Received: 21 February 2022 | Revised: 1 May 2022 | Accepted: 2 May 2022

DOI: 10.1111/ctr.14700

Clinical TRANSPLANTATION
The Journal of Clinical and Translational Research

WILEY

ORIGINAL ARTICLE

Impact of medical eligibility criteria and OPTN policy on simultaneous liver kidney allocation and utilization

Ashwani K. Singal[1,2] | Yong-Fang Kuo[3] | Paul Kwo[4] | Nadim Mahmud[5] | Pratima Sharma[6] | Mitra K. Nadim[7]

[1]Department of Medicine, University of South Dakota Sanford School of Medicine, Sioux Falls, South Dakota, USA

[2]Avera McKennan University Hospital and Transplant Institute, Sioux Falls, South Dakota, USA

[3]Department of Biostatistics and Preventive Medicine, University of Texas Medical Branch, Galveston, Texas, USA

[4]Division of Gastroenterology and Hepatology, Stanford University Medical University, Stanford, California, USA

[5]Division of Gastroenterology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania, USA

[6]Division of Gastroenterology and Hepatology, University of Michigan, Ann Arbor, Michigan, USA

[7]Division of Nephrology and Hypertension, University of Southern California, Los Angeles, California, USA

Correspondence
Ashwani K. Singal, University of South Dakota Sanford School of Medicine, Avera McKennan University Hospital and Transplant Institute, Avera Transplant Institute, Sioux Falls, SD 57105, USA
Email: ashwanisingal.com@gmail.com

Abstract

Background: Organ Procurement and Transplantation Network (OPTN) implemented medical eligibility and safety-net policy on 8/10/17 to optimize simultaneous liver-kidney (SLK) utilization. We examined impact of this policy on SLK listings and number of kidneys used within 1-yr. of receiving liver transplantation (LT) alone.

Methods and results: OPTN database (08/10/14-06/12/20) on adults (N = 66 709) without previous transplant stratified candidates to listings for SLK or LT alone with pre-LT renal dysfunction at listing (eGFR < 30 mL/min or on dialysis). Outcomes were compared for pre (08/10/14-08/09/17) vs. post (08/10/17-06/12/20) policy era. SLK listings decreased in post vs. pre policy era (8.7% vs. 9.6%; $P < .001$), with 22% reduced odds of SLK listing in the postpolicy era, with a decrease in all OPTN regions except regions 6 and 8, which showed an increase. Among LT-alone recipients with pre-LT renal dysfunction (N = 3272), cumulative 1-year probability was higher in post vs. prepolicy period for dialysis (5.6% vs. 2.3%; $P < .0001$), KT listing (11.4% vs. 2.0%; $P < .0001$), and KT (3.7% vs. .25%; $P < .0001$). Sixty-seven (2.4%) kidneys were saved in post policy era, with 18.1%, 16.6%, 4.3%, and 2.9% saving from regions 7, 2, 11, and 1, respectively.

Conclusion: Medical eligibility and safety-net OPTN policy resulted in decreased SLK use and improved access to LT alone among those with pre-LT renal dysfunction. Although decreased in postpolicy era, regional variation of SLK listings remains. In spite of increased use of KT within 1-year of receiving LT alone under safety net, less number of kidneys were used without impact on patient survival in postpolicy era.

KEYWORDS
cirrhosis, dialysis, ESRD, HRS, OPTN

1 | INTRODUCTION

Liver transplant candidates have a high prevalence of renal dysfunction. The spectrum of renal dysfunction varies from reversible to irreversible renal damage from acute kidney injury or chronic kidney disease with or without dialysis.[1–3] Although renal function may improve after liver transplantation (LT) alone,[4–6] many patients will require simultaneous liver kidney (SLK) in order to improve post-transplant outcomes.[2,7,8]

Since the introduction of the model for end-stage liver disease (MELD) score in 2002, the frequency of SLK has increased significantly by over 400% in the US.[9–11] The use of SLK was very heterogeneous across centers, and Organ Procurement and Transplantation Network (OPTN) regions,[9,12] because of the lack of medical eligibility criteria and regional sharing.[13–15] Although the access to donor kidneys has increased since the introduction of a new allocation system in 2014, the increasing use of SLK remains of concern, as there is a waiting period of over 5 years for kidney transplant (KT) alone.[16] Moreover, candidates listed for SLK compared to those listed for KT alone received better quality organs with Kidney Donor Profile Index < .35.[11] To overcome this clinical unmet need and unequal allocation of organs, the OPTN implemented a policy on August 10, 2017, as a basis for homogenizing the medical eligibility criteria for SLK listing and allocation.[9,11] This policy also provided a safety net for patients who did not recover renal function or developed advanced kidney disease with estimated glomerular filtration rate (eGFR) < 20 mL/min within 1-year of LT, with a priority to receive a donor kidney, if listed between 60 and 364 days after receiving LT alone.[9,11]

Data on the impact of this policy on the use of SLK, and patient outcomes among candidates with renal dysfunction who receive LT alone are scant.[17,18] A recent report showed that the implementation of the OPTN policy on SLK listing resulted in decreased frequency of SLK listings, and increased access to deceased donor KT among recipients of LT alone without negative impact on patient outcomes.[19] However, in the background of heterogeneous use of SLK across United Network for Organ Sharing (UNOS) regions and liver disease etiology before the policy was implemented,[10,12,20] the data are needed to examine the impact of policy on the variation on use of SLK and KT after LT alone (KAL) based on UNOS region and liver disease etiology. We performed this study to address this knowledge gap. The goal of our study was to examine the impact of policy change on regional differences in SLK utilization. Furthermore, we aimed to determine whether the policy implementation was associated with increased access to LT alone among candidates with pre-LT renal dysfunction.

2 | METHODS

2.1 | Study population and creation of cohorts

The UNOS database was used to extract a retrospective cohort of adults listed for LT from 8/1/14–06/12/20. Candidates with previous LT or KT were excluded (Figure 1). The study population was stratified to prepolicy (08/10/14 to 08/09/17) and postpolicy (08/10/17 to 06/12/20) eras. Liver disease etiology was stratified using the specific UNOS codes to alcohol-associated liver disease (ALD), nonalcoholic steatohepatitis (NASH), hepatitis C virus (HCV) infection, and other etiologies.

2.2 | Study outcomes

2.2.1 | Listings for simultaneous liver and kidney (SLK) transplant

SLK listings (listed for both liver and kidney within 90 days of each other) in the prepolicy era were compared with those listed in the postpolicy era for baseline characteristics.

2.2.2 | Waitlist outcomes among candidates listed for LT alone

Candidates listed for LT alone with renal dysfunction (eGFR < 30 mL/min as determined using the chronic kidney disease epidemiology collaboration or CKD-EPI equation),[21] or on dialysis at the time of listing were analyzed. The CKD-EPI equation for eGFR calculation was used as of all the equations which can be used using the UNOS registry, the eGFR using this equation is the closest to the measured GFR using the iothalamate clearance.[22] Baseline characteristics of the candidates and the frequency of renal dysfunction were compared between the pre- and postpolicy eras and also across UNOS regions. Chi-square ad analysis of variance tests were used for comparing categorical and continuous variables. This cohort was examined for 90-day probability of receiving LT and of waitlist mortality (removal from the list for death or being too sick for LT). As the MELD score predicts 3-month mortality in patients with cirrhosis,[23] we chose 90-day time point for this analysis. For this analysis, those listed between 04/01/2020 and 06/12/2020 were excluded to allow at least 90-day follow up for each candidate. Cumulative incidence rates for WL mortality and for receiving LT within 90 days were generated using competing risk analysis. The competing event was receiving LT or waitlist mortality for the respective outcomes of waitlist mortality and for receiving LT. Patients remaining on the waitlist through 90 days of follow-up were censored.

2.2.3 | Patient survival and renal outcomes among recipients of LT alone

Recipients of LT alone with renal dysfunction were analyzed for patient survival and renal outcomes (eGFR, dialysis, listings for KAL, and receiving KAL) within 1 year after receiving LT alone. For this analysis, LT recipients during 08/10/2016–08/09/2017 and during 08/10/2019–06/12/2020 were excluded to allow at least 1-year Follow-up for each recipient and avoid overlap of recipients across the policy era. For data on dialysis, kidney listing, and KT was obtained from the kidney waitlist file which was merged with the follow-up file of LT recipients using a unique patient code. It should be noted that information on dialysis after LT may be underestimated, as this information is available from the kidney waitlist file and hence only for those candidates listed for KAL. Kaplan-Meier survival curves were obtained on 1-year patient survival. Frequency of significant renal dysfunction (eGFR > 30 mL/min or needing dialysis) at 6 and 12 months was also examined and compared for the two policy eras. Cumulative incidence of 1-year listing for and receiving KAL were derived comparing post vs. prepolicy era using competing risk analysis. The competing event was patient mortality within a year of receiving LT alone. Patients were censored at their maximum follow-up period.

We examined the total number of kidneys used (number of SLK + number of KT within a year of receiving LT alone) in the pre- and postpolicy periods. For a fair comparison, kidneys used within a year of listing for SLK or for KAL were analyzed. For this analysis, SLK transplants within 1-year of listing were included to keep homogeneity with the

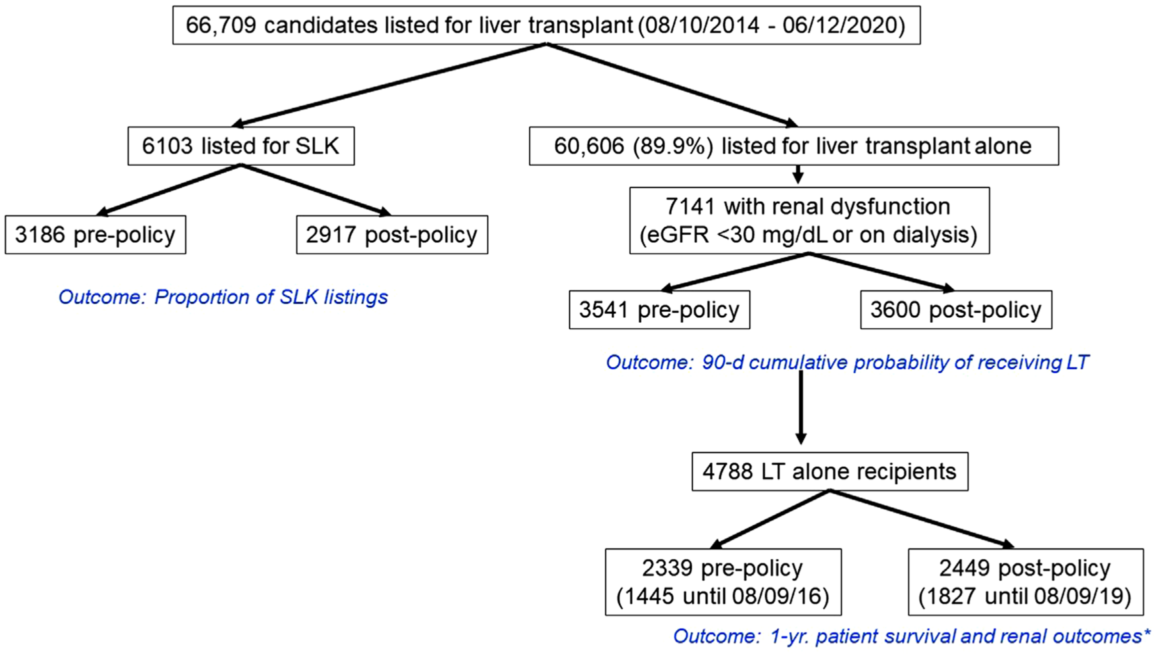

FIGURE 1 Schematic representation of study population and methodology for creation of study cohorts. *End-stage renal disease (estimated glomerular filtration rate < 30 mL/min or dialysis), listing for kidney, and receipt of kidney transplant

number of kidneys used within 1-year of receiving LT alone. As 2019–2020 data is only included from 08/10/19–06/12/20, the number of SLK and for KAL for this period was extrapolated as (N/10)*12.

2.3 | Statistical analyses

Chi-square and analysis of variance tests were used to compare categorical and continuous variables, respectively. Logistic regression model was built to examine the impact of policy era on the SLK listings. Variables different at baseline and those clinically relevant were added in the model. Results of logistic regression model were expressed as odds ratio (OR) with 95% confidence interval (CI). Gray's statistical test was used to compare the two policy eras on cumulative probabilities of receiving LT within 90-d of listing for LT alone and on kidney listing or KT within 1-year of receiving LT alone. Fine and Gray regression models were built to examine the impact of post vs. prepolicy period on receipt of LT within 90 days from listing and on kidney listing or KT within 1-year of receiving LT alone. Results were expressed as hazard ratio (HR) with 95% CI. Cox proportional hazards regression models were built to evaluate the impact of post vs. prepolicy period on patient survival at 1 year after LT. Variables different at baseline and those clinically relevant ones were entered in the model. Results of cox model were expressed as HR with 95% CI. Log rank test was used for statistical significance comparing the two policy eras on patient survival at 1-year of receiving LT alone. Interactions of policy era with the UNOS region and with liver disease etiology were examined for each outcome. If there was significant interaction, impact of policy era was examined across each UNOS region or liver disease etiology using separate logistic regression models. These models included the same variables as in the main models. *P*-values $< .05$ was considered significant for all the analyses. SAS version 9.4 (SAS Institute, Cary, NC, USA) was used for statistical analyses. Given a database study with de-identified data, the study qualified for waiver of consent and did not require any approval from the IRB.

3 | RESULTS

3.1 | Listings for simultaneous liver kidney

Of 66 709 candidates listed for first LT between 08/01/14 and 06/12/20, 6103 (9.1%) were listed for SLK (Figure 1). Proportion of SLK listings was 9.6% (3186 of 33 119) before and 8.7% (2917 of 33,590) after the implementation of policy, $P < .001$. Candidates listed for SLK during the postpolicy era vs. those listed during the prepolicy era were older, more likely to be females, listed for ALD, and on dialysis. Although the MELD scores in the two eras were not different, candidates listed during the postpolicy era had higher serum creatinine, but lower serum bilirubin and INR values (Table 1). Compared to prepolicy era, odds of SLK listings decreased by 22% during the years after the introduction of OPTN policy, .78 (.72-.84), $P < .001$. Other predictors for SLK listings were female gender, diabetes mellitus, on dialysis, black and Hispanic race, and ALD or NASH vs. HCV liver disease etiology. There was interaction of policy era with UNOS region ($P < .001$) but not with liver disease etiology ($P = .33$).

Among 2661 (1302 prepolicy) SLK transplants performed, futile SLK cases (deaths within 15 days) were similar comparing pre- and post-policy periods (2.5% vs. 2.2%, $P = .663$). Of 2598 SLK transplants with eGFR < 30 prior to transplant without being on dialysis, there were

TABLE 1 Baseline characteristics of candidates listed for simultaneous liver kidney (SLK) transplants comparing pre vs. post policy eras

Variable	Pre-policy era (N = 3186)	Post-policy era (N = 2917)	*P*
Age in years at listing	53 ± 16	54 ± 15	<.007
% Females	40	43	<.02
% C, AA, H	61, 14, 20	60, 13, 21	.66
% diabetes mellitus	56.4	55.9	.1
% on dialysis	48	51	<.03
Serum bilirubin (mean ± SD) mg/dL	5.4 ± 8.8	4.4 ± 7.7	<.001
INR (mean ± SD)	1.58 ± .7	1.51 ± .6	<.001
Serum creatinine (mean ± SD) mg/dL	3.5 ± 2.4	3.7 ± 2.4	<.001
Serum sodium (mean ± SD) mEq/L	136 ± 4	137 ± 4	<.08
MELD score (mean ± SD) at listing	23.2 ± 10.2	23 ± 9.3	.32
% HCV, ALD, NASH etiology	21, 25, 20	13, 28, 24	<.001

OR, Odds ratio; CI, Confidence interval; INR, Institutional normalized ratio; HCV, Hepatitis C virus; ALD, Alcohol-associated liver disease; NASH, Nonalcoholic steatohepatitis.

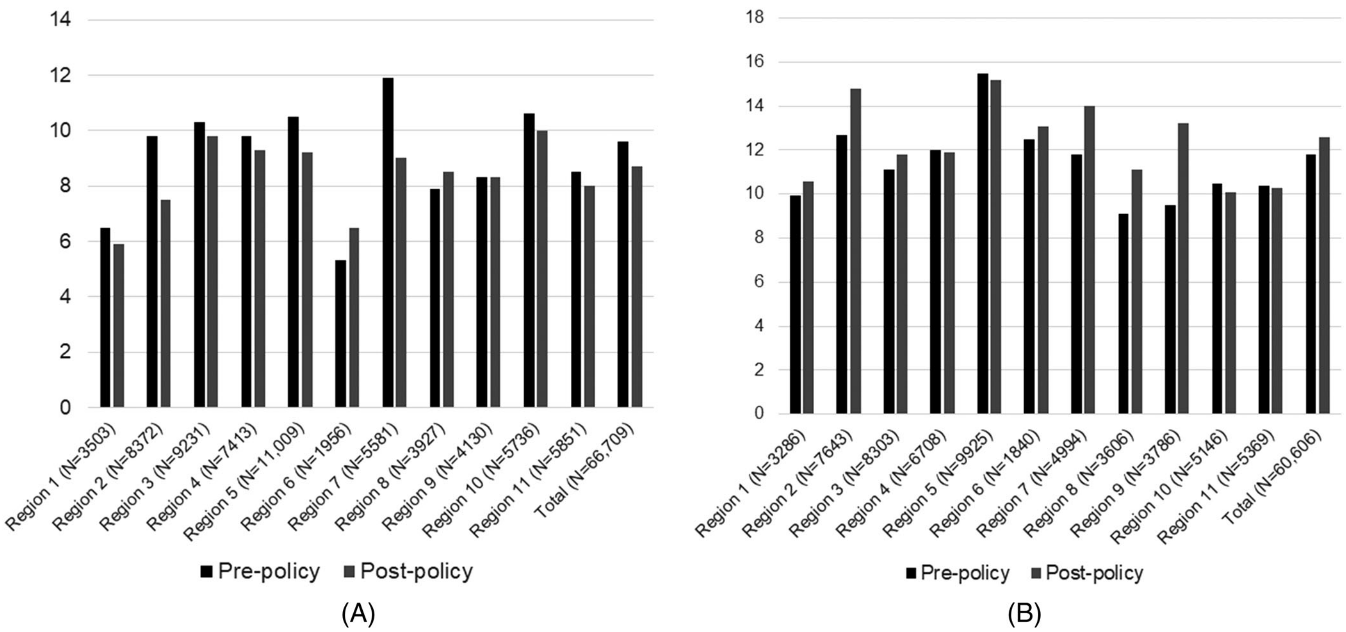

FIGURE 2 Frequency of listings for simultaneous liver and kidney transplantation across 11 UNOS regions (A) and of renal dysfunction (estimated glomerular filtration rate < 30 or on dialysis within previous week of listing) among listings for liver transplant alone (B) across 11 UNOS regions during the prepolicy (08/10/2014-08/09/2017) and the postpolicy era (08/10/2017-06/12/2020)

four recipients with delayed graft function (requirement of dialysis within first week of receiving SLK), one of 1341 in the pre- and three of 1257 in the postpolicy period, $P = .287$.

3.1.1 | Impact of UNOS region on SLK listings

SLK listings varied from 5.3% in region 6–11.9% in region 7 during the prepolicy era, and 5.9% in region 1–10% in region 10 during the postpolicy era (Figure 2A). Baseline characteristics were different across UNOS regions (Table S1). SLK listings in the postpolicy era decreased in all the regions except regions 6 and 8, which showed an increase and region 9 where the frequency of SLK use remained unchanged. Stratified logistic regression models for each UNOS region after controlling for all the variables as in the main model showed decrease in the use of SLK in the postpolicy era for regions 2, 5, and 7 and no difference for other regions (Table 2A).

3.2 | Renal dysfunction among candidates listed for liver transplant alone

Of the 60 606 candidates listed for LT alone, 7418 (12.2%) had renal dysfunction at the time of listing. The prevalence of renal dysfunction was 11.8% (3541 of 29 933) before and 12.6% (3877 of 30 673) after

TABLE 2 Logistic regression models for each UNOS region on odds of (A) SLK listing in the post vs. prepolicy era and (B) renal dysfunction among candidates listed for liver transplant alone

A)					
	Pre-policy	Post-policy	OR	95% CI	P
Region 1	111 (1699)	106 (1804)	.7	.18-1.01	.059
Region 2	430 (4375)	299 (3997)	.57	.46-.70	<.001
Region 3	467 (4519)	461 (4712)	.91	.76-1.09	.3
Region 4	352 (3603)	352 (3810)	.87	.70-1.07	.18
Region 5	576 (5468)	508 (5541)	.76	.64-.89	<.001
Region 6	53 (993)	63 (963)	1.08	.66-1.79	.76
Region 7	341 (2855)	246 (2746)	.63	.50-.79	<.001
Region 8	162 (2059)	159 (1868)	.88	.66-1.19	.41
Region 9	166 (1996)	178 (2134)	.92	.69-1.23	.59
Region 10	288 (2726)	302 (3010)	.9	.73-1.12	.33
Region 11	240 (2826)	242 (3025)	.83	.64-1.07	.15
B)					
	Pre-policy	Post-policy	OR	95% CI	P
Region 1	158 (1588)	180 (1698)	.94	.59-1.51	.8
Region 2	499 (3945)	546 (3698)	.98	.76-1.27	.9
Region 3	449 (4052)	503 (4251)	1.06	.81-1.39	.68
Region 4	391 (3251)	410 (3457)	.79	.58-1.08	.14
Region 5	760 (4892)	765 (5033)	1.14	.90-1.43	.28
Region 6	117 (940)	118 (900)	1.13	.63-2.03	.69
Region 7	296 (2514)	346 (2480)	1.13	.82-1.58	.45
Region 8	173 (1897)	190 (1709)	.97	.66-1.43	.88
Region 9	174 (1830)	260 (1956)	1.32	.89-1.96	.17
Region 10	256 (2430)	273 (2708)	.89	.64-1.23	.48
Region 11	268 (2586)	286 (2783)	.84	.60-1.18	.32

the implementation of OPTN policy, $P < .003$. Candidates with renal dysfunction and listed for LT alone during the postpolicy era vs. those listed during the prepolicy era were more likely to be listed for ALD and be on dialysis. Although the MELD scores in the two eras were not different, candidates listed during the postpolicy era had higher bilirubin values (Table 3). Compared to prepolicy era, odds of renal dysfunction among candidates listed for LT alone were not different in the post vs. prepolicy era, 1.01 (.96-1.07), $P = .67$. Other predictors for renal dysfunction among listings for LT alone were female gender, diabetes mellitus, serum bilirubin, INR, serum sodium, and NASH or ALD vs. HCV liver disease etiology. There was an interaction of policy era with UNOS region ($P < .03$) but not with liver disease etiology ($P = .32$).

3.2.1 | Impact of UNOS region on LT alone listings

Frequency of renal dysfunction among listings for LT alone decreased in region 10, remained unchanged in regions 4, 5, and 11, and increased in other UNOS regions (Figure 2B). None of the regions showed any change in frequency of listings for LT alone among candidates with renal dysfunction on analysis of stratified logistic regression models for each UNOS region (Table 2B).

3.2.2 | Liver transplant and mortality within 90 days of listing for LT alone with renal dysfunction

Of 7141 candidates listed for LT alone with renal dysfunction at the time of listing (3600 after and 3541 before implementation of the policy), 4334 (61%) received LT within 90 days from listing. The 90-day probability of receiving LT after the policy was implemented was 64% as compared to 61% before the policy implementation, $P < .001$ (Figure 3A). In a Fine and Gray competing risk model, 90-day cumulative probability of receiving LT was 7% higher in the post vs. prepolicy era, 1.07 (1.00-1.15), $P = .037$. Other predictors were young age, white race, male gender, and listing MELD score (data not shown). A total of 1223 (17.1%) candidates died within 90 days from listing, with lower cumulative probability among candidates listed after vs. before implementation of the policy, (14.4% vs. 16%, $P < .001$), (Figure 3B).

3.3 | One-year outcomes in recipients of LT alone with renal dysfunction

3.3.1 | Patient survival

Of 3272 recipients of LT alone, 1-year patient survival among 1445 recipients during prepolicy era was 91.5% and among 1827 transplanted during postpolicy era was 92.2%, $P = .67$ (Figure S1). LT recipients in the pre vs. post policy era were similar on age at transplant (43.2±22.8 vs. 42.3±23.4 years, $P = .26$), female gender (45% vs. 46%, $P = .40$), race/ethnicity Caucasians: blacks: Hispanics (67:10:18 vs. 65:9:19, $P = .30$), diabetes mellitus (20% vs. 19%, $P = .46$), and eGFR (80.8±232.7 vs. 120.6±984.8). After controlling for all the variables, there was no difference on patient survival comparing post vs. prepolicy period, .96 (.74-1.24), $P = .75$. Age at transplant, black race, and ALD vs. HCV liver disease etiology predicted 1-year patient survival.

3.4 | Renal outcomes

The renal outcomes at 1-year after LT alone were analyzed among 3230 LT alone recipients (1432 before and 1798 after policy implementation) who had renal dysfunction at the time of listing, but were not dialysis at the time of transplantation.

3.4.1 | Renal dysfunction

A total of 111 (3.4%) LT recipients (83 after policy introduction) needed dialysis within 1-year, with higher probability among LT recipients in the postvs. prepolicy era (5.6% vs. 2.3%, $P < .001$), Figure S2. In a

TABLE 3 Candidates with renal dysfunction (estimated glomerular filtration rate < 30 mL/min or on dialysis) listed for liver transplant alone: (A) comparing baseline characteristics for pre vs. post policy eras

Variable	Pre-policy era (N = 3541)	Post-policy era (N = 3600)	*P*
Age in years at listing	45 ± 23	45 ± 22	.82
% females	49	48	.45
% C, AA, H	66, 10, 18	65, 9, 19	.16
% diabetes mellitus	23	21	.22
% dialysis	33	37	<.001
Serum bilirubin (mean ± SD) mg/dL	14.3 ± 13.1	15.1 ± 13.6	<.02
INR (mean ± SD)	2.3 ± 1.4	2.4 ± 1.5	.73
Serum creatinine (mean ± SD) mg/dL	2.6 ± 2.0	2.6 ± 2.0	.25
Serum sodium (mean ± SD) mEq/L	136 ± 6	136 ± 5	.33
MELD score (mean ± SD)	27.8 ± 14.4	28.3 ± 14.8	.21
% HCV, ALD, NASH	14, 28, 14	6, 37, 17	

OR, Odds ratio; CI, Confidence interval; INR, Institutional normalized ratio; HCV, Hepatitis C virus; ALD, Alcohol-associated liver disease; NASH, Nonalcoholic steatohepatitis.

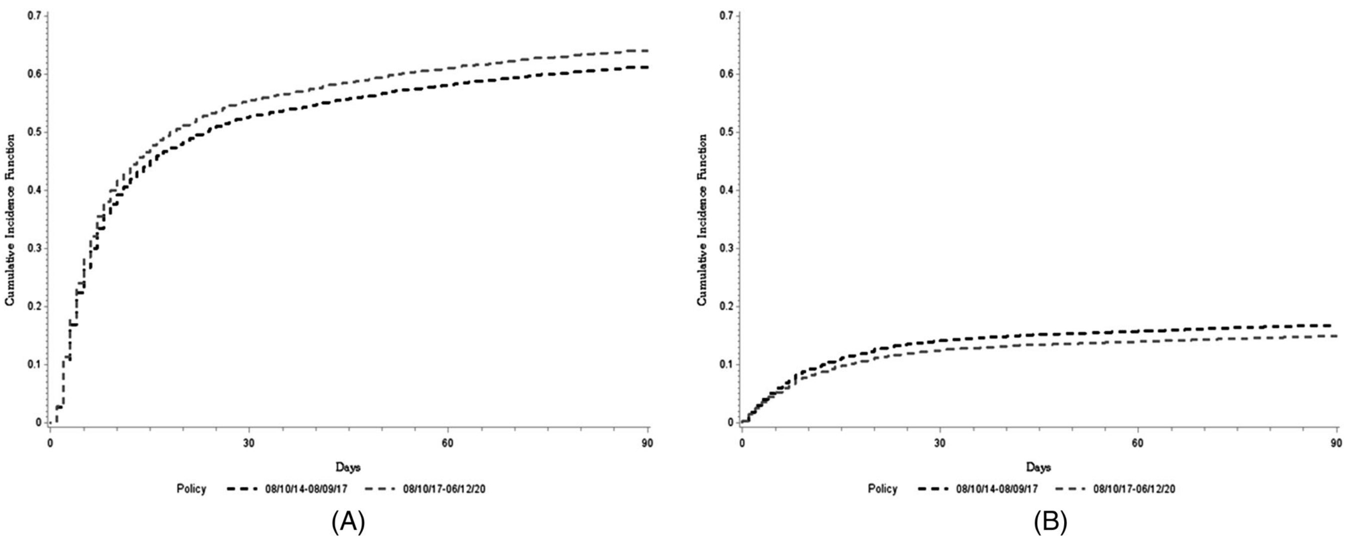

FIGURE 3 Cumulative 90-day probability of receiving liver transplant (A) and of patient mortality while waiting on the list (B) among candidates with renal dysfunction (serum creatinine > 1.5/dL at or on dialysis within previous week of listing) and listed for liver alone. Comparison for listed candidates after (08/10/17-03/31/20, gray line) vs. before (08/10/14-08/09/17, black line) implementation of the OPTN policy

competing risk model controlling for demographics (age, gender, and race), diabetes mellitus, eGFR, UNOS region, and liver disease etiology, the subhazard for requirement of dialysis within 1-year of receiving LT alone was higher by 2.5-folds in the post vs. prepolicy era, 2.46 (1.58-3.83), $P < .001$. None of the other variables predicted need for dialysis. There was no interaction of policy era with region ($P = .78$) or with liver disease etiology ($P = .76$).

Frequency of renal dysfunction (eGFR < 30 or on dialysis) at six months follow up was higher among recipients in the postpolicy (N = 1190) vs. prepolicy (N = 894) era (14.7% vs. 11.4%, $P = .028$). The frequency of renal dysfunction at 12 months tended to be higher among recipients in the postpolicy (N = 1095) vs. prepolicy (N = 1009) era (16.4% vs. 13.7%, $P = .087$).

3.4.2 | Listing for and receipt of KAL

A total of 153 (4.7%) recipients (133 in the postpolicy era) needed to be listed for KAL within 1-year, with a higher probability among LT recipients in the post vs. prepolicy era (11.4% vs. 2.0%, $P < .001$), Figure S3A. In a competing risk model, the subhazard for KAL listing within 1-year of receiving LT alone was higher by about 5.3-folds in the post vs. prepolicy era, 5.27 (3.27-8.50), $P < .001$. There was interaction of policy era with region ($P < .001$) but not with liver disease etiology ($P = .38$).

A total of 52 (1.6%) recipients (48 in the postpolicy era) received KAL within 1-year, with a higher probability among LT recipients in the post vs. prepolicy era (3.7% vs. 0.25%, $P < .001$), Figure S3B. In a competing risk model, the subhazard for KT within 1-year was higher by

TABLE 4 Impact of OPTN policy on the number of kidneys used (SLK within 1 year of listing and KT within 1 year of LT alone) in the pre- and post policy eras

	Pre-policy era (08/10/14-08/09/17)		Post-policy era (08/10/17-08/09/20)[a]			
	SLK transplants	KAL after LT alone	SLK transplants	KAL after LT alone	Net saving of kidneys	% change in post vs. pre-policy era
Region 1	37	0	32	3	2	2.9
Region 2	182	1	125	7	51	16.6
Region 3	277	0	276	12	−11	−2.0
Region 4	119	0	115	7	−3	−1.3
Region 5	238	2	224	13	3	.6
Region 6	28	0	32	0	−4	−6.7
Region 7	152	1	102	5	46	18.1
Region 8	94	0	103	2	−11	−5.6
Region 9	63	0	63	3	−3	−2.4
Region 10	147	0	158	3	−14	−4.6
Region 11	136	0	117	8	11	4.3
Total	1473	4	1347	63	67	2.4

[a]As 2019–2020 data is only included from 08/10/19–06/12/20, the number of SLK and for KAL for this period was extrapolated as (N/10)*12.
OPTN, Organ Procurement Transplant Network; SLK, Simultaneous liver kidney; KT, Kidney transplant; LT, Liver transplant.

about 15-folds in the post vs. prepolicy era, 14.6 (4.5-47.4), $P < .001$. There were no other predictors for listing or need for KAL within 1-year of receiving LT alone. There was an interaction of policy era with region and with liver disease etiology, $P < .001$ for both.

3.5 | Impact of OPTN policy on the donor kidney pool

Although there was an interaction between policy era and the UNOS region for KAL listing and for receiving KAL within 1-year of LT alone, we did not perform stratified cox models due to small number of events in each region (Table 4). Total number of kidneys used for SLK transplants or under safety net (KAL within 1-year after receiving LT alone) were calculated. Of 3194 SLK transplants (1785 in pre- and 1409 in postpolicy era), 2755 (1282 in postpolicy era) were performed within 1 year from the time of SLK listing. After extrapolating 323 SLK transplants and 23 KAL in the postpolicy era to until 08/09/20, a total of 2820 SLK (1347 in postpolicy era) and 67 KAL (63 in the postpolicy era), a total of 67 (2.4%) kidneys were saved in the postpolicy era. Across regions, 51 (16.6%) and 46 (18.1%), 11 (4.3%), and 2 (2.9%) kidneys were saved in the postpolicy era in the UNOS regions 2, 7, 11, and 1, respectively. There was no change in region 5, while in other regions, a total of 46 more kidneys were used in the postpolicy era (Table 4). As listing for KAL within a year of receiving LT alone does not mean that the candidate has to receive kidney within a period of 365 days, as the safety net priority continues as long as they are listed within 1 year of receiving liver alone. Presuming that every candidate listed for SLK or for KAL will end up receiving kidney, analysis on number of donor kidneys used was revised using SLK and KAL listings in the pre and post policy periods. Number of KAL listings remained unchanged with 3206 kidney listings (20 after LT alone) before policy and 3230 kidney listings (141 after LT alone) in the postpolicy period.

4 | DISCUSSION

Our study confirms that since the implementation of the OPTN policy on SLK allocation, there has been a decrease in listings for SLK, and an increase in 1-year probability of listing for and need for KT among recipients of LT alone. The net effect on the total number of kidneys used (SLK within 1-year listing and KAL within 1-year of LT alone) decreased by 2.4% in the postpolicy era. NASH as liver disease etiology had highest odds of being listed for SLK and to require KAL after receiving LT alone. In addition, our study provides novel observation that although regional variation on SLK and of KT among recipients of LT alone has decreased, there remains regional variation, with net decrease in total number of kidneys in UNOS regions 7, 2, and 11. We also showed an increased access to and probability of receiving LT within 90 days from listing among candidates with renal dysfunction, with highest odds of receiving LT in patients listed for ALD etiology.

The OPTN policy was introduced in August 2017 in order to optimize the use of SLK transplantation. The SLK listings decreased by about 10% (9.6% to 8.7%), with 22% reduced odds for SLK listing since the introduction of the OPTN policy. In another recently reported study using the UNOS database until 06/12/2019, the SLK transplant decreased by about 9% (13.4% to 11.8%) among transplant recipients with eGFR > 30 mL/min since the introduction of the OPTN policy.[19] Our study confirms the same findings using data with extended data analysis until 06/12/2020.

We also showed a higher probability of receiving LT alone within 90 days from listing in the postpolicy era among patients listed with renal dysfunction. It is likely that changes in liver allocation policy simultaneous to the implementation of OPTN policy and increasing number of donors with time resulted in better access to liver grafts. However, as the policy is more restrictive requiring transplant centers to meet certain criteria before getting approval for SLK listing, it is possible that better access to liver graft may be due to candidates waiting only for one rather than two simultaneous organs. In our analysis also, 56% of all LT alone were in the postpolicy period despite equal distribution of patients to before and after the policy implementation for patients listed for LTA. Decrease in waitlist time due to the need for only liver instead of both liver and kidney likely results in improved access to transplant and waitlist outcomes. Ethnic minorities (black, Hispanic, or other race) and females were less likely to receive LT as has been shown in previous studies.[24–26]

About 16% of LT alone recipients developed end-stage renal disease in the postpolicy era in our analysis. In another study from a single center, of 44 LT alone recipients who met the new SLK criteria, the prevalence of end-stage renal disease was lower at 4.8%. Lower prevalence in this study is likely due to definition of end-stage renal disease based on eGFR ≤20 mL/min, instead of 30 mL/min. in our analysis.[17] To address the concern of LT-alone recipients in the postpolicy era of being disadvantaged and potentially worse renal outcomes, a safety net approach was included within the new policy. Under this approach, recipients developing end-stage renal disease or requiring dialysis between 60 and 364 days after LT alone are prioritized for listing for and receipt of KAL. Our study findings of increase in listing for and receipt of KAL in the postpolicy era within 1-year of receiving LT alone are similar to a recently reported study using the UNOS database until 06/12/2019, with an increase in kidney listing and KT in the post vs. prepolicy era: 8.8% vs. 2.9% and 4.0% vs. .7%, respectively.[19] Importantly, the total number of kidneys used (SLK combined with KAL within a year of LT alone) reduced marginally by 2.4% in the postpolicy era.

LT-alone recipients in the postpolicy period were more likely to be listed for or require KAL, clearly suggesting a need for closer monitoring of their renal function in the post-transplant follow up period. However, this did not impact the patient's survival at 1 year after receiving LT alone, similar to another recently reported study using the UNOS database.[19] In another study reported from a single center on recipients of LT alone, 1-year patient survival of 44 patients meeting the new SLK criteria was similar to 302 who did not meet these criteria (95% vs. 94%, $P = .53$).[17] However, the small sample size and data from a single center probably explain difference on absolute patient survival rates in this compared to our UNOS database study. In a UNOS-based analysis, recipients of LT alone meeting the new SLK criteria had better 2-year patient survival compared to SLK recipients based on the SLK criteria before implementation of the policy. These findings suggest that although the new SLK criteria may decrease and homogenize the use of SLK across centers and regions, this policy may not result in improvement of post-transplant survival.[27] In another UNOS-based analysis on KSL listings, waitlist mortality reduced and access to KT increased since the implementation of OPTN policy, a finding similar to our study.[28] Although we did not patients patient or graft survival among KAL, 1-year patient and graft survival was similar to KT-alone recipients.[28]

The study findings demonstrate that the OPTN policy provides better access to liver among candidates with renal dysfunction listed for LT alone without affecting the patient outcomes. Although regional variation on the use of SLK has reduced since the new policy has been implemented, there remains regional heterogeneity on the use of SLK and on KAL within 1 year of receiving LT alone. This could be due to variations on baseline characteristics across regions in the population or on comfort level of centers with LT alone among patients meeting medical eligibility criteria, as these criteria are required if the centers would like to list the candidate for SLK, but do not mandate them to do so. In the new OPTN policy, SLK listing needs to be approved by the UNOS and patients need to meet a set of criteria proposed in this policy, but these criteria do not mandate SLK listing and the centers or providers may use their judgment and comfort level to proceed with LT alone in spite of candidates meeting the new criteria. An additional potential source of heterogeneity may be variation on the formula chosen to estimate eGFR, as the UNOS does not mandate a specific eGFR equation. Based on liver disease etiology, NASH etiology had the strongest association with SLK listing and for need of KAL after LT alone. This finding is in alignment to previous reports with NASH etiology as the fastest growing indication for use of SLK, likely due to concomitant comorbidities such as diabetes, hypertension, and obesity.[20] Among candidates listed for LT alone who have renal dysfunction at listing, ALD etiology was most strongly associated with receipt of LT, likely due to presence of concomitant alcoholic hepatitis with severe disease and younger age in this population.[29,30]

Analysis using the UNOS database with a large sample size is a strength of our study. Using extended data until June 2020, our study confirmed recently reported findings on SLK and use of kidney after LT alone. Further, we followed a rigorous approach to extract the study population, allowing at least 90-day follow-up for every listed candidate to examine 90-day wait list outcomes, and at least 1-year among those receiving LT alone to examine 1-year patient survival and renal outcomes. However, our studies suffer from some limitations. Being a database study without access to medical charts of patients, the study suffers from potential inaccuracy and content of any database. We did not examine the type of renal dysfunction requiring SLK, whether acute kidney injury or chronic kidney disease. It is also difficult to examine from the data whether the increased use of KAL within 1-year of LT alone is a true policy impact or confounded by increasing prevalence of NASH and elderly population receiving LT. Lastly, information on dialysis within a year of receiving LT alone may be underestimated, as this information was available only among recipients for KAL in the kidney waitlist file.

In summary, our UNOS database analysis shows that the OPTN policy for SLK allocation has resulted in decreased use of SLK and improved access to LT alone among those with renal dysfunction. In spite of increased use of KT within 1 year of receiving LT alone under safety net, less number of kidneys were used in the postpolicy era without impact on patient survival, mostly from regions 7, 2, and 11. NASH etiology is associated with SLK listings and KAL after LT alone, and ALD with receiving transplant after listing for LT alone. Studies with longer follow up are needed to assess the impact of OPTN policy on kidney donor pool and renal outcomes after receiving LT alone, and reexamine the new criteria as a basis to further optimize and homogenize regional allocation of SLK.

ACKNOWLEDGMENT

No funding was received for this study.

CONFLICTS OF INTEREST

None of the authors have any financial or any other conflicts of interest to disclose.

AUTHOR CONTRIBUTIONS

Ashwani K. Singal conceived the study idea. **Ashwani K. Singal, Pratima Sharma, Mitra Nadim, and Yong-Fang Kuo** designed the study and interpreted the data. **Yong-Fang Kuo** performed statistical analyses. **Ashwani K. Singal** wrote the initial draft. All the authors provided important input and reviewed to approve the final version.

DATA AVAILABILITY STATEMENT

Data supporting this study are available in the UNOS dataset.

ORCID

Ashwani K. Singal https://orcid.org/0000-0003-1207-3998
Nadim Mahmud https://orcid.org/0000-0003-1889-3954
Pratima Sharma https://orcid.org/0000-0002-1182-0579

REFERENCES

1. Angeli P, Garcia-Tsao G, Nadim MK, Parikh CR. News in pathophysiology, definition and classification of hepatorenal syndrome: a step beyond the International Club of Ascites (ICA) consensus document. *J Hepatol*. 2019;71(4):811-822.
2. Tariq R, Singal AK. Management of hepatorenal syndrome: a review. *J Clin Transl Hepatol*. 2020;8(2):192-199.
3. Francoz C, Durand F, Kahn JA, Genyk YS, Nadim MK. Hepatorenal syndrome. *Clin J Am Soc Nephrol*. 2019;14(5):774-781.
4. Boyer TD, Sanyal AJ, Garcia-Tsao G, et al. Impact of liver transplantation on the survival of patients treated for hepatorenal syndrome type 1. *Liver Transpl*. 2011;17(11):1328-1332.
5. Sharma P, Goodrich NP, Zhang M, Guidinger MK, Schaubel DE, Merion RM. Short-term pretransplant renal replacement therapy and renal nonrecovery after liver transplantation alone. *Clin J Am Soc Nephrol*. 2013;8(7):1135-1142.
6. Nadim MK, Genyk YS, Tokin C, et al. Impact of the etiology of acute kidney injury on outcomes following liver transplantation: acute tubular necrosis versus hepatorenal syndrome. *Liver Transpl*. 2012;18(5):539-548.
7. Hmoud B, Kuo YF, Wiesner RH, Singal AK. Outcomes of liver transplantation alone after listing for simultaneous kidney: comparison to simultaneous liver kidney transplantation. *Transplantation*. 2015;99(4):823-828.
8. Gonwa TA, McBride MA, Anderson K, Mai ML, Wadei H, Ahsan N. Continued influence of preoperative renal function on outcome of orthotopic liver transplant (OLTX) in the US: where will MELD lead us?. *Am J Transplant*. 2006;6(11):2651-2659.
9. Singal AK, Ong S, Satpathy S, Kamath PS, Wiesner RH. Simultaneous liver kidney transplantation. *Transpl Int*. 2018.
10. Singal AK, Salameh H, Kuo YF, Wiesner RH. Evolving frequency and outcomes of simultaneous liver kidney transplants based on liver disease etiology. *Transplantation*. 2014;98(2):216-221.
11. Formica RN, Aeder M, Boyle G, et al. Simultaneous liver-kidney allocation policy: a proposal to optimize appropriate utilization of scarce resources. *Am J Transplant*. 2016;16(3):758-766.
12. Nadim MK, Davis CL, Sung R, Kellum JA, Genyk YS. Simultaneous liver-kidney transplantation: a survey of US transplant centers. *Am J Transplant*. 2012;12(11):3119-3127.
13. Davis CL, Feng S, Sung R, et al. Simultaneous liver-kidney transplantation: evaluation to decision making. *Am J Transplant*. 2007;7(7):1702-1709.
14. Eason JD, Gonwa TA, Davis CL, Sung RS, Gerber D, Bloom RD. Proceedings of Consensus Conference on Simultaneous Liver Kidney Transplantation (SLK). *Am J Transplant*. 2008;8(11):2243-2251.
15. Nadim MK, Sung RS, Davis CL, et al. Simultaneous liver-kidney transplantation summit: current state and future directions. *Am J Transplant*. 2012;12(11):2901-2908.
16. Hart A, Smith JM, Skeans MA, et al. OPTN/SRTR 2016 annual data report: kidney. *Am J Transplant*. 2018;18(Suppl 1):18-113.
17. Jiang DD, Roayaie K, Woodland D, Orloff S, Scott D. Survival and renal function after liver transplantation alone in patients meeting the new United Network for Organ Sharing simultaneous liver-kidney criteria. *Clin Transplant*. 2020;34(10):e14020.
18. Jay CL, Washburn WK, Rogers J, Harriman D, Heimbach J, Stratta RJ. Difference in survival in early kidney after liver transplantation compared with simultaneous liver-kidney transplantation: evaluating the potential of the "safety net". *J Am Coll Surg*. 2020;230(4):463-473.
19. Samoylova ML, Wegermann K, Shaw BI, et al. The impact of the 2017 kidney allocation policy change on simultaneous liver kidney utilization and outcomes. *Liver Transpl*. 2021.
20. Singal AK, Hasanin M, Kaif M, Wiesner R, Kuo YF. Nonalcoholic steatohepatitis is the most rapidly growing indication for simultaneous liver kidney transplantation in the United States. *Transplantation*. 2016;100(3):607-612.
21. Levey AS, Stevens LA, Schmid CH, et al. A new equation to estimate glomerular filtration rate. *Ann Intern Med*. 2009;150(9):604-612.
22. Francoz C, Nadim MK, Baron A, et al. Glomerular filtration rate equations for liver-kidney transplantation in patients with cirrhosis: validation of current recommendations. *Hepatology*. 2014;59(4):1514-1521.
23. Kamath PS, Wiesner RH, Malinchoc M, et al. A model to predict survival in patients with end-stage liver disease. *Hepatology*. 2001;33(2):464-470.
24. Mathur AK, Schaubel DE, Gong Q, Guidinger MK, Merion RM. Racial and ethnic disparities in access to liver transplantation. *Liver Transpl*. 2010;16(9):1033-1040.
25. Rosenblatt R, Wahid N, Halazun KJ, et al. Black patients have unequal access to listing for liver transplantation in the United States. *Hepatology*. 2021.
26. Locke JE, Shelton BA, Olthoff KM, et al. Quantifying sex-based disparities in liver allocation. *JAMA Surg*. 2020;155(7):e201129.
27. Cullaro G, Hirose R, Lai JC. Changes in simultaneous liver kidney transplant allocation policy may impact post liver transplant outcomes. *Transplantation*. 2018.
28. Wilk AR, Booker SE, Stewart DE, et al. Developing simultaneous liver-kidney transplant medical eligibility criteria while providing a safety net: a 2-year review of the OPTN's allocation policy. *Am J Transplant*. 2021;21(11):3593-3607.
29. Xie C, Kuo YF, Singal AK. Changing population of liver transplant recipients in the era of direct-acting antiviral therapy. *J Clin Transl Hepatol*. 2020;8(3):262-266.

30. Cotter TG, Sandikci B, Paul S, et al. Liver transplantation for alcoholic hepatitis in the United States: excellent outcomes with profound temporal and geographic variation in frequency. *Am J Transplant*. 2021;21(3):1039-1055.

SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

How to cite this article: Singal AK, Kuo Y-F, Kwo P, Mahmud N, Sharma P, Nadim MK. Impact of medical eligibility criteria and OPTN policy on simultaneous liver kidney allocation and utilization. *Clin Transplant*. 2022;36:e14700. https://doi.org/10.1111/ctr.14700