Journal of Cardiac Failure Vol. 28 No. 11 2022

Outcomes in Patients With Chronic Kidney Disease and End-stage Renal Disease and Durable Left Ventricular Assist Device: Insights From the United States Renal Data System Database

TARUN DALIA, MD,[1,#] WAN-CHI CHAN, MD, MPH,[1,#] ANDREW J. SAUER, MD,[1] SAGAR RANKA, MD,[1] AMANDEEP GOYAL, MD,[1] IOANNIS MASTORIS, MD,[1] SUVEENKRISHNA POTHURU, MD,[3] TRAVIS ABICHT, MD,[2] MATTHEW DANTER, MD,[2] ANDRIJA VIDIC, DO,[1] KAMAL GUPTA, MD,[1] RYAN J. TEDFORD, MD,[4] JENNIFER COWGER, MD, MS,[6] JAMES C. FANG, MD,[5] AND ZUBAIR SHAH, MD[1]

Kansas City, and Manhattan, Kansas; Charleston, South Carolina; Salt Lake City, Utah; and Detroit, Michigan

ABSTRACT

Background: There is paucity of data regarding durable left ventricular assist device (LVAD) outcomes in patients with chronic kidney disease (CKD) stages 3−5 and CKD stage 5 on dialysis (end-stage renal disease [ESRD]).

Methods and Results: We conducted a retrospective study of Medicare beneficiaries with ESRD and a 5% sample of patients with CKD with an LVAD (2006−2018) to determine 1-year outcomes using the United States Renal Data System database. The LVAD implantation, comorbidities, and outcomes were identified using appropriate *International Classification of Diseases,* 9th and 10th edition codes. We identified 496 patients with CKD and 95 patients with ESRD who underwent LVAD implantation. The patients with ESRD were younger (59 years vs 66 years; $P < .001$), had more Blacks (40% vs 24.6%, $P = .009$), compared with the CKD group. The 1-year mortality (49.5% vs 30.9%, $P < .001$) and index mortality (27.4% vs 16.7%, $P = .014$) rates were higher for patients with ESRD. A subgroup analysis showed significantly higher mortality in ESRD vs CKD 3 (49.5% vs 30.2%, adjusted $P = .009$), but no significant difference in mortality between stage 3 vs 4/5 (30.2% vs 30.8%, adjusted $P = .941$). There was no significant difference in secondary outcomes (bleeding, stroke, and sepsis/infection) during follow-up between the 2 groups.

Conclusions: Patients with ESRD undergoing LVAD implantation had significantly higher index and 1-year mortality rates compared with patients with CKD. (*J Cardiac Fail 2022;28:1604−1614*)

Key Words: Left ventricular assist device (LVAD), chronic kidney disease (CKD), end-stage renal/kidney disease (ESRD), dialysis, mortality.

In patients with advanced heart failure, studies have shown improved survival and quality of life in the patients who undergo left ventricular assist device (LVAD) implantation when compared with conventional medical therapy alone.[1−3] There are few data and societal guidelines regarding LVAD

From the [1]Department of Cardiovascular Medicine, University of Kansas Medical Center, Kansas City, Kansas; [2]Department of Cardiothoracic Surgery, University of Kansas Medical Center, Kansas City, Kansas; [3]Department of Internal Medicine, Ascension Via Christi Hospital, Manhattan, Kansas; [4]Division of Cardiology, Department of Medicine, Medical University of South Carolina, Charleston, South Carolina; [5]Division of Cardiovascular Medicine, University of Utah, Salt Lake City, Utah and [6]Department of Cardiovascular Medicine, Henry Ford Hospitals, Detroit, Michigan.

Manuscript received December 12, 2021; revised manuscript received March 23, 2022; revised manuscript accepted March 26, 2022.

Reprint requests: Zubair Shah, MD, Assistant Professor, Department of Advance Heart Failure and Transplant, Medical Director of Mechanical Circulatory Support Devices, Department of Cardiovascular Medicine, The University of Kansas Medical Center. Phone: 913 588 3827. E-mail: zshah2@kumc.edu

[#]Dr Dalia and Dr Chan contributed equally to this article.

1071-9164/$ - see front matter

https://doi.org/10.1016/j.cardfail.2022.03.355

use in patients with advanced CKD and end-stage renal disease (ESRD). As such, the decision regarding durable LVAD implantation in these patients varies by program.[4] Retrospective and observational studies have shown that patients with preexisting CKD and ESRD who underwent temporary and durable LVAD implantation, have worse outcomes when compared with normal kidney function.[5–7] There had been significant improvement in LVAD technology over the years, with the vast majority of contemporary LVAD implants involving continuous centrifugal flow (including magnetically levitating) impellers.[8] Consequently, patient outcomes involving these more contemporary LVAD devices have improved compared with earlier LVAD devices involving predominately pulsatile or axial flow.[9] To address these knowledge gaps, we conducted this study to determine outcomes in patients with advanced CKD and patients with ESRD who underwent durable LVAD implantation using the national United States Renal Data System (USRDS) database. Our main objectives were to determine the (1) baseline characteristics of patients with preexisting CKD and ESRD who underwent LVAD implantation and the (2) relative outcomes including mortality in CKD and patients with ESRD during index LVAD implant admission and at the 1-year follow-up.

Methods

Data Source

The study cohort was derived from USRDS analytical files from 2006 to 2018, which was the most recent data available at time of inception of this study. December 31, 2017, was used as last date of LVAD implant to include 1 year of follow-up. The USRDS collects, analyzes, and distributes information about CKD and ESRD in United States in collaboration with the Centers for Medicare and Medicaid Services (CMS).[10] The USRDS is funded directly by the National Institute of Diabetes and Digestive and Kidney Disease. This study was reviewed and approved by institutional review board of University of Kansas Medical Center and the National Institute of Diabetes and Digestive and Kidney Disease. The interpretation and reporting of this data in no way should be seen as an official policy or interpretation of the US government.

Study Population

For the ESRD Group

ESRD in the USRDS database is defined as chronic renal failure requiring renal replacement treatment—dialysis or transplantation—to sustain life. Nephrologists complete a medical evidence form for all patients with ESRD and certify the disease, after which the patients are included in the CMS ESRD database.

Our study only included those Medicare beneficiaries with ESRD who were dialysis dependent, 18 years or older, and underwent durable LVAD implantation between 2006 and 2017. We excluded patients who underwent kidney transplant before LVAD implantation. The *International Classification of Diseases*, Ninth (ICD-9) and Tenth (ICD-10) editions procedure codes 37.66 and 02HA0QZ were used to identify LVAD patients. This yielded an initial sample of 321 patients. Patients who are living outside the United States and do not have continuous Medicare AB coverage during 1 year of follow-up ($n = 164$), who received LVAD before the onset of ESRD ($n = 27$), who underwent kidney transplantation, before or during LVAD implantation ($n = 20$), and those who were not on continued dialysis (continued dialysis means that they were on dialysis for at least 60 days before LVAD implantation, $n = 15$) were excluded. This process yielded a final sample size of 95 patients with ESRD who were dependent on hemodialysis for 60 days or more before admission (Fig. 1A).

For the CKD Group

To incorporate patients with CKD in this analysis, data from the CMS Medicare 5% sample linked to the USRDS registry were used. The CMS uses 1 inpatient claim or 2 outpatient claims with a specified diagnosis code to determine the presence of CKD in the USRDS database. If the patient has more than 1 claim with stage codes, the stage on the last claim was used. If the last claim has more than 1 stage, the highest stage was used.

We included patients with CKD who underwent durable LVAD implantation from 2006 to 2017. This criterion yielded an initial sample size of 605 patients. Patients who are living outside the United States, did not have continuous Medicare AB coverage during 1 year of follow-up, and who has already developed ESRD before LVAD implantation ($n = 109$) were excluded. This process yielded final sample size of 496 patients (Fig. 1B). The baseline CKD staging information was collected from the index hospitalization. The baseline CKD staging data was available for 193 patients (39%); of these patients, 91% had advanced CKD (stage 3 or higher).

Baseline Characteristics and Comorbidities

The demographics included were age, gender, and self-reported race (White, Black, Asian, or others). The comorbidities included were nonischemic cardiomyopathy, hypertension, diabetes mellitus, atherosclerotic heart disease, peripheral vascular disease, stroke or transient ischemic attack,

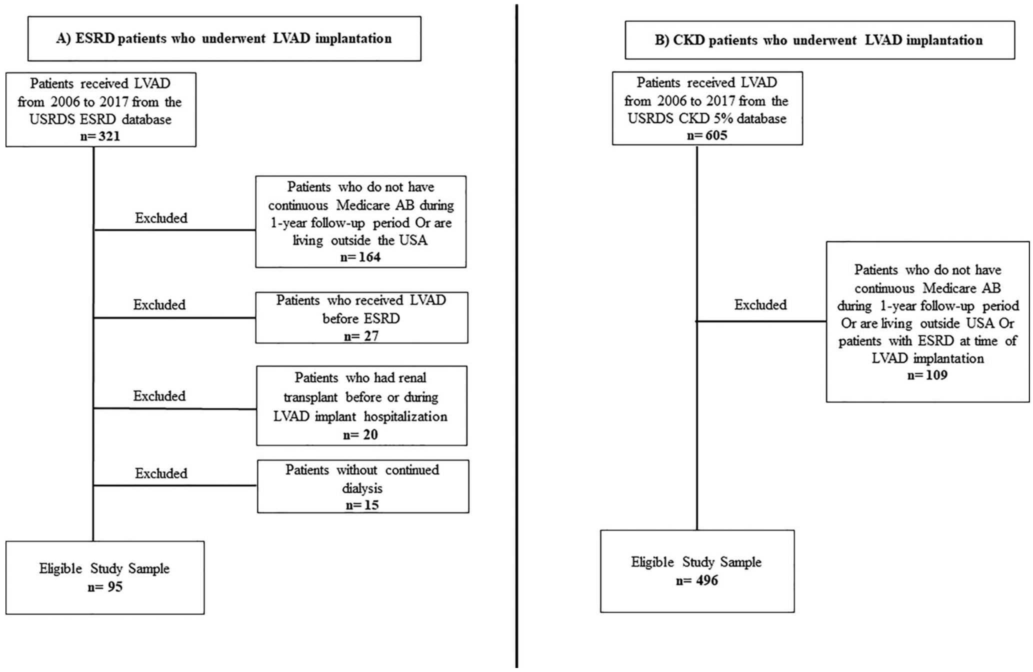

Fig. 1. Study population. (**A**) Patients with end-stage renal disease (ESRD) who underwent left ventricular assist device (LVAD) implantation. (**B**) Patients with chronic kidney disease (CKD) who underwent LVAD implantation between 2006 and 2017.

and atrial fibrillation. CMS Form 2728 and ICD-9-CM and ICD-10-CM codes that were used to determine these comorbidities are provided in the Supplementary file (Supplementary Table 1). The information regarding concomitant valvular surgeries during LVAD implantation, length of stay, primary cause of renal failure, dialysis type, and time on hemodialysis before implant was also reported.

Follow-up and Outcomes

The patients were followed for 1 year after LVAD implantation. The primary outcome was all-cause mortality during 1 year of follow-up and during the index admission. The 1-year follow-up for the primary outcome was started from the admission date of index hospitalization. We also performed a subanalysis to investigate all-cause mortality during follow-up period after hospital discharge, excluding patients who underwent orthotopic heart transplantation (OHT). As an exploratory analysis, we investigated the 1-year rate mortality in OHT patients and also evaluated those 20 patients who underwent renal transplantation before LVAD implantation to determine how many of them underwent a subsequent OHT during the follow-up. We also performed a subanalysis to investigate index mortality outcomes in LVAD patients who underwent concomitant valve surgeries.

Other secondary outcomes included were significant bleeding (bleeding requiring admission owing to gastrointestinal bleeding, choroidal hemorrhage, orbit hemorrhage, vitreous hemorrhage, hemorrhage in the optic sheath, hemarthrosis, hemoperitoneum, and hemorrhage owing to prosthetic device), pump thrombosis, hemorrhagic and ischemic stroke, sepsis, and infection of the LVAD within the 1-year follow-up. The 1-year follow-up in secondary outcomes was started from discharge date of index hospitalization. The ICD-9-CM and ICD-10-CM used to define these outcome variables are provided in Supplementary file (Supplementary Table 1). The subgroup analysis of patients with available CKD staging ($n = 193$ patients) was done to determine impact of CKD staging on the primary outcome.

Statistical Analysis

Baseline characteristics and outcomes were compared between patients with CKD and patients with ESRD. Continuous variables were expressed as median with interquartile range (IQR) values and compared using the 2-samples t test or Wilcoxon rank-sum test. Categoric variables were expressed as count with percent of total population and compared using Pearson's χ^2 test. The incidence of death was represented with cumulative incidence function (CIF) curves, treating heart transplantation as a competing outcome. Gray's test was used to compare the incidence of death between ESRD with LVAD and CKD with LVAD, and also compared the incidence of death between LVAD patients in CKD 3, CKD 4/5, and ESRD. We used the Cox proportional hazards model to calculate hazard ratios for mortality comparing patients with CKD stage 4/5 and ESRD vs those with CKD 3. The model included adjustment for age, race, nonischemic cardiomyopathy, hypertension, diabetes mellitus, atherosclerotic heart disease, peripheral vascular disease, and years of LVAD implantation. Pearson's χ^2 test was used to compare the secondary outcomes. We further adjusted for multiple comparisons with the false discovery rate. We used the Cochran−Armitage trend test in these 2 groups to determine trend of change in LVAD implantation over the years. We further conducted a Spearman correlation to see if these 2 groups share the same trend or not. All *P* values were 2 sided, and a *P* value of less than .05 was considered significant. Statistical analysis was conducted using SAS 9.4 software (SAS Institute Inc, Cary, NC).

Results

Baseline Characteristics

Between 2006 and 2017, 95 Medicare beneficiaries with ESRD and 496 beneficiaries with CKD in the Medicare 5% sample underwent a durable LVAD implantation. The details of baseline characteristics including comorbidities are shown in Table 1. The patients with ESRD were almost 7 years younger (59 years vs 66 years, $P \leq .0001$) compared with the CKD group. African American patients were more common in the ESRD group (40.0% vs 24.6%, $P \leq .01$). The ESRD group had more patients with hypertension (90.5% vs 38.3%, $P \leq .0001$), peripheral vascular disease (13.7% vs 7.3%, $P = .04$), atherosclerotic heart disease (62.1% vs 50.6%, $P = .04$), and diabetes mellitus (48.4% vs 20.2%, $P \leq .001$). There were more patients with nonischemic cardiomyopathy in the CKD group (50.0% vs 32.6%, $P \leq .002$). The most common valve repair or replacement was the aortic valve in patients with ESRD (13.7%) and in patients with CKD (9.1%). In the ESRD group, more patients underwent any surgical valve repair or replacement (28.4% vs 14.3%, $P \leq .001$) when compared with the CKD group during the index LVAD admission. In the ESRD group, the major form of maintenance dialysis was hemodialysis (84.2%); very few patients were on peritoneal dialysis. The median time on hemodialysis for our patients was 3.3 years (IQR 0.8−6.0 years). Hence, the majority of patients in our study were on long standing hemodialysis before LVAD implantation. The percentage of LVAD implanted in CKD group over the course of study years were: 74 (14.9%) in 2006−2009, 187 (37.7%) in 2010−2013, and 235 (47.4%) in 2014−2017 ($P = .06$). Whereas in the ESRD group, LVADs implanted over course of study years were 23 (24%) in 2006−2009, 36 (37.9%) in 2010−2013, and 36 (37.9%) in 2014−2017 ($P = .06$). There was no significant change in the trend of LVAD implantation in patients with ESRD (11.3 per 1,000,000 patients in 2006 and 13.5 per 1,000,000 patients in 2017, $P_{trend} = .910$). LVAD implantation in patients with CKD increased from 90.3 per 1,000,000 patients to 236 per 1,000,000 patients from 2006 to 2017 ($P_{trend} < .001$). Spearman correlation showed that there is a mild positive correlation between ESRD and CKD, with a Spearman correlation coefficient of 0.523 ($P = .081$) (Supplementary Fig. 1),

Outcomes

Outcome During the Index LVAD Admission

During the index admission for LVAD implantation, 26 patients (27.4%) died in the ESRD group and 83 patients (16.7%) died in the CKD group (Table 2). Of 496 total patients with CKD, 33 required kidney replacement therapy (KRT) during the index admission (any KRT type like continuous renal replacement therapy, continuous venovenous hemofiltration, continuous venovenous hemodialysis, continuous venovenous hemodiafiltration, and intermittent hemodialysis were included). Of those 33 patients with CKD who required KRT during index admission, 21 (63.6%) died. Of the 463 patients with CKD who did not require KRT during the index admission, only 62 (13.4%) died. The mortality rate was significantly higher in patients with CKD who require KRT (63.6% vs 13.4%, $P < .001$) when compared with patients who did not required KRT.

We further analyzed those LVAD patients who underwent concomitant surgical valve repair or replacement during the LVAD index admission. The patients with ESRD who underwent any concomitant surgical valve (aortic, mitral, or tricuspid) repair or replacement had a higher index mortality rate (44.4% vs 20.6%, $P = .02$) compared with those who did not undergo valve surgery (details in Supplementary Table 2). Similarly, in the CKD group, those patients who underwent any concomitant valve repair or replacement during the index LVAD admission had a higher mortality (33.8% vs 13.9%, $P \leq .0001$) as compared with those who did not (details in Supplementary Table 3).

Primary Outcome

The 1-year all-cause mortality was higher among patients with ESRD who underwent LVAD implantation when compared with patients with CKD (49.5% vs 30.9%, $P \leq .001$) (Table 2). Because 12.6% of patients in the ESRD group and 9.9% of patients in the CKD group underwent heart transplantation during follow-up (details in secondary outcomes elsewhere in this article), we treated heart

Table 1. Baseline Characteristics of Patients With an LVAD with CKD and ESRD, 2006–2018

Baseline Characteristics	Median (IQR)/No. (%) ESRD ($n = 95$)	Median (IQR)/No. (%) CKD ($n = 496$)	*P* value
Age	58.9 (49.5–65.0)	66.0 (56.0–71.0)	<.0001
Gender			.39
Male	72 (75.8)	395 (79.6)	
Female	23 (24.2)	101 (20.4)	
Race			.01
White	54 (56.8)	339 (68.4)	
Black	38 (40.0)	122 (24.6)	
Asian	<11*	<11*	
Other	<11*	25 (5.04)	
Comorbidities			
Nonischemic cardiomyopathy	31 (32.6)	248 (50.0)	.002
Hypertension	86 (90.5)	190 (38.3)	<.0001
Diabetes mellitus	46 (48.4)	100 (20.2)	<.0001
Atrial fibrillation	22 (23.2)	148 (29.8)	.19
Atherosclerotic heart disease	59 (62.1)	251 (50.6)	.04
Peripheral vascular disease	13 (13.7)	36 (7.3)	.04
Stroke/TIA	<11	24 (4.8)	.15
Concomitant valvular procedures			
Aortic valve replacement/repair	13 (13.7)	45 (9.1)	.17
Mitral valve replacement/repair	11 (11.6)	12 (2.4)	<.0001
Tricuspid valve replacement/repair	11 (11.6)	21 (4.2)	.004
Any one of the valve procedures	27 (28.4)	71 (14.3)	<.001
Length of stay			
Overall group	25.5 (15.0–42.0)	30.0 (21.0–43.0)	.03
Subgroup: patients who survived at index hospitalization	30.0 (19.9–51.0)	30.0 (22.0–42.0)	.99
Primary cause of renal failure			
Diabetes	39 (41.1)		
Hypertension	25 (26.3)		
Glomerulonephritis	11 (11.6)		
Dialysis type			
Hemodialysis	80 (84.2)		
CAPD	<11*		
CCPD	<11*		
Hemodialysis duration (years)	3.3 (0.8–6.0)		
Dates of LVAD Implantation			.06
2006–2009	23 (24.2)	74 (14.9)	
2010–2013	36 (37.9)	187 (37.7)	
2014–2017	36 (37.9)	235 (47.4)	

CAPD, continuous ambulatory peritoneal dialysis; CCPD, continuous cyclic peritoneal dialysis; CKD, chronic kidney disease, ESRD, end-stage renal disease; IQR, interquartile range; LVAD, left ventricular assist device; TIA, transient ischemic attack.
*Absolute value cannot be reported if n is <11 as per United States Renal Data System reporting policy.

Table 2. Primary Outcome (All-cause Mortality) Among Patients with CKD and ESRD Who Underwent LVAD Implantation, 2006–2018

Outcomes	No. (%) ESRD ($n = 95$)	No. (%) CKD ($n = 496$)	*P* Value
1-Year all-cause mortality	47 (49.5)	153 (30.9)	.0004
Mortality during index LVAD implantation admission	26 (27.4)	83 (16.7)	.0144
	ESRD ($n = 57$) *	CKD ($n = 364$)*	
Mortality during follow-up period*	21 (36.8)	64 (17.6)	.0008
Days from discharge to death among patients who died (days); median, (Q1, Q3)*	48 (21, 98)	149.5 (71.5, 235.5)	.0015

All-cause mortality segregated according to study years

Years	ESRD		CKD		*P* Value
	No. of LVAD	Mortality; *n* (%)	No. of LVAD	Mortality; *n* (%)	
2006–2009	23	15 (65.2)	74	36 (48.7)	.1646
2010–2013	36	16 (44.4)	187	55 (29.4)	.0762
2014–2017	36	16 (44.4)	235	62 (26.4)	.0258

*Including patients who survived the index admission and excluding those who received heart transplant during 1 year of follow-up. Abbreviations as in Table 1.

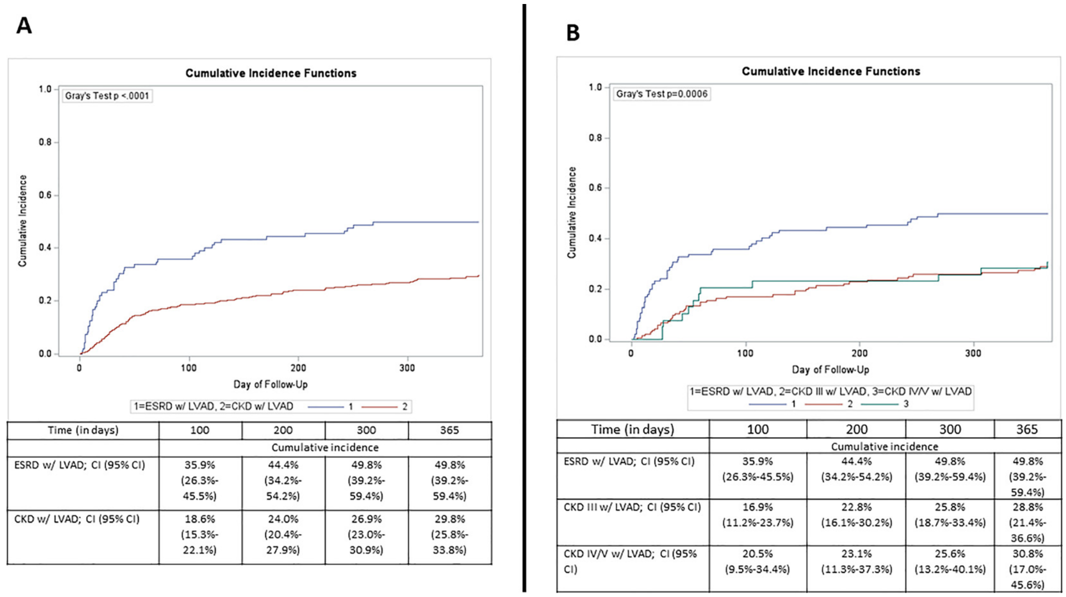

Fig. 2. (**A**) Incidence of death compared between patients with with end-stage renal disease (ESRD) with a left ventricular assist device (LVAD) and patients with chronic kidney disease (CKD) with an LVAD, as estimated using cumulative incidence functions. (**B**) Incidence of death compared between patients with ESRD with an LVAD, patients with CKD stage III with an LVAD, and patients with CKD stage IV/V with an LVAD, as estimated using cumulative incidence functions. CI, confidence interval.

transplantation as a competing outcome and presented the incidence of death with CIF curves (Fig. 2). Fig. 2A shows a higher incidence of mortality in patients with ESRD with LVAD at 1-year follow-up. The complement of the Kaplan–Meier survival estimate is provided in Supplementary Fig. 2A. Over the 12 years of follow-up, we found higher mortality among ESRD group compared with CKD group using CIF curve (showing the incidence of death for 2006–2018) (Supplementary Fig. 3A). After excluding patients who died during the index hospitalization and those who underwent OHT, the overall 1-year mortality among patients with ESRD and patients with CKD was 36.8% and 17.6%, respectively ($P \leq .001$). The median time to mortality in those LVAD patients who survived index admission and excluding those who underwent OHT was 48 days (IQR 21–98 days) in patients with ESRD and 149.5 days (IQR 71.5–235.5 days) in patients with CKD, during the 1-year follow-up. On comparing the patients with CKD who received KRT and survived the index hospitalization (12 patients) to those who did not require KRT and survived the index hospitalization (401 patients), no significant difference in 1-year mortality was noted between the 2 groups (25% vs 16.7%, $P = .45$). When segregated according to study years, the mortality in patients with ESRD was significantly higher than patients with CKD even with the newer generation LVAD pumps (Table 2). After using a multivariable Cox proportional hazard model, ESRD (HR 1.86, 1.12–3.06, $P = .016$) was an independent predictor of mortality (Fig. 3).

When stratified by CKD stage, there was no significant difference in mortality between CKD stages 3 vs 4/5 (30.2% vs 30.8%, adjusted $P = .941$) and patients with ESRD compared with CKD stage 4/5 (49.5% vs 30.8%, adjusted $P = .071$). There was significantly higher mortality in patients with ESRD compared with CKD stage 3 (49.5% vs 30.2%, adjusted $P = .009$) (Table 3). The CIF curve showing the incidence of death and treating heart transplantation as a competing outcome comparing ESRD to CKD III to CKD IV/V LVAD recipients is shown in Fig. 2B. The complement of the Kaplan–Meier survival estimate is provided in Supplementary Fig 2B. The incidence of death using CIF curves for 2006–2018 (12-year outcome) comparing ESRD to CKD III to CKD IV/V group is shown in Supplementary Fig. 3B.

Table 3. All-Cause 1-year Mortality Stratified According to CKD Staging, 2006–2018

Baseline CKD staging	People in subgroup,* *n* (%)	Mortality, *n* (%)
CKD stage 3[†]	136 (70.5)	41(30.2)
CKD stage 4/5[‡]	39 (20.2)	12 (30.8)
ESRD[§]	95 (100)	47 (49.5)

Abbreviation as in Table 1.
*There were 193 patients with CKD who have the baseline CKD staging data.
[†]The 1-year mortality in CKD stage 3 vs stage 4/5 was 30.2% vs 30.8%; adjusted $P = .941$.
[‡]One year mortality in CKD stage 4/5 vs ESRD was 30.8% vs 49.5%; adjusted $P = .071$.
[§]One year mortality in CKD stage 3 vs ESRD was 30.2% vs 49.5%; adjusted $P = .009$.

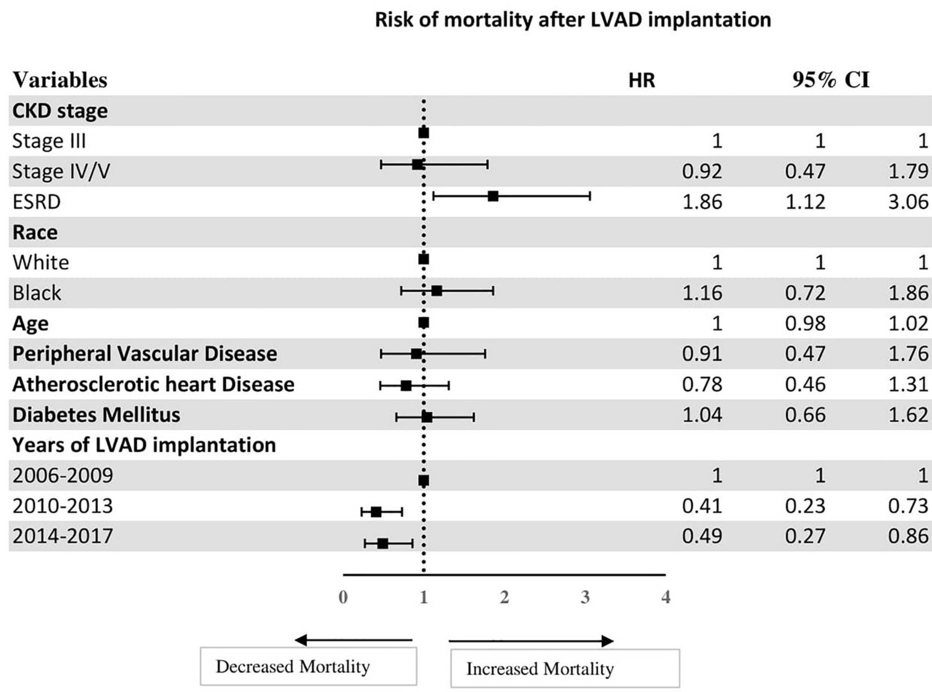

Fig. 3. Forest plot of multivariable Cox proportional hazard model.* *The model included adjustment for age, race, nonischemic cardiomyopathy, hypertension, diabetes mellitus, atherosclerotic heart disease, peripheral vascular disease, and years of left ventricular assist device (LVAD) implantation. CI, confidence interval; CKD, chronic kidney disease.

Secondary Outcomes

In the ESRD group, 12 (12.6%) and 49 (9.9%) patients in the CKD group underwent OHT within 1 year of LVAD implantation (Table 4). In the ESRD group, all the patients who underwent OHT survived for 1 year after transplantation. For patients who underwent OHT in the CKD group, fewer than 11 patients (14.3%) died during follow-up (per USRDS agreement for release of information, we were unable to report absolute values) (Supplementary Table 4). We also investigated the 20 patients with ESRD who underwent renal transplantation before or during their LVAD implant admission (they were excluded from the primary and secondary analyses because our focus in this study was patients with ESRD on HD) and found that 25% of these 20 patients underwent OHT within 1 year (Supplementary Table 5).

There was no significant difference in secondary LVAD outcomes, including significant bleeding (20.0% vs 16.1%, $P = .355$), ischemic stroke (9.5% vs 9.3%, $P = .951$), hemorrhagic stroke (3.2% vs 3.4%, $P = .894$) pump thrombosis (4.2% vs 6.7%, $P = .368$), and sepsis/infection (25.3% vs 18.8%, $P = .144$) between the ESRD group and the CKD group during 1 year of follow-up (Table 4).

Table 4. Secondary Outcomes in Patients With CKD and ESRD Who Underwent LVAD Implantation, 2006–2018

Outcomes	No. of events, *n* (%) ESRD (*n* = 95)	No. of events, *n* (%) CKD (*n* = 496)	*P* Value
Heart transplant	12 (12.6)	49 (9.9)	.4192
Secondary outcomes	No. of events ESRD (*n* = 95)	No. of events CKD (*n* = 496)	*P* Value
Significant bleeding	19 (20.0)	80 (16.1)	.3547
Pump thrombosis	<11	33 (6.7)	.3679
Ischemic stroke	<11	46 (9.3)	.9511
Hemorrhagic stroke	<11	17 (3.4)	.8941
Sepsis/ infection	24 (25.3)	93 (18.8)	.1444

Abbreviations as in Table 1.
Absolute value for $n < 11$ cannot be reported owing to United States Renal Data System agreement of release of information.

Discussion

There are several noteworthy findings in this nationwide study of Medicare beneficiaries with CKD and ESRD. First, there was high 1-year mortality among patient with CKD and patients with ESRD who underwent LVAD implantation. Second, patients with ESRD who underwent LVAD implantation had a significantly higher index and 1-year mortality rates when compared with patients with CKD. Third, the mortality among patients with CKD who required KRT during the index LVAD admission was higher compared with patients with CKD who did not. Fourth, the CKD and patients with ESRD who underwent concomitant surgical valve replacement or repair during index LVAD admission had a higher index mortality. Fifth, after using a multivariable Cox proportional model, ESRD was an independent predictor of mortality.

The Interagency Registry for Mechanically Assisted Circulatory Support (INTERMACS) is a national database of FDA-approved mechanical circulatory support (MCS) devices. Their eighth annual report, which included patients from June 2006 to December 2016 and had predominant continuous flow axial devices, showed am overall mortality of approximately 20% at 1 year.[11] It also showed that abnormal kidney function, especially preimplant dialysis, is a significant risk factor for mortality (hazard ratio 3.29). In our study, which only had patients with CKD and patients with ESRD, the 1-year all-cause mortality was higher (49.5% in the ESRD group and 30.9% in the CKD group) compared with overall all-cause 1-year mortality in the eighth annual INTERMACS report. In general, it is known that worsening kidney function (CKD and ESRD on maintenance dialysis) is associated with higher mortality as compared with patients with normal kidney function.[12] Hence, the 1 possible explanation for the higher mortality in our study can be underlying CKD and ESRD status of patients at time of LVAD implantation.

A prior study from the USRDS database included LVAD patients from 2003 to 2013 with a median follow-up of 762 days showed higher mortality in the ESRD group (81.2%) compared with patients without ESRD (36.4%).[7] Unlike our study, this study included both temporary MCS devices (ICD-9-CM 37.62 and 37.65) and durable LVAD. The temporary MCS devices are mostly used in dire circumstances like cardiogenic shock and refractory arrhythmias.[13] This factor may explain higher index mortality noted in their study (51.6%) compared with our study (27.4%) in ESRD group. Another study from the USRDS database including patients with ESRD from 2006 to 2014 who underwent LVAD implantation showed a 1-year mortality rate of 61.5%.[14] In this study, outcomes were not compared with patients with CKD or patients without ESRD. We only included patients with a durable LVAD, and our study includes most patients with newer generation centrifugal LVADs. Our study updates prior reports and confirms similar higher 1-year mortality among patients with ESRD who underwent LVAD implantation. Our study also shows that, in recent years (2014–2017), the mortality rate in patients with CKD has decreased as compared with prior years; this finding is most likely due to better patient selection, improvements in surgical techniques, and better perioperative management.

The mechanisms behind kidney dysfunction and worse outcomes in LVAD patients is poorly understood. In patients with kidney dysfunction there is decreased clearance of urea, uremic toxins, proteins like fibroblast growth factor 23 and Klotho, which all had been associated with increased cardiovascular events and mortality.[15–18] Studies have shown kidney dysfunction before LVAD implantation can lead to increased incidence of early right ventricular failure and increased heart failure hospitalizations.[19] Several studies have identified postimplantation right ventricular failure as a risk factor for worse outcomes in LVAD patients.[20,21] Ventricular–arterial coupling is assessed as the ratio between arterial elastance (E(a)) and end-systolic ventricular elastance (E(es)).[22] Ventricular–vascular coupling can be altered in patients with ESRD and is associated with increased mortality.[23,24] ESRD carries a high risk of death compared with CKD.[25] The reasons discussed elsewhere in this article may explain the worse outcomes noted in LVAD recipients in the ESRD population compared with the CKD population.

We found a high mortality during the index LVAD admission in patients with CKD (17%) and patients with ESRD on maintenance dialysis (27%). On further subanalysis, we found that patients with CKD who required KRT during index admission had a higher mortality rate compared with patients with CKD who did not (63.6% vs 13.4%, $P < .001$). We also found ESRD (on maintenance dialysis) status was an independent predictor of mortality in patients undergoing LVAD implantation. In prior studies not including LVAD patients, it is well-known in the nephrology literature that mortality among dialysis patients is higher than patients with CKD.[26,27] Our study also suggests that LVAD patients who require dialysis have a higher mortality compared with patients with CKD with LVAD. We found those LVAD patients (in both CKD and ESRD) who undergo concomitant valve surgeries have higher index mortality. Few prior studies had also shown a higher in-hospital mortality in LVAD patients who undergo concomitant valve surgeries, irrespective of their renal function.[28]

There were no major differences in adverse events (bleeding, infection, and stroke) between the 2 groups during the 1-year follow-up, suggesting that ESRD remains a major contributor to mortality, independent of LVAD complications. Infection and bleeding were the most common adverse effects. The INTERMACS registry also showed that after bleeding, infection is the most common adverse in first 3 months and then most common adverse event thereafter.[11]

Per the scientific statement for MCS devices in 2017, durable MCS should be avoided in patients with irreversible kidney damage.[29] Each program has their own approach in selecting patients with underlying kidney disease for LVAD implantation. Based on our findings, we would like to stress the importance of the careful selection of patients with advanced CKD and patients with ESRD for LVAD consideration. The Heart Failure Society of America Guidelines committee for stage D heart failure patients recommends incorporating a palliative team care approach for patients considered for MCS.[30] We also echo the incorporation of a palliative team care and integrated team discussion before implantation of an LVAD in this unique cohort. Our study results will not only aid physicians in decision-making regarding the use of LVAD therapies in the CKD and ESRD groups, but also aid in the end-of-life discussions with the family.

Limitations

Even though our study represents the most recent data available from USRDS national Medicare database regarding outcomes for durable LVAD devices, it has some important limitations. First, because it is based on administrative data, we are unable to determine details or types of implantable devices. Second, we were missing several key clinical parameters of preoperative patient illness that may have impacted mortality, including the INTERMACS profile, preoperative use of temporary mechanical support, and markers of frailty or cachexia. Additionally, we lacked information on preoperative and postoperative right heart function. Third, we were unable to find information on LVAD intent or ,indication like bridge to transplantation, bridge to recovery, or destination therapy, which may impact mortality after LVAD implantation. Fourth, we relied on diagnostic and procedural codes to determine the comorbidities and outcomes. However, given the inability to perform a manual review of the administrative data, this approach had been used in prior studies. Fifth, the median age of our population is more than 55 years; hence, the generalizability of our results to a younger population may be limited. Sixth, we were unable to find information on patients with acute renal failure requiring hemodialysis and awaiting LVAD implantation.

Conclusions

During 1 year of follow-up, patients with ESRD on maintenance dialysis with an LVAD had an increased mortality rate when compared with patients with CKD during the index admission and during 1 year of follow-up. The patients with CKD who required KRT during their index admission had a higher mortality compared with those who did not. LVADs in patients with advanced CKD and ESRD should only be considered after shared decision-making between physicians and their patients and may be best used in patients with ESRD who are being stabilized for expedited dual organ transplantation.

Lay Summary

- Very few patients with end-stage renal disease (ESRD) on maintenance dialysis undergo LVAD implantation.
- Mortality among patients with ESRD on maintenance dialysis who undergo LVAD implantation was significantly higher during 1 year of follow-up when compared with patients with chronic kidney disease (CKD).
- LVADs in patients with advanced CKD and ESRD on maintenance dialysis should only be considered after shared decision-making between physicians and their patients. We believe the incorporation of a palliative team care and an integrated team discussion before the implantation of an LVAD is crucial in this unique cohort of patients.

Declaration of Competing Interest

None of the authors have any direct conflicts of interest related to this article.

Funding: None.

Other Relevant Disclosures: Dr Sauer reports general disclosures to include consulting relationships with Medtronic and Abbott.

Dr Tedford reports general disclosures to include consulting relationships with Medtronic, Abbott, Aria CV Inc., Acceleron, CareDx, Itamar, Edwards LifeSciences, Eidos Therapeutics, Lexicon Pharmaceuticals, Gradient, and United Therapeutics. Dr Tedford is on a steering committee for Acceleron and Abbott as well as a research advisory board for Abiomed. He also does hemodynamic core lab work for Actelion and Merk.

Dr Cowger reports general disclosures to include consulting relationship with Medtronic and Abbott. She is on a steering committee for Medtronic, Procyrion, Endotronix, and Bioventrix. She also serves as speaker for Zoll.

Dr Fang reports general disclosures to include consulting relationship with Cytokinetics, AstraZeneca, Amgen, J&J, Boehringer-Ingelheim/Lilly, Windtree, and Capricor.

Supplementary materials

Supplementary material associated with this article can be found in the online version at doi:10.1016/j.cardfail.2022.03.355.

References

1. Rose EA, Gelijns AC, Moskowitz AJ, Heitjan DF, Stevenson LW, Dembitsky W, et al. Long-term use of a left ventricular assist device for end-stage heart failure. N Engl J Med 2001;345:1435–43.
2. Grady KL, Meyer PM, Dressler D, Mattea A, Chillcott S, Loo A, et al. Longitudinal change in quality of life and impact on survival after left ventricular assist device implantation. Ann Thorac Surg 2004;77:1321–7.
3. Park SJ, Milano CA, Tatooles AJ, Rogers JG, Adamson RM, Steidley DE, et al. Outcomes in advanced heart failure patients with left ventricular assist devices for destination therapy. Circ Heart Fail 2012;5:241–8.
4. Daimee UA, Kutyifa V. Left ventricular assist devices in patients with renal dysfunction: where are we heading? Exp Rev Med Device 2017;14:413–5.
5. Sandner SE, Zimpfer D, Zrunek P, Rajek A, Schima H, Dunkler D, et al. Renal function and outcome after continuous flow left ventricular assist device implantation. Ann Thorac Surg 2009;87:1072–8.
6. Yoshioka D, Sakaguchi T, Saito S, Miyagawa S, Nishi H, Yoshikawa Y, et al. Predictor of early mortality for severe heart failure patients with left ventricular assist device implantation. Circ J 2012;76:1631–8.
7. Bansal N, Hailpern SM, Katz R, Hall YN, Tamura MK, Kreuter W, et al. Outcomes associated with left ventricular assist devices among recipients with and without end-stage renal disease. JAMA Intern Med 2018;178:204–9.
8. Kamboj M, Kazory A. Left ventricular assist device and the kidney: getting to the heart of the matter. Blood Purif 2019;48:289–98.
9. Mehra MR, Uriel N, Naka Y, Cleveland JC Jr, Yuzefpolskaya M, Salerno CT, et al. A fully magnetically levitated left ventricular assist device. N Engl J Med 2019;380:1618–27.
10. United States Renal Data System. 2020 USRDS annual data report: epidemiology of kidney disease in the United States. Bethesda, MD: National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases; 2020.
11. Kirklin JK, Pagani FD, Kormos RL, Stevenson LW, Blume ED, Myers SL, et al. Eighth annual INTERMACS report: special focus on framing the impact of adverse events. J Heart Lung Transplant 2017;36:1080–6.
12. Tonelli M, Wiebe N, Culleton B, House A, Rabbat C, Fok M, et al. Chronic kidney disease and mortality risk: a systematic review. J Am Soc Nephrol 2006;17:2034–47.
13. Rihal CS, Naidu SS, Givertz MM, Szeto WY, Burke JA, Kapur NK, et al. 2015 SCAI/ACC/HFSA/STS clinical expert consensus statement on the use of percutaneous mechanical circulatory support devices in cardiovascular care (Endorsed by the American Heart Association, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of value by the Canadian Association of Interventional Cardiology−Association Canadienne de Cardiologie d'Intervention). Catheter Cardiovasc Interv 2015;85:1112–4.
14. Walther CP, Niu J, Winkelmayer WC, Cheema FH, Nair AP, Morgan JA, et al. Implantable ventricular assist device use and outcomes in people with end-stage renal disease. J Am Heart Assoc 2018;7:e008664.
15. Obi Y, Rhee CM, Mathew AT, Shah G, Streja E, Brunelli SM, et al. Residual kidney function decline and mortality in incident hemodialysis patients. J Am Soc Nephrol 2016;27:3758–68.
16. Brandenburg VM, Kleber ME, Vervloet MG, Tomaschitz A, Pilz S, Stojakovic T, et al. Fibroblast growth factor 23 (FGF23) and mortality: the Ludwigshafen Risk and Cardiovascular Health Study. Atherosclerosis 2014;237:53–9.
17. Memmos E, Sarafidis P, Pateinakis P, Tsiantoulas A, Faitatzidou D, Giamalis P, et al. Soluble Klotho is associated with mortality and cardiovascular events in hemodialysis. BMC Nephrol 2019;20:217.
18. Lisowska-Myjak B. Uremic toxins and their effects on multiple organ systems. Nephron Clin Pract 2014;128:303–11.
19. Mohamedali B, Bhat G. The influence of pre-left ventricular assist device (LVAD) implantation glomerular filtration rate on long-term LVAD outcomes. Heart Lung Circ 2017;26:1216–23.
20. Kormos RL, Teuteberg JJ, Pagani FD, Russell SD, John R, Miller LW, et al. Right ventricular failure in patients with the HeartMate II continuous-flow left ventricular assist device: incidence, risk factors, and effect on outcomes. J Thorac Cardiovasc Surg 2010;139:1316–24.
21. LaRue SJ, Raymer DS, Pierce BR, Nassif ME, Sparrow CT, Vader JM. Clinical outcomes associated with INTERMACS-defined right heart failure after left ventricular assist device implantation. J Heart Lung Transplant 2017;36:475–7.
22. Ikonomidis I, Aboyans V, Blacher J, Brodmann M, Brutsaert DL, Chirinos JA, et al. The role of ventricular−arterial coupling in cardiac disease and heart failure: assessment, clinical implications and therapeutic interventions. A consensus document of the European Society of Cardiology Working Group on Aorta & Peripheral Vascular Diseases, European Association of Cardiovascular Imaging, and Heart Failure Association. Eur J Heart Fail 2019;21:402–24.
23. Antonini-Canterin F, Enache R, Popescu BA, Popescu AC, Ginghina C, Leiballi E, et al. Prognostic value of ventricular-arterial coupling and B-type natriuretic peptide in patients after myocardial infarction: a five-year follow-up study. J Am Soc Echocardiogr 2009;22:1239–45.
24. Lane AD, Wu PT, Kistler B, Fitschen P, Tomayko E, Jeong JH, et al. Arterial stiffness and walk time in patients with end-stage renal disease. Kidney Blood Pressure Res 2013;37:142–50.
25. Foster BJ, Mitsnefes MM, Dahhou M, Zhang X, Laskin BL. Changes in excess mortality from end stage renal disease in the United States from 1995 to 2013. Clin J Am Soc Nephrol 2018;13:91–9.
26. Neovius M, Jacobson SH, Eriksson JK, Elinder C-G, Hylander B. Mortality in chronic kidney disease and renal replacement therapy: a population-based cohort study. BMJ Open 2014;4:e004251.
27. Go AS, Chertow GM, Fan D, McCulloch CE, Hsu C-y. Chronic kidney disease and the risks of death, cardiovascular events, and hospitalization. N Engl J Med 2004;351:1296–305.
28. Briasoulis A, Yokoyama Y, Kuno T, Ueyama H, Shetty S, Alvarez P, et al. In-hospital outcomes of left ventricular assist device implantation and concomitant valvular surgery. Am J Cardiol 2020;132:87–92.

29. Cook JL, Colvin M, Francis GS, Grady KL, Hoffman TM, Jessup M, et al. Recommendations for the use of mechanical circulatory support: ambulatory and community patient care: a scientific statement from the American Heart Association. Circulation 2017;135:e1145–e58.

30. Fang JC, Ewald GA, Allen LA, Butler J, Westlake Canary CA, Colvin-Adams M, et al. Advanced (stage D) heart failure: a statement from the Heart Failure Society of America Guidelines Committee. J Card Fail 2015;21:519–34.