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Cardiologist Evaluation and Approval Was the Primary Predictor of Kidney Transplant Candidacy and Transplantation Among Patients With Reduced Left Ventricular Ejection Fraction

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Background. End-stage kidney disease patients with concomitant heart failure (HF) with reduced ejection fraction are often denied kidney transplantation. The aims of this study were to explore factors predictive of suitability for kidney transplant and to assess cardiovascular outcomes in patients with impaired left ventricular ejection fraction (LVEF) after transplant. **Methods.** We evaluated 109 consecutive adults with LVEF ≤40% at the time of initial kidney transplant evaluation between 2013 and 2018. Posttransplant cardiovascular outcomes were defined as nonfatal myocardial infarction (MI), admission for HF, cardiovascular death, and all-cause mortality. **Results.** A cardiologist participated in kidney transplant evaluation for 87% of patients and was present at 49% of transplant selection conferences. Twenty-four patients (22%) were denied by a cardiologist for kidney transplant, and 59 (54%) were denied by the selection committee, of whom 43 were because of cardiovascular risk. Forty-two (38%) patients were approved for kidney transplant. On univariate analysis, the variables associated with denial for kidney transplant included cardiologist denial, higher cardiac troponin T, prior coronary intervention, cardiovascular event, positive stress study, lower ejection fraction, and lower VO_2 max (all $P < 0.05$). Cardiologist denial was the most significant predictor of denial for kidney transplant in different multivariate models. At a median follow-up of 15 mo, 5 (5%) suffered nonfatal MI, 13 (12%) were hospitalized for HF exacerbation, and 17 (16%) died. Only 22 patients, 52% of those approved, underwent kidney transplant. After kidney transplant, there was 1 death, 1 nonfatal MI, and 3 hospitalizations for HF. Median LVEF improved from 38% before listing to 55% posttransplant. **Conclusions.** Cardiologist denial was the primary predictor of rejection for kidney transplant. Despite careful selection, prevalence of cardiovascular events and mortality after kidney transplant was 23%. There is need for a structured multidisciplinary approach for patients with impaired LVEF.

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Prevalence of left ventricular systolic dysfunction in patients with end-stage kidney disease (ESKD) is high, with an estimated 16% to 18% of ESKD patients affected in the literature. Of these, 60% had presumed nonischemic cardiomyopathy as diagnosed by the absence of myocardial ischemia on perfusion imaging.[1,2] Left ventricular systolic dysfunction is an independent risk factor for all-cause mortality in ESKD patients.[1] The pathophysiology of left ventricular dysfunction in ESKD is thought to relate to the uremic milieu leading to alterations in cardiac structure and function. The risk of uremic cardiomyopathy increases with time spent on dialysis[2]; data from Medicare billing estimated the incidence of new-onset heart failure (HF) at 12.0% and 32.3% of patients at 12 and 36 mo after listing for kidney transplant,

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respectively.[3] Patients with ESKD also have a high prevalence of coronary artery disease, which predisposes to ischemic cardiomyopathy.

Although there is no cutoff value of ejection fraction, patients with left ventricular systolic dysfunction and ESKD are often considered poor candidates for renal transplant because they are at high risk for perioperative complications: a 5-fold increase in cardiac mortality, a 2-fold increase in all-cause mortality, and a 70% increase in posttransplant cardiac complications with left ventricular ejection fraction (LVEF) ≤45%.[2] However, several small observational studies have shown that, in certain subsets, kidney transplantation can lead to improvements in LV function and normalization of ejection fraction.[4–9]

Stratifying cardiovascular risk for patients with left ventricular dysfunction remains a challenge that faces cardiologists and nephrologists alike. Protocols for cardiac evaluation vary from center to center, and this reflects heterogeneity in society guidelines. The joint American Heart Association/American College of Cardiology Foundation statement suggests that it is reasonable to perform preoperative assessment of LV function by echocardiography in potential kidney transplant candidates (class IIa recommendation).[10] They recommend that all transplant candidates with LVEF ≤50% be referred to a cardiologist for evaluation (class I recommendation), as well as suggest that a transplantation program should identify a primary cardiology consultant for questions related to potential kidney transplantation candidates. However, the Renal Association suggests that there is no compelling evidence that pretransplant screening for coronary artery disease in asymptomatic patients with established kidney failure is effective and make no comment regarding echocardiography.[11] The European Renal Best Practice guideline recommends cardiac ultrasound and a standard exercise stress test in asymptomatic "high-risk" patients—defined as those of an older age, with diabetes, or with history of cardiovascular disease.[12] More recently, Kidney Disease Improving Global Outcomes (KDIGO) guidelines recommend that asymptomatic patients who have been on dialysis for at least 2 y or have risk factors for pulmonary hypertension undergo echocardiography.[13] All guidelines have a consensus opinion that symptomatic patients warrant further evaluation. Similar heterogeneity is seen in screening for coronary artery disease, because retrospective studies did not suggest a mortality benefit with cardiac stress testing, or coronary artery assessment and intervention, before kidney transplantation.[14,15] It is not surprising, then, that how to proceed once abnormal echocardiogram findings have been identified is not clear, and how to identify which patients would benefit from transplantation in the setting of a depressed ejection fraction remains a topic of debate.

Our primary aim is to evaluate predictors of approval for kidney transplant in patients with reduced ejection fraction at our center. Our secondary aim is to assess cardiovascular outcomes for those who underwent kidney transplantation.

MATERIALS AND METHODS

This was a retrospective study involving patients who underwent first evaluation for kidney transplant at Mayo Clinic Arizona between January 2013 and December 2018. This study was approved by the Mayo Clinic institutional review board and deemed low risk. All patients who had an echocardiogram showing an LVEF ≤40% within a week of their initial transplant evaluation were included. All data were collected by review of the electronic medical records. Ejection fraction ≤40% was chosen as the cutoff because this is the widely accepted definition of HF with reduced ejection fraction. It is also the same inclusion criteria that were used in the largest published study of outcomes of patients with systolic HF post–kidney transplantation.[8]

Our kidney transplant center is a referral center for nephrologists across Arizona and neighboring states. Patients are referred by their primary nephrologist with a formal letter. They undergo initial consultation with a transplant nephrologist who determines if additional workup is required. The procedure of our transplant center for cardiovascular testing includes the following: (1) electrocardiogram, (2) echocardiogram to evaluate valves and pulmonary pressure on all patients except recipients <50 y of age not on dialysis and without a history of diabetes, and (3) any type of cardiac stress test for patients with diabetes, older than 59 y of age, history of coronary artery disease, or with history of tobacco use. Carotid duplex ultrasound is required for patients with history of stroke, transient ischemic attack, or limb amputation.

When transplant nephrologists feel that a cardiologist opinion should be sought based on clinical history or abnormal findings on cardiovascular tests, they refer to a cardiologist within the transplantation center who reviews the patient in person and corresponds with a detailed consultation note. If further tests such as cardiac catheterization, functional testing, or repeat echocardiography following targeted intervention are required, these are performed at Mayo Clinic. Should the transplant nephrologist or cardiologist recommend an intensification in dialysis regime, this is communicated to the referring nephrologist, who receives a copy of all consultation letters.

The cardiologist determines the number of visits required for them to satisfactorily make their recommendation. At any point in the consultation process, the cardiologist may give a written opinion on the suitability for proceeding with transplantation, specifically in relation to perceived cardiovascular risk rather than overall suitability of the candidate.

Progress in the transplant evaluation process is monitored by the transplant coordinators, and once it is deemed complete, the patient is put forward for discussion at a conference that is attended by members of the transplant committee: the transplant surgeon, nephrologist, social worker, assigned pretransplant nursing team, transplant center director, dietician, and any other member of the transplant team that interacted with the patient. The cardiologist who reviewed the patient is invited to attend the meeting. For patients for whom there is concern regarding their cardiovascular status, they are usually discussed at a conference when a cardiologist who specializes in HF is present. All patients referred for evaluation are discussed at a transplant conference unless they withdraw or are deceased.

Demographic data were collected including age, sex, ethnicity, presence of cardiovascular risk factors, a prior diagnosis of HF, etiology of kidney disease, estimated glomerular filtration rate at time of referral, and time spent on dialysis, as well as type of dialysis. Cardiovascular events at the time of evaluation were defined as history of angina or acute coronary syndrome, coronary intervention (percutaneous or bypass grafting), history of HF, history of cardiac arrest, peripheral arterial disease requiring intervention, or cerebrovascular disease.

Transthoracic echocardiograms originally reported by an experienced cardiologist at Mayo Clinic Arizona were reviewed to allow extraction of several variables. Data were collected regarding the initial echocardiogram and subsequent follow-up echocardiograms, both pre- and posttransplant (if performed).

Cardiovascular workup before transplant was recorded, including nuclear stress testing, functional testing (VO_2 max testing or 6-minute walk test), and coronary angiography. Patient referral to a cardiologist and the outcome of that referral—approval, further testing, change to medication regimen, or interventional procedures—was reviewed.

Date of initial transplant evaluation, date of the transplant conference meeting, and date of listing for transplant were recorded. Also recorded was the presence of a cardiologist at the transplant selection meeting and whether this was the cardiologist who reviewed the patient before the selection conference. Cardiovascular outcomes, cardiovascular death, all-cause mortality, and date of occurrence were evaluated for all patients.

Demographics and clinical characteristics between patients who have been approved and patients who have been denied or never discussed for transplant were compared using the chi-square test for categorical variables and the Kruskal-Wallis rank sum test for continuous variables. Multivariable logistic regression was used to investigate which factors are associated with transplant outcome denial or never discussed. The variables chosen in the multivariable models are based on statistical significance along with clinical relevance. Kaplan-Meier curves and the log-rank test were used to assess cardiac event-free survival by the 3 groups of interest (patients who had been approved and transplanted, patients who had been approved but were still in waitlisting, and patients who had been denied or never discussed). Cardiovascular events were defined as HF requiring hospitalization, nonfatal myocardial infarction (MI), cardiovascular death, and all-cause mortality. All statistical analyses were performed using SAS software, version 9.3 (SAS Institute, Cary, NC). $P < 0.05$ was defined as statistical significance.

RESULTS

We evaluated 109 consecutive adults with LVEF ≤40% at the time of initial kidney transplant evaluation between 2013 and 2018. Median age was 61 y (range 20–76 y); 85 (78%) were male; 56 (51%) were White, 13 (12%) Black, 6 (6%) Native American, 24 (22%) Hispanic, and 7 (6%) Asian. Sixty-three (58%) had diabetes mellitus, 89 (82%) had a history of cardiovascular events, and 42% had ischemic cardiomyopathy. Etiology of cardiomyopathy is outlined in **Figure S1, SDC,** http://links.lww.com/TXD/A487.

Ninety-nine patients in our cohort (91%) required dialysis at the time of transplant evaluation. Seventy-six patients were utilizing hemodialysis, and 23 patients were utilizing peritoneal dialysis. Data regarding residual renal function were not available. Cause of ESKD is as follows: diabetic nephropathy, 46 patients (42%); hypertensive nephrosclerosis, 7 patients (6%); glomerulonephritis, 19 patients (17%); autosomal dominant polycystic kidney disease, 6 patients (6%). The remaining 31 patients had various other diagnoses, including reflux nephropathy, tubulointerstitial disease, drug-induced chronic kidney disease, and unknown. In terms of nutritional status, the median Body Mass Index was 28 kg/m^2 (range 19–44) and the median serum albumin level 4.2 g/dL (range 2.8–5.5 g/dL).

TABLE 1.

Description of the cardiac evaluation for the entire cohort

Cardiac evaluation	Number of patients (%)	Test result
Cardiologist consultation	92 (84)	
Echocardiogram		
Mean (SD) LVEF at initial evaluation	109 (100)	31.4% (6.46)
Median (range) LVEF at initial evaluation		33.0% (10.0, 40.0)
Mean (SD) LVEF at time of committee decision	38 (35)	38.5 (11.32)
Median (range) LVEF at time of committee decision		37.5 (12.0, 66.0)
Stress myocardial perfusion scan	80 (73)	
Positive for reversible ischemia	8 (10)	
Positive for prior infarct	34 (43)	
Negative for ischemia	38 (48)	
Functional testing	31 (28)	
Mean (SD) VO_2 max mL/kg/min		14.4 (5.71)
Median (range) VO_2 max (mL/kg/min)		12.2 (6.7, 34.7)
Catheterization (left or right heart)	39 (36)	

LVEF, left ventricular ejection fraction.

Cardiac evaluation for the entire cohort is shown in Table 1. Median LVEF was 33% (range 10%–40%). Eighty patients had nuclear stress imaging; 7% were positive for reversible ischemia and 31% for prior infarct. Median VO_2 max was 12.2 (6.7–34.7) mL/kg/min (31 patients). Ninety-two patients had a cardiology consultation during the transplant evaluation process, whereas 5 patients had cardiologist input solely during discussion at the selection committee. Overall, a cardiologist was present at the time of selection committee decision in 49% of cases (for 14 patients, the primary cardiologist who completed the evaluation was present, and for 35 patients, another cardiologist who did not participate in the initial consultation was present). Thirty-seven patients (35%) had a repeat echocardiogram undertaken before the transplant conference; median LVEF at this time was 37.5% (12–66) versus an initial median LVEF of 34% in these 37 patients.

Twenty-four patients (22%) were denied by a cardiologist for kidney transplant following cardiology consultation, and 45 patients (41%) were approved; 23 patients (21%) were still under review by the cardiologist at the time of transplant conference, and 17 patients (16%) never saw a cardiologist for a consultation, as shown in **Figure S2, SDC**, http://links.lww.com/TXD/A487. Fifty-nine (54%) were denied by the selection committee, of whom 43 were because of cardiovascular risk. Ten patients were referred for consideration of combined heart-kidney transplantation, and 2 patients ultimately underwent dual transplantation.

Sixty-six patients underwent goal-directed therapeutic approaches to optimize cardiovascular risk during kidney transplant evaluation process, as shown in **Figure S3, SDC**, http://links.lww.com/TXD/A487. Most patients (n = 47, 43%) had medication changes, followed by a similar number of patients (n = 10, 9%) who required an increase in dialysis time or frequency to optimize fluid management, and 9 patients (8.3%) required percutaneous coronary intervention. There was no difference in the likelihood of being denied by the selection committee between patients who underwent

TABLE 2.

Clinical and biochemical variables associated with denial for kidney transplant on univariate analysis

	Transplant selection committee decision: Approved (n = 42)	Selection committee decision: Denied or never discussed (n = 67)	Total (N = 109)	*P*
Female gender, n (%)	9 (21.4)	15 (22.4)	24 (22.0)	0.906[a]
Age (median, range, y)	60.0 (27.0, 74.0)	61.0 (20.0, 76.0)	61.0 (20.0, 76.0)	0.138[a]
(mean, SD, y)	56.2 (12.07)	59.6 (11.53)	58.3 (11.81)	0.138[a]
Race, n (%)				0.037[a]
Caucasian	18 (42.9)	38 (56.7)	56 (51.4)	
African American	8 (19.0)	5 (7.5)	13 (11.9)	
Native American	0 (0.0)	6 (9.0)	6 (5.5)	
Hispanic	9 (21.4)	15 (22.4)	24 (22.0)	
Asian	5 (11.9)	2 (3.0)	7 (6.4)	
Others	2 (4.8)	1 (1.5)	3 (2.8)	
BMI (median, range, kg/m^2)	27.1 (18.7, 40.7)	28.5 (21.0, 43.6)	28.2 (18.7, 43.6)	0.493[b]
(mean, SD, kg/m^2)	28.1 (5.51)	29.0 (5.10)	28.6 (5.26)	0.493[b]
Smoking, n (%)	15 (35.7)	27 (40.3)	42 (38.5)	0.632[a]
Diabetes, n (%)	20 (47.6)	43 (64.2)	63 (57.8)	0.088[a]
Hypertension, n (%)	39 (92.9)	62 (92.5)	101 (92.7)	0.950[a]
Dyslipidemia, n (%)	19 (45.2)	43 (64.2)	62 (56.9)	0.052[a]
Coronary Intervention, n (%)				0.003[a]
Percutaneous coronary intervention	7 (16.7)	22 (32.8)	29 (26.6)	
Coronary artery bypass surgery	4 (9.5)	18 (26.9)	22 (20.2)	
History of cardiac arrest, n (%)	4 (9.5)	3 (4.5)	7 (6.4)	0.296[a]
Peripheral arterial disease, clinical or subclinical, n (%)				0.091[a]
Abnormal Ankle Brachial Index only	2 (4.8)	2 (3.0)	4 (3.7)	
Claudication	0 (0.0)	5 (7.5)	5 (4.6)	
Angioplasty/bypass	1 (2.4)	5 (7.5)	6 (5.5)	
Amputation	1 (2.4)	7 (10.4)	8 (7.3)	
Cerebrovascular disease, n (%)				0.473[a]
Transient ischemic attack	2 (4.8)	2 (3.0)	4 (3.7)	
Stroke	5 (11.9)	4 (6.0)	9 (8.3)	
Cardiovascular events, n (%)	30 (71.4)	59 (88.1)	89 (81.7)	0.029[a]
Dialysis at the time of transplant evaluation				0.301[a]
Hemodialysis	27 (64.3)	49 (73.1)	76 (69.7)	
Peritoneal dialysis	12 (28.6)	11 (16.4)	23 (21.1)	
Cardiology clearance, n (%)				<0.001[a]
Denied	2 (4.8)	22 (32.8)	24 (22.0)	
Approved	32 (76.2)	13 (19.4)	45 (41.3)	
Pending review	3 (7.1)	20 (29.9)	23 (21.1)	
Never saw	5 (11.9)	12 (17.9)	17 (15.6)	
Stress test performed during kidney transplant process, n (%)				<0.001[a]
No	7 (16.7)	22 (32.8)	29 (26.6)	
Yes	25 (59.5)	13 (19.4)	38 (34.9)	
Yes, fixed infarct	9 (21.4)	25 (37.3)	34 (31.2)	
Yes, reversible ischemia	1 (2.4)	7 (10.4)	8 (7.3)	
VO_2 max categorical, n (%)				0.007[a]
VO_2 >14	11 (26.2)	4 (6.2)	15 (14.0)	
VO_2 <14	4 (26.7)	12 (75.0)	16 (51.6)	
NT_Pro-BNP, median (range)	7727.5 (672.0, 52 001.0)	40 758.0 (3000.0, 52 001.0)	26 786.0 (672.0, 52 001.0)	0.009[b]
Mean (SD)	14 983.6 (18 138.11)	34 709.3 (18 798.45)	27 946.2 (20 623.85)	0.009[b]
cTniT, median (range)	0.1 (0.0, 232.0)	0.1 (0.0, 209.0)	0.1 (0.0, 232.0)	0.021[b]
Mean (SD)	6.7 (36.31)	8.8 (37.33)	8.0 (36.78)	0.021[b]
Serum albumin (g/dL), median (range)	4.2 (3.0, 5.0)	4.0 (0.0, 5.5)	4.2 (3.7, 4.4)	0.048[b]
Mean (SD)	4.2 (0.48)	3.9 (0.70)	4.0 (0.63)	0.048[b]
LVEF (%) median (range)	35.0 (20.0, 40.0)	31.0 (10.0, 39.0)	33.0 (10.0, 40.0)	0.003[b]
Mean (SD)	33.9 (4.14)	29.8 (7.16)	31.4 (6.46)	0.003[b]

[a]Chi-square *P* value.
[b]Wilcoxon rank sum *P* value.
BMI, Body Mass Index; cTniT, cardiac troponin T; LVEF, left ventricular ejection fraction; NT-Pro-BNP, N-terminal (NT)-pro hormone b-type natriuretic peptide.

therapeutic interventions versus those who did not (n = 33 [54%] versus n = 26 [65%], $P = 0.3$).

The variables associated with denial for kidney transplant are shown in Table 2 and summarized here: history of coronary artery intervention and cardiovascular events at the time of transplant evaluation, cardiologist's input regarding transplant candidacy, presence of fixed or reversible ischemia on stress testing, lower VO_2 max, higher N-terminal (NT)-pro hormone b-type natriuretic peptide, higher cardiac troponin T, hypoalbuminemia, and lower LVEF (all $P \leq 0.05$).

Clinical characteristics of patients that were not significantly different between approved and nonapproved groups were age, gender, Body Mass Index, history of smoking, diabetes, hypertension, dyslipidemia, peripheral arterial disease, and stroke. Approximately 50% of patients in both the approved and denied groups had a clinical history of a decompensated HF episode; thus, there was no difference between groups.

In terms of kidney disease parameters, serum hemoglobin and serum phosphorus at time of evaluation did not influence candidacy for transplant, nor did duration of months on dialysis at time of evaluation. Patients who were preemptive to renal replacement therapy did not have a higher rate of approval for transplant.

Patients who were approved for kidney transplant were, on average, evaluated for a longer period from date of initial evaluation to date of transplant selection committee outcome, although this was not statistically significant (median 231.5 versus 106.0 d, $P = 0.059$).

Three multivariate models were built to account for clinically and statistically relevant predictors of denial for kidney transplant, as shown in Table 3. Cardiologist denial was the most significant and consistent predictor of denial for kidney transplant. A history of a prior cardiovascular event also increased risk of denial (odds ratio 3.98; 95% confidence interval, 1.26-12.58). The results were similar when the cohort was restricted to the 69 patients with cardiology input, as shown in **Table S1, SDC**, http://links.lww.com/TXD/A488.

At a median follow-up of 15 mo, 5 (5%) suffered nonfatal MI, 13 (12%) were hospitalized for HF exacerbation, and 17 (16%) died. Only 22 (20%) underwent kidney transplant. Six of 22 were living donors and the remainder deceased donor kidney transplants. Twelve patients (55%) had delayed graft function. Median creatinine was 1.61 mg/dL at 1 mo (0.9–7.04 mg/dL) and 1.46 mg/dL at 12 mo (0.81–4.7 mg/dL). After kidney transplant, there was 1 death, 1 nonfatal MI, and 3 hospitalizations for HF. Of the patients who had an echocardiogram posttransplant, 13 of 15 (86%) showed improvement in their LVEF, with 12 patients (80%) having ejection fraction >50%. Median LVEF improved from 33% at initial evaluation and 38% at time of transplant conference to 55% posttransplant.

Differences in cardiac event-free survival between the approved and denied groups and transplanted and nontransplanted groups are demonstrated in Figure 1. Cardiac event-free survival was higher for patients on the waitlist (hazard ratio 0.45 [0.17-1.14], $P = 0.09$) and those transplanted (hazard ratio 0.27 [0.10-0.74], $P = 0.01$) than for those denied.

DISCUSSION

Although attempts have been made to standardize the kidney transplant evaluation with measures such as proposed prognostic indicators, expert guidelines, and multidisciplinary involvement on transplant committee teams, subjective input continues to play a role. There are several published qualitative studies that examine a nephrologist's perceptions and practices regarding transplant candidacy,[16–18] but quantitative data are sparse. Lenihan et al[19] used multivariate logistic regression to explore factors associated with waitlisting for transplant specifically in the elderly population and found that older age, coronary artery disease, and poor mobility adversely affected listing.

To our knowledge, this is the first study published in the literature that examines the factors that are predictive of kidney transplant candidacy in patients with HF with reduced ejection fraction. It is also the first study to explore factors that are outside of the baseline patient characteristics, in particular, the influence of the cardiac evaluation on kidney transplant candidacy. It is unique in highlighting the importance of the input

TABLE 3.

Factors associated with denial for kidney transplant on multivariate model

	Model 1			Model 2			Model 3		
Variables	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***	**OR**	**95% CI**	***P***
Age	1.01	0.98-1.05	0.506	1.01	0.97-1.05	0.588	1.01	0.97-1.04	0.701
Any cardiovascular event									
No	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Yes	2.40	0.75-7.64	0.139	3.25	1.07-9.91	0.038	3.98	1.26-12.58	0.019
Cardiology clearance									
Yes/pending	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref	Ref
Review/never saw									
No	7.12	1.41-35.90	0.017	10.28	2.13-49.61	0.004	9.68	2.02-46.30	0.004
Serum albumin	0.59	0.24-1.42	0.237						
LVEF	0.90	0.82-0.99	0.027						
cTnT (binary)									
cTnT < 0.1				Ref	Ref	Ref			
cTnT ≥0.1				2.02	0.84-4.88	0.117			
Race									
White							Ref	Ref	Ref
Other							0.52	0.21-1.26	0.145

CI, confidence Interval; cTnT, cardiac troponin T; LVEF, left ventricular ejection fraction; OR, odds ratio.

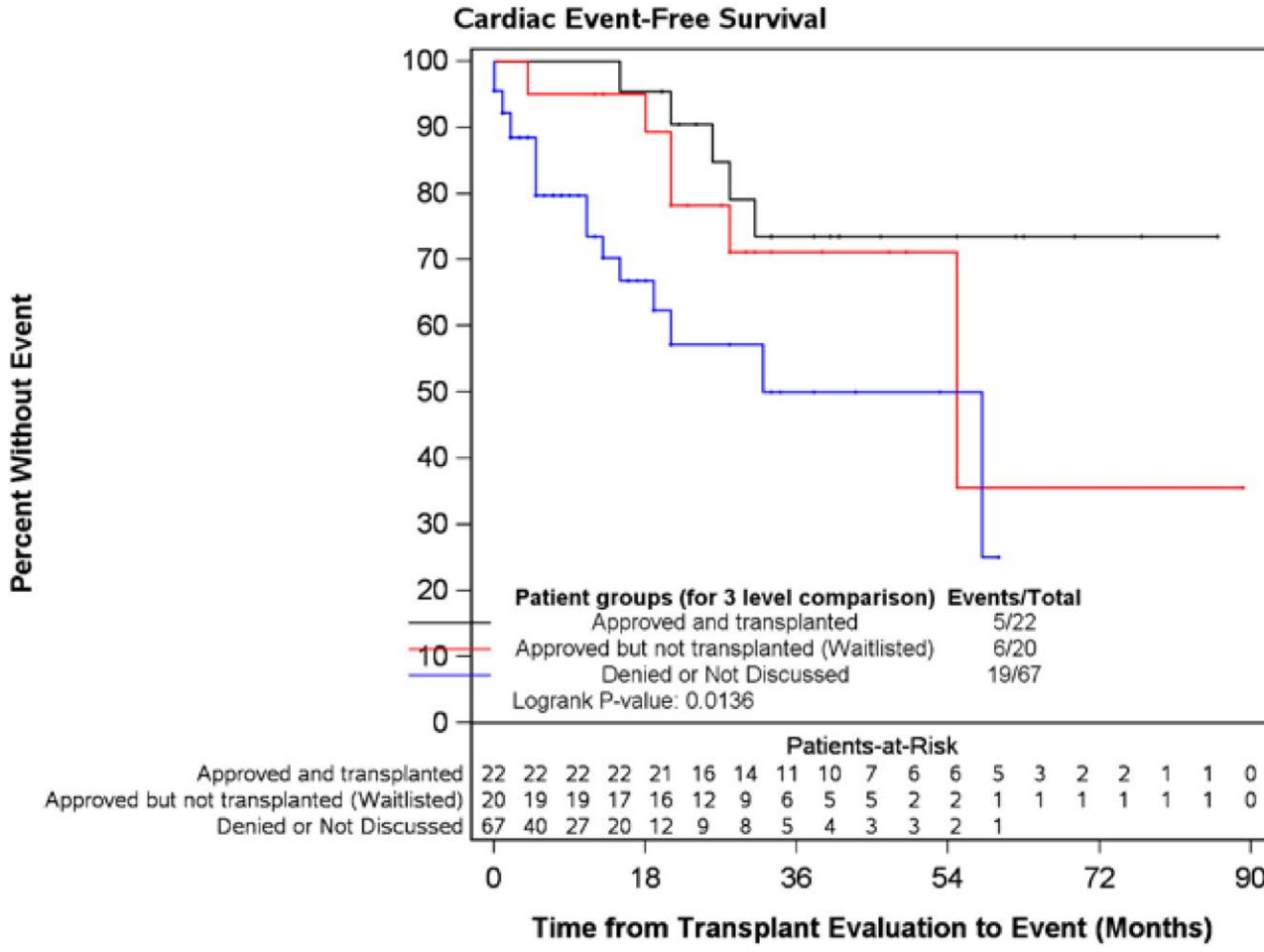

FIGURE 1. Cardiac event-free survival by group.

from the cardiologist in terms of deciding who among these high-risk patients are suitable for transplant, given that cardiologist denial was the most significant factor on multivariate analysis for negatively influencing transplant candidacy.

As well as being pivotal in selecting patients for transplant, cardiologist input is an opportunity to optimize the patients' cardiac status; based on the initial evaluation, most patients (60%) had an intervention including optimization of goal-directed therapy and alteration of dialysis regime, and this led to a mean improvement in ejection fraction. However, it is not possible to differentiate the impact of transplantation from cardiologist input on the improved ejection fraction after kidney transplant. A total of 11% of studied patients did not have a cardiologist involved in their transplant evaluation, missing this potential opportunity. We would argue that all patients with LV dysfunction should be reviewed by a cardiologist before consideration for transplantation, as recommended by the American Heart Association/ American College of Cardiology Foundation.[10] There was a nonsignificant increased rate of selection committee approval for patients who underwent cardiology consultation before selection conference compared with patients who did not have preconference cardiology consultation (n = 37 [43%] versus n = 5 [33%], $P = 0.5$).

Prior observational studies showed both improved echocardiographic parameters and improved rates of cardiovascular morbidity and mortality post–kidney transplant.[4,8] After transplantation, LVEF >50% was associated with a lower hazard for death or hospitalizations for HF (relative risk 0.900; 95% confidence interval, 0.860-0.950; P < 0.0001).[8]

In our study, the majority of patients achieved LVEF >50%. Time of posttransplant echocardiogram was not standardized in this retrospective study, and further studies evaluating the value of standardized imaging for patients with pretransplant reduced LVEF are necessary.

The KDIGO guidelines suggest that patients with symptomatic New York Heart Association class III/IV HF with *uncorrectable* left ventricular dysfunction with ejection fraction <30% be excluded from kidney transplantation alone, unless there are mitigating factors that give patients an acceptable estimated survival.[20] The KDIGO group describes "uncorrectable" dysfunction as a persistent LVEF <30% despite adequate fluid removal on dialysis. In clinical practice, dialysis centers often function independently from transplant evaluation centers, and objective determinants of adequacy of fluid removal are lacking.[21] A trial of intensified dialysis was often recommended at our center, but whether this was truly achieved is unclear. Thus, although it is a desirable recommendation, whether LV dysfunction is categorically uncorrectable is difficult to ascertain. The KDIGO group recommends that these patients be referred for combined kidney-heart transplant evaluation, which occurred for just 10 of our patients. The low number of transplanted patients with LV dysfunction reflects the ongoing uncertainty in choosing which of these patients will improve posttransplant.

In our study, although the rate of posttransplant cardiovascular morbidity and mortality was high at 23%, absolute numbers were small with 5 of 22 patients affected. Much of this morbidity comes from admissions for HF—3 of 5 events. The etiology of HF was varied in these patients: ischemic, nonischemic, and hypertensive heart disease. All the HF admissions occurred within the first 6 mo, and there were no further episodes beyond this early time, which may suggest that it was still in the early posttransplant phase when ventricular remodeling was still underway.

There were over 1500 kidney transplants performed between 2013 and 2018 at Mayo Clinic Arizona. Despite the estimated prevalence of LV dysfunction in up to 18% of patients with ESKD, our study period showed only an average of 3.6 patients per year with moderate-severe LV dysfunction undergoing kidney transplant, which is <1% of total transplant recipients. In addition, there were only 109 patients over a 5-y period with reduced ejection fraction who were referred for kidney transplant evaluation, despite the high prevalence of HF with reduced ejection fraction in ESKD patients. We hypothesize that many patients are deemed unsuitable candidates by their primary nephrologist and not referred for evaluation by a transplant center. When we retrospectively chose a 5-y period, we were hoping to have sufficient posttransplant data to analyze which variables influenced cardiovascular outcomes after kidney transplant, but because of the low number of transplanted patients, this was not possible. We were also unable to compare outcomes between patients established on dialysis and those preemptive at time of transplantation because only 1 patient had not yet commenced dialysis. These areas warrant further study.

Several limitations warrant discussion; first, our study did not capture data regarding whether patients were symptomatic or asymptomatic in relation to HF because New York Heart Association class was not consistently recorded. We did, however, record whether they had a preexisting diagnosis of HF at initial transplant evaluation, which was only 54 of 109 or half of patients. New York Heart Association class may have influenced decisions at transplant selection meetings.

Second, this is a retrospective study, which cannot infer causality, and further prospective studies are required to evaluate the transplant evaluation process in real time. It also reflects the experience of a single center with the advantage of easy access to a team of cardiologists, several of whom specialize in advanced HF and heart transplantation. This is not readily available to many other centers in the United States and other countries and limits the generalizability of this study. What is consistently clear is the complexity of managing these patients.

Our median follow-up time was relatively short at 15 mo, and critical data on cardiovascular outcomes for patients who did not undergo kidney transplant during this study's follow-up time may be missed because we were only able to capture data collected by our transplant center. As mentioned previously, patients travel from state-wide and from out of state to be evaluated for transplant candidacy at our center. Many patients, once denied suitability for kidney transplant, return to the care of their primary nephrologist and no longer follow-up at Mayo Clinic. Thus, our data regarding cardiovascular events in the nontransplanted group (ie, majority of patients) during follow-up are limited. Mortality data are complete, however, based on registry data.

In contrast, all patients who were actively listed for transplant or underwent kidney transplant had ongoing follow-up for at least 5 y posttransplant. This means that it is not possible to compare the prevalence of cardiovascular events in the transplanted group to those in the nontransplanted group because it is likely that the rate of events in the nontransplanted group is much higher than what we captured via our records. Despite this lack of data, there was a higher rate of cardiac event-free survival in the transplant group than in the nontransplanted group.

There is ongoing research into the area of evaluation and screening of patients for coronary artery disease while on the kidney transplant waitlist. In a subgroup analysis from ISCHEMIA-CKD, an invasive strategy for revascularization in kidney transplant candidates with stable coronary disease did not improve outcomes compared with conservative management.[22] The CARSK study is a multicenter, randomized control trial that is randomizing patients after initial screening for coronary artery disease at time of waitlisting to either no further screening or screening at regular intervals. The focus of this study, however, is on patients already accepted on the waitlist and evaluation for coronary ischemia rather than cardiac failure; patients with "active cardiac issues" are excluded. Whether patients with low ejection fraction are included is not specified on the protocol.[23] The transplantation community eagerly awaits the completion of this trial to add to the evidence regarding screening for transplantation. In the interim with the current evidence available, the authors of this article agree with Sharif[22] that the variation in guidance from international groups reflects a lack of evidence to support cardiac screening or intervention in asymptomatic kidney transplantation candidates, but abandoning screening altogether is likely a step too far, and we must careful evaluate "cardiac fitness" with a multidisciplinary approach. Specifically, how to assess patients with LV dysfunction has not been adequately addressed to date.

In conclusion, patients with left ventricular systolic dysfunction represent a unique patient group that is particularly complex to evaluate for kidney transplantation. Involvement of a cardiologist is recommended based on cardiologist denial having a significant impact on transplant selection committee denial and waitlisting. Posttransplant cardiovascular morbidity and mortality remain high, particularly with regard to HF admissions in the early posttransplant period, but improvements in left ventricular function are seen posttransplant. Standardized echocardiography at 12 mo posttransplant would be helpful in assessing this in these high-risk patients because normalization of ejection fraction posttransplant has led to reduced cardiovascular morbidity and mortality in prior studies.[8] Because of the absolute number of patients with LVEF <40% being referred for transplant evaluation and furthermore transplanted being low, research on posttransplant outcomes is mainly limited to retrospective single-center studies. Larger studies to examine posttransplant outcomes in this group are required to further guide important factors for selection for transplant.

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