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And Then There Were Three: Effects of Pretransplant Dialysis on Multiorgan Transplantation

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Background. Simultaneous liver-kidney (SLK) and simultaneous heart-kidney (SHK) transplantation currently utilize 6% of deceased donor kidneys in the United States. To what extent residual kidney function accounts for apparent kidney allograft survival is unknown. **Methods.** We examined all adult SLK and SHK transplants in the United States during 1995–2014. We considered the duration of dialysis preceding SLK or SHK (≥90 d, 1–89 d, or none) as a proxy of residual kidney function. We used multinomial logistic regression to estimate the difference in the adjusted likelihood of 6- and 12-month apparent kidney allograft failure between the no dialysis versus ≥90 days dialysis groups. **Results.** Of 4875 SLK and 848 SHK recipients, 1775 (36%) SLK and 449 (53%) SHK recipients received no dialysis before transplant. The likelihood of apparent kidney allograft failure was 1%–3% lower at 12 months in SLK and SHK recipients who did not require pretransplant dialysis relative to recipients who required ≥90 days of pretransplant dialysis. Among 3978 SLK recipients who survived to 1 year, no pretransplant dialysis was associated with a lower risk of apparent kidney allograft failure over a median follow-up of 5.7 years (adjusted hazard ratio 0.73 [0.55–0.96]). **Conclusions.** Patients with residual kidney function at the time of multiorgan transplantation are less likely to have apparent failure of the kidney allograft. Whether residual kidney function facilitates function of the allograft or whether some SLK and SHK recipients have 3 functional kidneys is unknown. Sustained kidney function after SLK and SHK transplants does not necessarily indicate successful MOT.

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INTRODUCTION

The number of multiorgan transplants (MOTs) is rising. A large proportion of MOTs are simultaneous liver-kidney (SLK) and simultaneous heart-kidney (SHK) transplants. These transplants treat the kidney as a "secondary" organ, offered to individuals with a failing nonrenal organ and concomitant kidney disease. According to United Network of Organ Sharing (UNOS) data, 6% of deceased donor kidneys in 2018 and 2019 were allocated as "secondary" organs in this manner. The rise of SLK and SHKs against a background of organ shortage has been the center of a vigorous controversy.[1,2] In 2019, UNOS released a white paper, "Ethical Implications of Multi-Organ Transplants," recommending, among other things, that "[d]ata for each MOT combination should be made publicly available to foster transparency."[3]

A prerequisite to fostering transparency in MOT is the proper selection of metrics that reflect what they measure. In the case of MOTs using kidney as a secondary organ, the current kidney outcome metric, observed kidney allograft survival, is flawed. In contrast to orthotopic liver and heart transplants, requiring removal of the native liver or heart, the native kidneys remain in place in heterotopic kidney transplants. Consequently, when allograft failure is defined as returning to dialysis or requiring another kidney transplant, what it reflects is failure of *both* the transplant kidney and the native kidneys (Figure 1). In the setting of deceased donor kidney transplantation, especially in the current era of prolonged wait time on dialysis, residual kidney function is usually negligible. In MOTs, however, kidney transplantation can occur at a much higher level of kidney function than what

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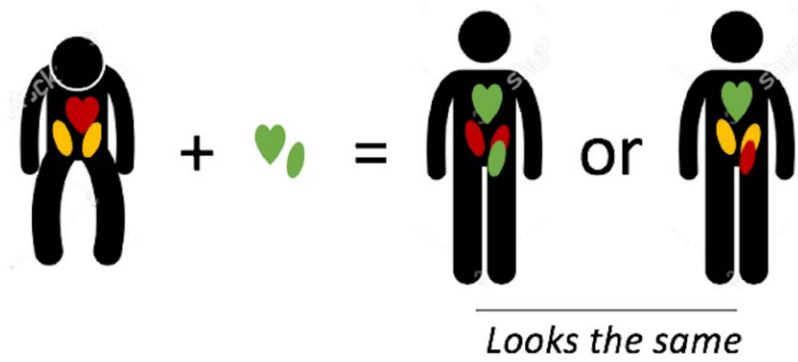

FIGURE 1. Apparent kidney allograft survival in multiorgan transplantation involving the kidney. We cannot distinguish between native kidney recovery or transplant kidney function without specific imaging. Red, poor function; orange, suboptimal function; green, full function.

is allowed in kidney-alone transplantation. In the OPTN/UNOS medical eligibility criteria for simultaneous liver-kidney (SLK) transplants, for instance, a patient may become eligible for SLK if he/she had an estimated glomerular filtration rate (eGFR) <60 mL/min for 3 months and 1 eGFR value <35 mL/min.[4] Such liberal criteria can create a lead time bias, as has been proposed in preemptive kidney transplantation.[5] Furthermore, the cause of kidney disease in SLK and SHK transplants is frequently acute kidney injury, the reversibility of which is difficult to predict. Nuclear imaging studies have previously demonstrated significant native kidney function in selected SLK recipients,[6-8] but these findings have not been generalized to the larger transplant population. The extent to which native kidney function may skew observed kidney allograft survival is therefore unknown.

In addition to carrying implications for monitoring programs, the extent to which observed kidney allograft outcome reflects native kidney function also indirectly estimates the extent of "prophylactic" transplant under current practice. Prophylactic transplants refer to SLK or SHK in nondialysis-dependent patients, in an attempt to improve overall patient survival posttransplant.[3] In an era of worsening organ shortage, directing kidneys away from dialysis-dependent patients who nearly always *will* benefit from a transplanted kidney to nonrenal organ candidates who *may* benefit from a transplanted kidney is controversial. Quantifying the magnitude of prophylactic kidney transplantation, which are perhaps premature or even "unnecessary," helps inform more rational MOT policy development.

We hypothesize that residual (native) kidney function attenuates the risk of apparent kidney allograft failure, as defined as return to dialysis or a low level of eGFR qualifying for kidney retransplantation. Because information on residual kidney function is not readily available, we use pretransplant dialysis duration as a practical, albeit imperfect, proxy. Apparent kidney allograft failure is typically blamed on allograft failure, but it may represent allograft failure plus accelerated loss of native kidney function after SLK and SHK. Studying the association between pretransplant dialysis duration and apparent kidney allograft failure may help quantify the extent of this phenomenon.

MATERIALS AND METHODS

Data Source and Cohort Assembly

We used the Scientific Registry of Transplant Recipients (SRTR), which contains deidentified data on all solid organ transplant donors, candidates, and recipients in the United States. The SRTR incorporates dialysis start dates from the Centers of Medicare and Medicaid Services, thus ensuring accurate ascertainment of apparent kidney allograft failure.[9]

We identified all adult SLK and SHK recipients from January 1, 1995, through December 31, 2014, who had complete kidney outcome data (either death, kidney allograft failure, or a reported serum creatinine during follow-up to enable us to calculate eGFR by the CKD-EPI formula) at 6 and 12 months. We defined SLK and SHK transplantation as deceased donor liver/heart and kidney transplantations occurring within 2 days in the same recipient. We chose the study start date as a full complement of donor characteristics became available in 1995. We chose the study end date as our database version is dated November 2017: the end date of December 2014 therefore allowed enough time to complete nearly 3 years of follow-up before censoring of survival time. Exclusion criteria included other concomitant solid organ transplantations, duplicate entries in the dataset, omission of primary outcome (eGFR at 6 and 12 mo), and omission of model covariates (Figure 2).

Exposure and Covariates

We used pretransplant dialysis duration as a proxy for residual kidney function, dividing pretransplant dialysis duration into 3 categories: ≥90 days (low residual kidney function), <90 days (intermediate residual kidney function), and no dialysis (high residual kidney function). We stratified each analysis by SLK and SHK and, unless stated otherwise, adjusted all analyses for the following covariates:

(1) Era: year of transplant;
(2) Donor characteristics: Kidney Donor Recipient Index, a marker of donor kidney quality, calculated from 10 donor characteristics, normalized to the 2017 median[10];
(3) Recipient comorbidities: Age, sex, race, insurance status, kidney diagnosis, liver/heart diagnoses, nonkidney life support at time of transplant;
(4) Transplant characteristics: Kidney and liver/heart cold ischemia times. Where cold ischemia time is missing for 1 organ but not the other, we imputed missing time using the assumption that the liver and heart precede the kidney implantation by 5 and 10 hours, respectively. (Five and 10 h were the mean difference in heart/kidney and liver/kidney cold ischemia time, respectively, in the nonmissing data.)

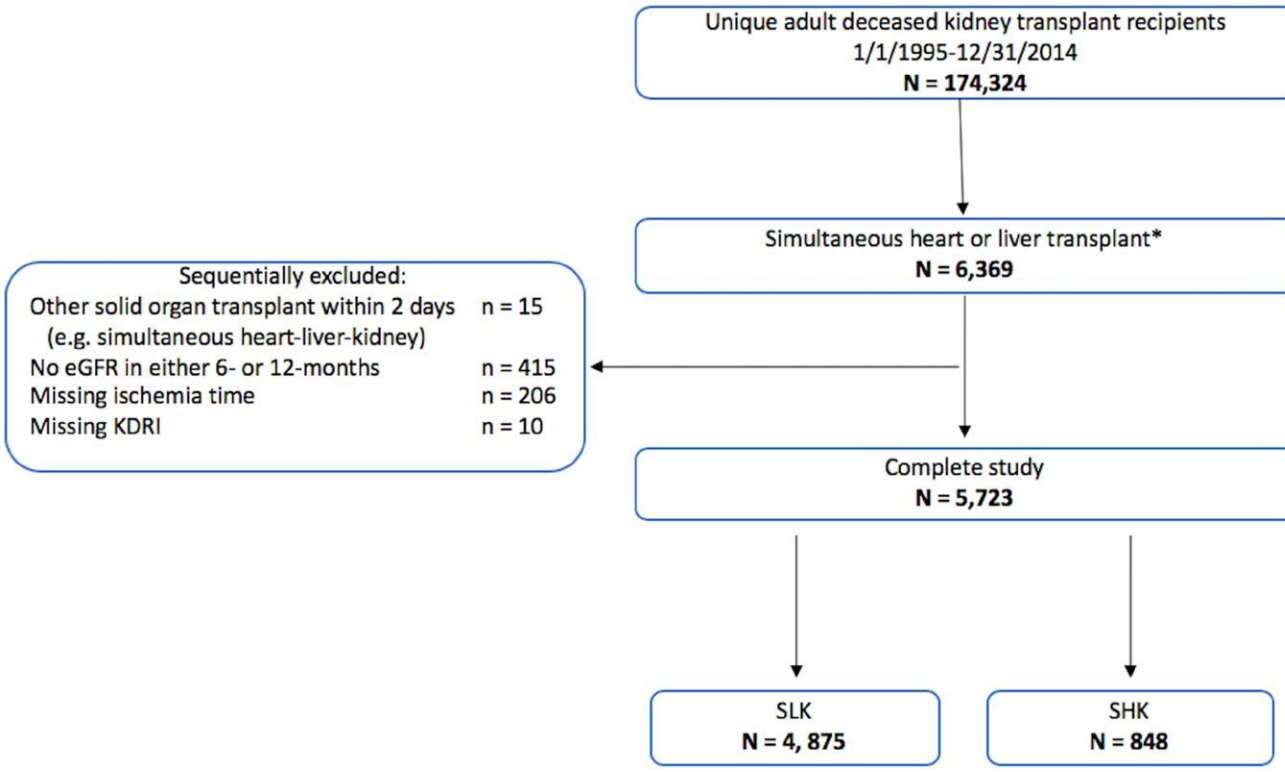

FIGURE 2. Cohort assembly. *Simultaneous transplant: heart or liver transplant preceding the kidney transplant by 2 or fewer d. eGFR, estimated glomerular filtrate rate; KDRI, Kidney Donor Risk Index; SHK, simultaneous heart-kidney; SLK, simultaneous liver-kidney.

Primary Outcome

Our primary outcome was the difference in the probability of apparent kidney allograft failure between the groups with no dialysis exposure (presumed high residual kidney function) and >90 days dialysis exposure (presumed low residual kidney function) at 6- and 12-month posttransplant, adjusted for differences in baseline characteristics including disease severity. This outcome was our best indirect estimate for the extent of "prophylactic" transplantation. To calculate the frequency of this outcome, we examined mutually exclusive occurrences of death, apparent kidney allograft failure (reported kidney allograft failure or eGFR < 20 mL/min), and no event (alive with eGFR ≥ 20 mL/min) at 6 and 12 months by a multinomial regression model. The multinomial regression model[11] is an extension of the logistic regression model allowing for >2 outcomes. In the 25% of cases where both death and allograft failure occurred by month 6 or 12, we chose to adjudicate the event as death although allograft failure may precede death. We made this decision because disease severity confounds the relation between pretransplant dialysis duration and apparent allograft failure. We therefore made the conservative estimate that *all* episodes of allograft failure shortly preceding death were due to disease severity rather than residual kidney function. Such a choice biased our primary outcome toward the null, underestimating the true association of residual kidney function with apparent allograft survival. We used predicted probabilities from the multinomial model[11] to estimate the difference in apparent kidney allograft failure between the different pretransplant dialysis duration (residual kidney function) groups, with and without adjustment for covariates.

Secondary Outcomes

Our secondary outcomes included:

(1) Delayed kidney allograft function: Results among the 3 groups were compared using the chi-square test.
(2) eGFR at 1 year in patients without death or apparent allograft failure: Results among the 3 groups were compared using the t-test.
(3) Death and apparent allograft failure after 1 year: In a landmark analysis, we restricted our analysis to patients who survived to 1 year without death or apparent kidney allograft failure. We applied the Fine and Gray extension to the traditional proportional hazards (Cox) regression model, employing the proportional subdistribution hazards model[12] to examine the association between pretransplant dialysis exposure and death or apparent kidney allograft failure in a competing risk framework. We examined Schoenfeld residuals to examine the validity of the proportional hazards assumption.

We conducted statistical analyses using SAS 9.4 (Cary, NC) and STATA 14.1 (StataCorp). Stanford University's Institutional Review Board approved this study in accordance with the Declaration of Helsinki (protocol number IRB-32753). The data reported here have been supplied by the Minneapolis Medical Research Foundation (MMRF) as the contractor for the SRTR. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the SRTR or the US government. Findings in this article were partly reported in abstract form at the American Society of Transplantation Cutting Edge of Transplantation Meeting in March 2020.

RESULTS

Cohort and Baseline Characteristics

Our final cohort consisted of 5723 adult MOT recipients (4875 SLK recipients and 848 SHK recipients). Of the SLK

recipients, 1533 (31%) received ≥90 days of dialysis, 1567 (32%) received <90 days of dialysis, and 1775 (36%) received no dialysis before transplant. Of the SHK recipients, 304 (36%) received ≥90 days of dialysis, 95 (11%) received <90 days of dialysis, and 449 (53%) received no dialysis before transplant. Table 1 outlines their baseline characteristics. Markers of disease severity, as manifested by nonkidney life support and biochemical indices (available for SLK), were highest in the groups receiving <90 days of dialysis and lowest in the groups receiving no dialysis. Acute kidney injury (often hepatorenal syndrome in the case of SLK) was the primary kidney diagnosis in 36% and 24% of SLK and SHK recipients, respectively. Diabetes mellitus and prior solid organ transplants, on the other hand, were most common in SLK patients receiving no dialysis and not significantly different among the SHK groups. Other comorbidities were generally present in <10% of all groups.

Primary Outcome

At 6 and 12 months, the likelihood of event-free survival (no death or apparent kidney allograft failure) was highest in SLK and SHK recipients with no pretransplant dialysis exposure (Figure 3). Figure S1 (SDC, http://links.lww.com/TXD/A303) shows results before multivariable adjustment. When the events were parsed into death and apparent kidney allograft failure, no pretransplant dialysis exposure was associated with a 1%–3% lower probability of apparent kidney allograft failure at 12 months in SLK and SHK recipients (Table 2). Intermediate dialysis exposure, or <90 days of dialysis exposure, was associated with a statistically nonsignificant 1%–5% increase in likelihood of death at 12 months in SLK and SHK recipients (Table 2, also in Table S1, SDC, http://links.lww.com/TXD/A303, where *P* values are available in parentheses). In 25% of all events before 1 year, apparent kidney allograft failure preceded death by 47 ± 70 days (Table S2, SDC, http://links.lww.com/TXD/A303).

Secondary Outcomes

Delayed Graft Function

After SLK, delayed kidney allograft function occurred in 26%, 25%, and 10% of patients requiring ≥90 days of dialysis, <90 days of dialysis, and no dialysis pretransplant, respectively ($P < 0.001$). After SHK, delayed kidney allograft function occurred in 38%, 26%, and 16% of patients requiring ≥90 days of dialysis, <90 days of dialysis, and no dialysis pretransplant, respectively ($P < 0.001$).

eGFR at 1 year in patients with no events: 3978 SLK and 706 SHK recipients survived to 1 year without apparent kidney allograft failure. eGFR was highest in SHK recipients with <90 days dialysis exposure (Table 3; $P = 0.004$).

Death and apparent kidney allograft failure beyond 1 year: over a median follow-up of 5.7 years, 859 (22%) SLK recipients died and 292 (7%) experienced kidney allograft failure. No pretransplant dialysis exposure (presumed high residual kidney function) was associated with a higher risk of death and a lower hazard for apparent kidney allograft failure (Table 3). Over a median follow-up of 6.2 years, 131 (19%) SHK recipients died and 61 (9%) experienced kidney allograft failure. In SHK recipients, a similar trend in apparent kidney allograft failure to SLK was observed, but the association was not statistically significant after multivariable adjustment (Table 3).

DISCUSSION

In this registry-based study, we demonstrate that pretransplant dialysis duration, an imperfect proxy of residual kidney function at the time of transplant, is associated with apparent kidney allograft failure after multiorgan transplantation involving the kidneys, that is, SLK and SHK. We find a 1%–3% lower risk of kidney allograft failure at 12 months in SLK/SHK recipients who did not require dialysis compared with SLK/SHK recipients who required >90 days of dialysis before transplant. This association remains significant after adjusting for donor, recipient, and transplant characteristics, including markers of disease severity. We submit that at least 1%–3% SLK/SHK transplants in patients who did not require pretransplant dialysis may be considered "prophylactic"; that is, even without the kidney component of these MOTs, these recipients may have had sufficient residual kidney function to stave off dialysis at 1-year posttransplant. While the estimated effect size is small, we feel that it is a *lower* bound for the extent of "prophylactic" kidney transplants, for reasons we will discuss below. More studies are warranted to uncover the upper bound of the true effect.

Our results complement prior single-center nuclear imaging studies examining native kidney function in SLK recipients.[6-8] In the largest of these studies,[6] 39 of 78 SLK recipients (51%) had native GFRs >20 mL/min at an average of 1-year posttransplant. Given the high geographic variability in the SLK/SHK use, extrapolating from single-center studies is challenging. Our estimate of 1%–3% should be regarded as the lowest estimate of prophylactic kidney transplant, as native kidneys may be contributing concurrently with the transplant kidney and thus evade recognition by the endpoint of apparent kidney allograft failure. Indeed, the lower long-term apparent kidney allograft failure rate in SLK recipients without pretransplant dialysis exposure suggests that a subset of SLK recipients have 3 functional kidneys. We also used a very conservative estimate of allograft failure, adjudicating cases in which both allograft failure and death occurred within 1 year as death. An alternative adjudication will likely increase the estimate of prophylactic kidney transplant.

While several studies have addressed these issues in SLK transplantation, we are not aware of prior studies examining the association between dialysis exposure and apparent kidney allograft failure in SHK recipients. Our findings in SHK are similar in direction and magnitude to those observed in SLK transplantation; the precision of our estimates is limited owing to much smaller sample size. Thus, our analyses confirm and extend previously published findings from single-center studies of SLK recipients to the entire SLK/SHK transplant population in the United States.

Our analysis has several strengths. We utilized a national dataset (the SRTR), improving generalizability relative to single-center or regional studies. The sample size was relatively large, increasing the power to detect modest associations. We conducted multivariable analyses to account for confounding by factors related to kidney function over time.

There are also several important limitations to our analysis. First and foremost, the SRTR data had no direct measure of residual kidney function. The need for, and duration of, preoperative dialysis are the closest proxies, but are clearly imperfect. For instance, if in the throes of end-stage liver or heart failure a patient with normal or near normal kidney function at experiences an episode of reversible acute kidney injury

TABLE 1.

Baseline characteristics in SLK and SHK transplants, stratified by pretransplant dialysis exposure

	SLK (N = 4875)				*SHK* (N = 848)			
	Pretransplant dialysis duration (presumed residual kidney function)				Pretransplant dialysis duration (presumed residual kidney function)			
	≥90 d (low)	<90 d (intermediate)	None (high)		≥90 d (low)	<90 d (intermediate)	None (high)	
Baseline characteristic	**N = 1533**	**N = 1567**	**N = 1775**	***P***	**N = 304**	**N = 95**	**N = 449**	***P***
Recipient								
Age (y)	56 (49–62)	57 (51–63)	58 (52–63)	<0.001	52 (43–60)	56 (45–62)	59 (52–64)	<0.001
Sex (% female)	508 (33%)	561 (36%)	621 (35%)	0.3	63 (21%)	20 (21%)	101 (22%)	0.8
Race (%)								0.05
White	1177 (77%)	1296 (83%)	1429 (81%)	<0.001	190 (63%)	69 (73%)	321 (71%)	
Black	265 (17%)	196 (13%)	275 (15%)		97 (32%)	24 (25%)	115 (26%)	
Others	91 (6%)	75 (5%)	71 (4%)		17 (6%)	2 (2%)	13 (3%)	
Ethnicity (% Hispanic)	275 (18%)	274 (17%)	235 (13%)	<0.001	32 (11%)	6 (6%)	29 (6%)	0.1
Education (% college or higher)	600 (39%)	548 (35%)	604 (34%)	0.006	123 (40%	34 (36%)	177 (39%)	0.7
Primary payer(% private/self-pay)	581 (38%)	836 (53%)	953 (54%)	<0.001	98 (32%)	56 (59%)	250 (56%)	
Primary kidney disease diagnosis (%)				<0.001				<0.001
AKI/Hepatorenal syndrome[d]	341 (22%)	849 (54%)	580 (33%)		55 (18%)	38 (40%)	108 (24%)	
Diabetic nephropathy	309 (20%)	230 (15%)	318 (18%)		58 (19%)	17 (18%)	92 (29%)	
Glomerulonephritis	244 (16%)	124 (8%)	232 (13%)		40 (13%)	7 (7%)	31 (7%)	
PKD/Hypertension	313 (29%)	109 (7%)	266 (15%)		79 (26%)	8 (8%)	79 (18%)	
Other	231 (15%)	160 (10%)	266 (15%)		56 (18%)	18 (19%)	103 (23%)	
Unknown	95 (6%)	95 (6%)	146 (8%)		16 (5%)	7 (7%)	36 (8%)	
Primary liver disease diagnosis (%)				<0.001				
Alcohol	271 (18%)	305 (19%)	236 (13%)					
Viral	622 (41%)	581 (37%)	721 (41%)					
Crytotogenic	112 (7%)	163 (10%)	155 (9%)					
Other	424 (28%)	353 (23%)	499 (28%)					
Unknown	4 (<1%)	3 (<1%)	2 (<1%)					
INR at transplant	1.3 (1.1–1.6)	1.8 (1.4–2.7)	1.5 (1.2–1.9)	<0.001				
Bilirubin at transplant	1.4 (0.7–3.5)	8.7 (3.0–27.0)	1.4 (0.7–3.5)	<0.001				
Primary heart disease diagnosis (%)								0.3
Ischemic cardiomyopathy					17 (6%)	6 (6%)	21 (5%)	
Dilated cardiomyopathy					257 (85%)	74 (78%)	362 (81%)	
Other					30 (10%)	15 (16%)	66 (15%)	
Nonkidney life support at transplant[e]	110 (7%)	387 (25%)	134 (8%)	<0.001	211 (69%)	79 (83%)	337 (75%)	0.02
Diabetes mellitus (%)	347 (23%)	276 (18%)	523 (29%)	<0.001	88 (28%)	24 (25%)	112 (25%)	0.5
Prior solid organ transplant (%)	236 (15%)	281 (18%)	380 (21%)	<0.001	51 (17%)	18 (19%)	88 (20%)	0.6
Cerebrovascular disease (%)[b]	33 (2%)	21 (1%)	12 (1%)	<0.001	16 (5%)	9 (9%)	26 (6%)	0.01
Peripheral artery disease (%)[a]	41 (3%)	25 (2%)	32 (2%)	0.1	13 (4%)	8 (8%)	28 (6%)	0.005
COPD (%)[a]	26 (2%)	24 (2%)	20 (1%)	0.01	4 (1%)	5 (5%)	18 (4%)	0.01
Malignancy history (%)[a]	95 (6%)	94 (6%)	145 (8%)	0.003	19 (6%)	6 (6%)	28 (6%)	0.01
Donor and Transplant								
$KDRI_{2017}$	0.85 (0.71–1.08)	0.87 (0.71–1.10)	0.86 (0.71–1.10)	0.1	0.77 (0.67–0.96)	0.72 (0.62–0.85)	0.76 (0.67–0.89)	0.005
Year of transplant (%)				<0.001				0.8
1995–1999	82 (5%)	65 (4%)	173 (10%)		37 (12%)	8 (8%)	43 (10%)	
2000–2004	233 (15%)	207 (13%)	319 (18%)		45 (15%)	17 (18%)	66 (15%)	
2005–2009	516 (34%)	570 (36%)	585 (33%)		86 (28%)	28 (29%)	141 (31%)	
2010–2014	702 (46%)	725 (46%)	698 (39%)		136 (45%)	42 (44%)	199 (44%)	
Cold ischemia time (h)								
Liver/heart	7 (5–9)	6 (5–8)	7 (5–9)	0.04	3 (2–4)	3 (3–4)	3 (2–4)	0.6
Kidney	11 (8–14)	10 (8–13)	11 (8–14)	0.01	13 (8–16)	13 (9–16)	12 (8–16)	0.6
cPRA at transplant[c]				0.1				0.5
0–20	899 (59%)	792 (51%)	954 (54%)		232 (76%)	79 (83%)	341 (76%)	
20.1–80	225 (15%)	202 (13%)	225 (13%)		53 (17%)	10 (11%)	79 (18%)	
80.1–100	173 (11%)	122 (8%)	133 (7%)		15 (5%)	4 (4%)	22 (5%)	
Number of HLA mismatches[b]	4 (4–5)	4 (4–5)	4 (4–5)	0.3	4 (3–4)	4 (3–4)	4 (3–4)	
Cross-match result (% positive)	125 (8%)	94 (6%)	109 (6%)	0.4	16 (5%)	0 (0%)	13 (3%)	0.3

Covariates included in the multivariable analysis are underlined. Continuous variables are represented as median (25–75th percentile range). Categorical variables are represented as count (percentage). *P* are generated by the Wilcoxon rank sum (continuous) and Chi-square test (categorical). Data missingness is <1% unless stated otherwise.

[a]1–10% missing.

[b]11–20% missing.

[c]21–30% missing.

[d]AKI applies to both SLK and SHK. Hepatorenal syndrome only applies to SLK.

[e]Nonkidney life support includes ventilator, inotrope, artificial liver (SLK), or advanced circulatory support devices (SHK).

Number refers to the hazard ratio of allograft failure compared with the median transplant deceased donor kidney for 2017.

AKI, acute kidney injury; COPD, chronic obstructive pulmonary disease; cPRA, calculated panel reactive antibodies; HCV, hepatitis C virus; HLA, human leukocyte antigen; INR, international normalized ratio; KDRI2017, Kidney Donor Risk Index, normalized to the 2017 scale; NASH, nonalcoholic steatohepatitis; PKD, polycystic kidney disease; SHK, simultaneous heart-kidney; SLK, simultaneous liver-kidney.

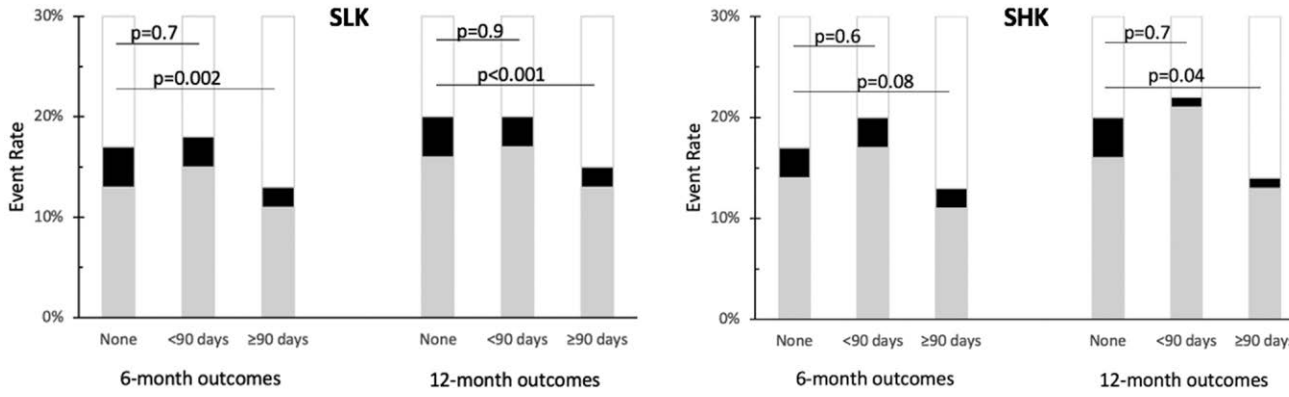

FIGURE 3. Adjusted event rate at 6- and 12-mo in SLK and SHK recipients, by presumed residual kidney function at time of transplant. Gray, death; black, apparent allograft failure; white, event-free survival. Dialysis ≥90 d (presumed lowest residual kidney function) is the reference group. *P* values refer to the test for difference between the likelihood of event-free survival compared with the reference group, in dialysis <90 d group (shorter line) and no dialysis group (longer line). SHK, simultaneous heart-kidney; SLK, simultaneous liver-kidney.

TABLE 2.

Unadjusted and adjusted differences in event risk at 6 and 12 mo in SLK and SHK patients, by pretransplant dialysis duration (presumed residual kidney function)

	Difference in event risk			
	<90 d vs ≥90 d dialysis		None vs ≥90 d dialysis	
	Unadjusted	Adjusted	Unadjusted	Adjusted
SLK				
6-mo				
Apparent allograft failure	–1%	**–1%**	**–2%**	**–2%**
Death	**+4%**	+2%	+0%	–2%
12-mo				
Apparent allograft failure	–1%	+1%	–1%	**–1%**
Death	**+3%**	+1%	–2%	**–3%**
SHK				
6-mo				
Apparent allograft failure	+1%	+0%	–1%	–2%
Death	+1%	+3%	–4%	–3%
12-mo				
Apparent llograft failure	–3%	**–3%**	**–3%**	**–3%**
Death	+4%	+5%	–4%	–3%

Dialysis ≥90 d (presumed lowest residual kidney function) is the reference group. Results are represented as the difference in event risk. Bolded cells denote statistical significance ($P < 0.05$). SHK, simultaneous heart-kidney; SLK, simultaneous liver-kidney.

requiring 1 session of dialysis and ends up receiving a MOT, such a patient may be misclassified as having intermediate residual kidney function when in fact residual kidney function might be high and recover soon after transplant. Indeed, that we found the highest eGFR in SHK candidates with pretransplant dialysis duration <90 days is an illustration of the above scenario. For this reason, we limited our primary outcome to comparison of apparent allograft failure rate between patients with no dialysis and patients with ≥90 days of dialysis, as the former almost certainly have higher residual kidney function than the latter. More detailed quantification of glomerular filtration, proteinuria, and other manifestations of kidney disease (eg, kidney size and symmetry by ultrasound) ought to be systematically collected in prospective MOT candidates in a multicenter effort to study our topic in more detail. As with all observational studies, there may be residual confounding for which we were unable to adjust. For example, the need for dialysis pre-MOT may indicate more severe end-stage liver or heart disease, which may itself modify the posttransplant course and the subsequent risk of kidney allograft failure. That the difference in apparent kidney allograft failure rate persists despite comparable death rates and despite a conservative adjudication of allograft failure lends confidence to the conclusion that residual kidney function, not disease acuity, explains the differences in apparent kidney allograft failure by pretransplant dialysis exposure.

Our findings suggest that apparent kidney allograft failure may *not* be an appropriate outcome to measure the success of the kidney transplant in multiorgan transplantation. As the 2017 SLK eligibility criteria is meant to be a minimal eligibility criteria and is generous in its allowance for SLK,[13,14] transplant programs still have the autonomy and responsibility to decide which of their patients meeting the criteria actually need a concurrent kidney transplant. Rates of kidney allograft failure will likely be lower for programs that are more liberal with SLK transplants, irrespective of the actual quality of kidney selection or posttransplant care. A counterweighing measure, such as mandated reporting of measured native and transplant kidney GFR to the SRTR after MOT, may be considered in refining the SLK policy and in drafting the future SHK policy.

Our study does not answer the question of whether the extent of seemingly "prophylactic" kidney transplants is appropriate. Some degree of kidney impairment is almost ubiquitous in end-stage heart and liver disease. A functioning kidney allograft does more than avert dialysis in the immediate perioperative setting; it also carries out complex metabolic and immunomodulatory roles. In other words, the kidney allograft, in reducing the need for dialysis need and kidney failure-associated complications, may also have "protected" the native kidneys postoperatively in SHK and SLK. From the individual SHK and SLK candidate's perspective, having 3 functioning kidneys is thus preferable to incurring the risk of having none. Although these salutary effects are doubtlessly present clinically, the incremental benefit of the kidney in MOT is less well-established *at a population level*. For SLK, the best available study, a propensity-matched cohort study, reported a significantly lower mortality (roughly half) in the first-year posttransplant of SLK compared with liver-alone transplant, but this only translated to a 1–4 month gain in 5-year mean posttransplant survival owing to the overall high

TABLE 3.

Subdistribution hazard ratios for allograft failure and death in SLK and SHK recipients, unadjusted and adjusted, by pretransplant dialysis exposure (presumed residual kidney function), conditional on an event-free first year

Pretransplant dialysis duration (presumed residual kidney function)	N	eGFR at 1 y	Apparent allograft failure		Death	
			Unadjusted	Adjusted	Unadjusted	Adjusted
SLK						
≥90 d (low)	1244	63 ± 21	Ref	Ref	Ref	Ref
<90 d (intermediate)	1246	63 ± 22	0.78 (0.58–1.04)	0.78 (0.57–1.07)	0.93 (0.78–1.12)	0.94 (0.78–1.14)
No dialysis (high)	1488	61 ± 20	0.77 (0.58–1.01)	**0.73 (0.55–0.96)**	**1.19 (1.01–1.40)**	1.11 (0.94–1.31)
SHK						
≥90 d (low)	243	60 ± 21	Ref	Ref	Ref	Ref
<90 d (intermediate)	75	69 ± 21	0.57 (0.25–1.33)	0.82 (0.33–2.03)	0.98 (0.53–1.79)	1.08 (0.58–2.02)
No dialysis (high)	388	61 ± 20	**0.45 (0.26–0.77)**	0.70 (0.37–1.32)	1.03 (0.72–1.48)	0.89 (0.61–1.30)

Bolded cells denote statistical significance ($P < 0.05$).
eGFR, estimated glomerular filtrate rate (in mL/min); SHK, simultaneous heart-kidney; SLK, simultaneous liver-kidney.

mortality of SLK recipients.[15] This gain in quite modest compared with the years gained for kidney-alone transplant as estimated by Wolfe et al[16] For SHK, the results are similar (as reviewed by Cheng et al[14]). Furthermore, all studies comparing the mortality of SLK/SHK to liver-/heart-alone transplant recipients have been subject to confounding by indication: the difference in survival was the most marked in the first-day posttransplant, suggesting confounding by indication where some of the sickest patients received only liver-/heart-alone *because* they were too sick to undergo dual-organ transplant. Our study does not directly address many of the clinical challenges in the management of patients with dual-organ failure. Rather, our study sheds light on the population level and policy question of how many kidney transplants used in MOT *may* have been better utilized in kidney-alone transplants.

One may argue that whether "prophylactic" kidney transplant should be offered is a supply-side question—the answer ought to depend on the availability of deceased donor kidney organs. In that case, the facts are unambiguous. There is a growing group of almost 100 000 patients awaiting deceased donor kidney transplants, all of whom have demonstrated advanced or dialysis-requiring kidney disease and stand to benefit immensely from a kidney transplant. These patients experience diminished access to transplant each time a prophylactic kidney transplant is performed, in which a heart or liver transplant candidate, who is not dialysis-dependent and likely won't be dialysis-dependent even without a kidney transplant, receives a kidney *ahead of kidney-alone candidates*.[1,2,17]

As a nontransplant option to kidney failure exists in the form dialysis, a lifetime approach to management of heart and liver transplant candidates with kidney disease would be to reserve kidney transplants for when residual kidney function is truly exhausted, that is, when the patient becomes truly dialysis-dependent.[14] Changes to the MOT allocation system to reflect this would include:

(1) mandated reporting of measured native and transplant kidney GFR to the SRTR after MOT, as discussed previously, and incorporation of these data into assessments of the center's posttransplant kidney allograft survival;
2) more stringent criteria for SLK/SHK;
3) a Safety Net option to enable liver/heart transplant recipients to obtain allocation priority for deceased donor kidneys.[14,17]

Such changes would reduce the likelihood of seemingly prophylactic transplants and shift kidneys toward patients who unambiguously need them. As a move in this direction, UNOS's 2017 SLK policy set criteria for SLK (where none existed before) and implemented a Safety Net option; whether and how this policy change altered outcomes for liver transplant recipients and access for kidney-alone transplant candidates is not yet known.

In summary, we find an association between the need for, and duration of, dialysis in advance of SLK and SHK transplantation, with a suggestion of seemingly "prophylactic" kidney transplantation in some SLK and SHK recipients. The estimated effect sizes are statistically significant but clinically modest and warrant verification in future studies with better quantifications of residual kidney function. Our findings challenge the validity of apparent kidney allograft failure as a metric of kidney transplant program quality in multiorgan transplantation. Whether the extent of seemingly prophylactic kidney transplant is warranted in the age of critical organ shortage deserves vigorous debate and discourse in the ethics and policy arenas.

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