failure disease state, and is associated with decreased survival after left ventricular assist device (LVAD) therapy or heart transplantation (HT). Combined heart-kidney transplantation (HKT) compared with isolated HT recently has been shown to have survival advantage among patients whose estimated glomerular filtration rate is less than 37 ml/min/m2. Data on LVAD to HKT are limited.

Methods

At our center, a total of 803 patients have received HT, 594 patients LVAD therapy, and 23 patients HKT from single donors; of those 23, 15 were without the use of LVAD and 8 were after support with LVAD.

Results

Kaplan-Meier survival analysis found LVAD-supported patients with CKD stages 4 or 5 had statistically worse 24-month survival after HT as compared with those with CKD stage 1, 2, and 3 (58% versus 88%, p=0.01). Patients who received

combined HKT after LVAD had comparable 24-month survival with those who received HKT without LVAD (87% and 85%, p=NS); both groups had numerically better survival compared with those who had CKD (stage 4-5) with isolated HT (58%).

Conclusions

Patients supported with LVAD who demonstrate advanced CKD (stage 4-5) have worse 24-month post-HT survival compared with those with less advanced CKD (stage 1-3). Combined HKT after LVAD support is feasible and confers comparable 24-month survival compared with HKT without prior LVAD therapy. Our study supports combined HKT for select LVAD patients with advanced CKD (stage 4-5).

Keywords: Left ventricular assist device, heart transplant, chronic kidney disease

Introduction

Chronic kidney disease (CKD) as reflected by a lower estimated glomerular filtration rate (eGFR) is a strong and independent risk factor for both incident cardiovascular disease and subsequent cardiovascular morbidity and mortality.[1-3] Among heart failure patients, lower eGFR is associated with worsening functional capacity[4,5] and nearly double the risk of 12-month hospitalizations or death.[6,7] Accordingly, measures of renal function used to develop a variety of acute and chronic heart failure models confers a proportionally higher risk than many other common clinical variables.[8-10] Patients with heart failure who have deterioration of renal function exhibit impaired neurohormonal activation, abnormal central hemodynamics, and reduced cardiac perfusion to the kidneys, commonly described as cardiorenal syndrome (CRS).[11,12] The identification and, especially, the irreversibility of CRS can signify a clinical spiral characterized by worsening functional capacity, intolerance to conventional heart failure therapy, and increased heart failure-related death – a state, often termed advanced heart failure, in which heart replacement options (left ventricular assist device [LVAD] therapy or heart transplantation [HT]) are advocated.

LVAD therapy is an excellent treatment option for patients with advanced heart failure, providing substantive improvements in both quality and quantity of life.[13-17] Clinical trials and INTERMACs data have consistently demonstrated that a high proportion of patients receiving LVAD therapy have CKD.[18,19] Unfortunately, advanced CKD (stages 3-5) at the time of heart replacement option is a strong independent predictor of worse 12-month survival with either HT or LVAD.[20,21] Most recently, an analysis of the United Network of Organ Sharing (UNOS) database demonstrated a survival advantage to combined heart-kidney transplantation (HKT) for heart failure patients with advanced CKD (eGFR<37 ml/min).[22] However, limited data exist on the feasibility of LVAD therapy as a bridge to HKT.[23,24] We document safety and favorable outcomes on a small retrospective cohort of patients who underwent combined HKT after chronic LVAD therapy.

Methods

A total of 803 patients underwent HT from 1988-2013; among these, 15 received combined HKT. A total of 594 patients underwent LVAD therapy, with 256 patients having had an LVAD prior to HT, including 8 patients who received HKT (1991-2013). Each HKT was from a single donor with all procedures performed at Aurora St. Luke's Medical Center (Milwaukee, WI). This retrospective investigation was approved by the institutional review board prior to initiation and chart review. All 256 patients had complete clinical data and comprised the final cohort for analysis. The eGFR was estimated using Modification of Diet in Renal Disease (MDRD) formulas, and patients were grouped according to established CKD stages.

Statistics

Continuous variables are summarized as mean ± SD and categorical variables are presented as frequency and percentage, respectively. Differences in continuous and categorical variables were compared using Wilcoxon Rank-Sum tests and Pearson chi-square tests, respectively (Table 1). Comparison of survival post-transplant between the LVAD and no LVAD groups were performed using Kaplan-Meier curves and Log-Rank test (Figures 1 and 2).

Table 1. Baseline characteristics of patient population

	LVAD to HT (n=256)	CKD 1-3 (n=241)	CKD 4-5 (n=15)	p	LVAD to HKT (n=8)	HKT no LVAD (n=15)	p
Age	54±12	54±12	58±9	0.02	54±9.7	56±8.3	NS
BMI	28±6	28±6	30±7	NS	31±8	27±4.1	NS
Female	48 (19%)	42 (17%)	5 (33%)	0.02	1 (12%)	6 (40%)	0.03
AA race	55 (21%)	48 (20%)	7 (47%)	NS	3 (38%)	1 (7%)	NS
CAD	132 (52%)	125 (52%)	7 (47%)	0.06	4 (50%)	9 (60%)	NS
eGFR	66±27	69±24	21±11	<0.01	19±14	16±12	<0.01
Support, days	211±214	212±217	190±155	NS	166±100		NS

CKD, chronic kidney disease; LVAD, left ventricular assist device; HKT, heart-kidney transplant; BMI, body mass index; AA, African American; CAD, coronary artery disease; eGFR, estimated glomerular filtration rate.

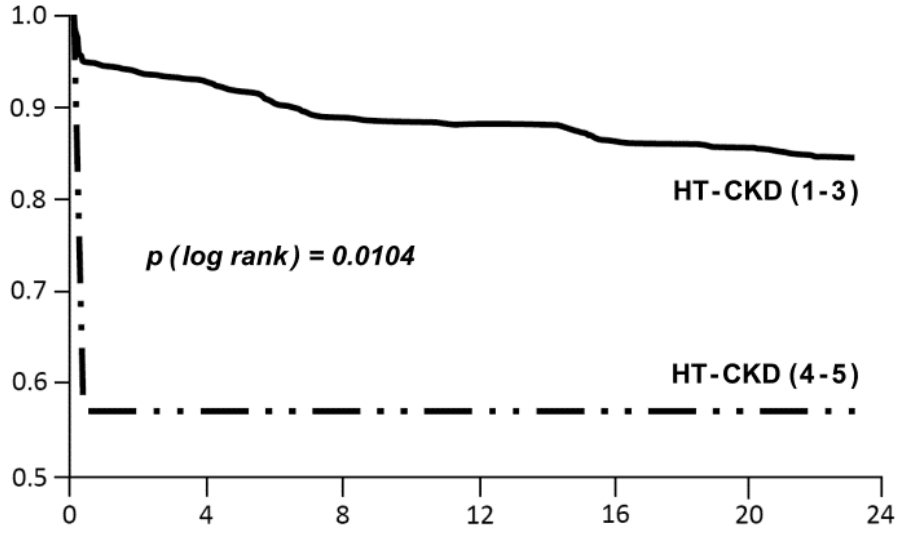

Figure 1. Two-year Kaplan-Meier curve showing survival among patients with chronic kidney disease (CKD) supported with a left ventricular assist device (LVAD) (1-3) compared with patients with CKD and no LVAD (4-5). HT, heart transplantation.

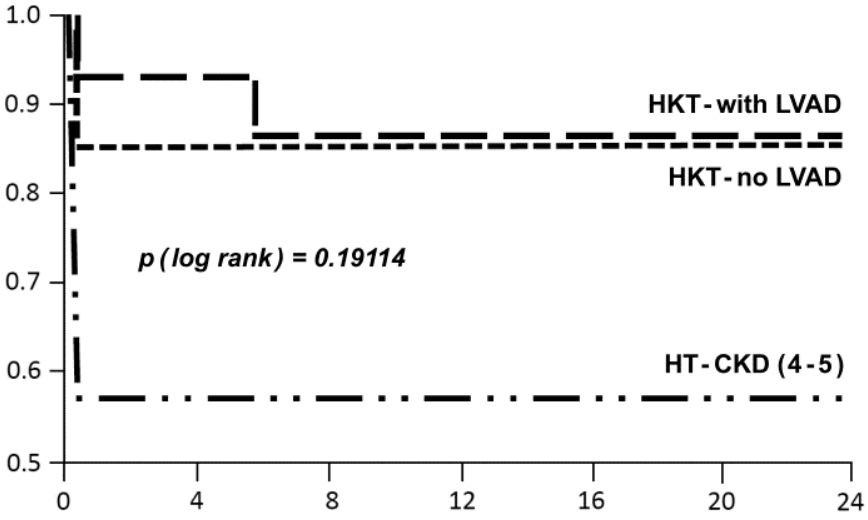

Figure 2. Two-year Kaplan-Meier curve showing survival among patients with combined heart-kidney transplantation (HKT) with and without left ventricular assist device therapy (LVAD) compared with patients with chronic kidney disease (CKD) who undergo heart transplantation (HT) alone (4-5).

Results

Table 1 describes the total cohort of 256 patients; most were young (mean age 54±12) men (n=208, 81%) with coronary artery disease (n=132, 52%), and the majority (94%) had mild CKD (stage 1-3) at the time of HT, with a mean group eGFR of 69±24 ml/min. A total of 15 patients had severe CKD (stage 4-5) at the time of HT, with a mean group eGFR of 21±11; these patients were older (mean age 58±9) and more often female (n=5, 33%). Comparatively, patients receiving LVAD to HKT (n=8) vs HKT without LVAD (n=15) were less often female (12% vs 40%, p=0.03) and had slightly higher eGFR (19±14 vs 16±12).

Kaplan-Meier survival analysis (Figure 1) found LVAD-supported patients with CKD stage 4 or 5 had statistically worse 24-month survival after HT compared with those with CKD stage 1, 2, or 3 (58% vs 88%, p=0.01). Patients who received combined HKT after LVAD had comparable 24-month survival with those that received HKT without LVAD (87% and 85%, p=NS); both groups had numerically better survival compared with those who had CKD (stages 4 or 5) with isolated HT (58%).

Discussion

Higher CKD stage, characterized by lower eGFR, is an established risk factor for incident cardiovascular disease and progression of heart failure disease state, and impairs survival after advanced heart failure therapies (LVAD or HT).[1,4,20,21] Select studies have demonstrated survival advantages to combined HKT for heart failure patients with advanced CKD.[22,25] Our data demonstrate two important observations. First, it confirms that patients with advanced CKD (stage 4 and 5) confer a mortality benefit from combined HKT. Second, patients supported with LVAD therapy who have advanced CKD (stages 4 or 5) who receive combined HKT have a 2-year survival rate comparable to those who do not have advanced CKD who receive isolated HT and patients who receive HKT without prior LVAD therapy, and numerically higher survival than those patients with advanced CKD who receive HT alone.

UNOS data reported that between 2008 and 2013, the era encompassing continuous-flow LVAD therapy and the present research, a total of 370 patients received HKT, among whom 57 (15.4%) patients where supported with LVAD therapy; our program has performed combined HKT on 23 patients, among whom 8 (34.8%) were supported with LVAD prior to HKT. Only one prior investigation has evaluated the feasibility and clinical outcomes of patients supported with LVAD therapy who received HKT.[23] Our cohort is larger, extends follow-up beyond 6 months and demonstrates comparable survival outcomes to a contemporary cohort of patients who underwent either HKT without LVAD therapy or HT with advanced CKD. The retrospective and single-center nature of this investigation is associated with selection bias. However, patients who received HKT irrespective of LVAD therapy in our program were similar with the exception of female gender; which was more common among those not receiving LVAD therapy, likely reflecting the known bias associated with LVAD treatment and body size.

Conclusions

Patients supported with LVAD therapy who demonstrate advanced CKD (stages 4-5) have worse 24-month post-HT survival compared with those with less-advanced CKD (stages 1-3). Combined HKT after LVAD support is feasible and confers comparable 24-month survival compared with HKT without prior LVAD therapy. Our study supports combined HKT for select LVAD patients with advanced CKD (stages 4-5).

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