

Short informative title: SLK Transplantation and OPTN Policy

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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.

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Abbreviations (in alphabetical order): **ALD**: Alcohol-associated Liver Disease; **CI**: Confidence Interval; **eGFR**: estimated Glomerular Filtration Rate; **HR**: Hazard Ratio; **HCV**: Hepatitis C virus; **KT**: Kidney Transplant; **LT**: Liver Transplantation; **MELD**: Model for End-stage Disease; **NASH**: Non Alcoholic Steato-Hepatitis; **OR**: Odds Ratio; **OPTN**: Organ Procurement Transplant Network; **SLK**: Simultaneous Liver Kidney; **UNOS**: United Network for Organ Sharing

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Impact of Medical Eligibility Criteria and OPTN Policy on Simultaneous Liver Kidney Allocation And Utilization

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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<30mL/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<0.001), with 22% reduced odds of SLK listing in the post-policy era, with 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-yr. probability was higher in post vs. pre-policy period for dialysis (5.6 vs. 2.3%; P<0.0001), KT listing (11.4 vs. 2.0%; P<0.0001) and KT (3.7 vs. 0.25%; P<0.0001). 67 (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 post-policy era, regional variation of SLK listings remains. In spite of increased use of KT within 1-yr of receiving LT alone under safety net, less number of kidneys were used without impact on patient survival in post-policy era.

Keywords: HRS; ESRD; Dialysis; Cirrhosis; OPTN

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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 <0.35.¹¹ To overcome this clinical unmet need and unequal allocation of organs, the OPTN implemented a policy on August 10th 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-yr. 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.

METHODS

Study Population and Creation of Cohorts (Figure 1)

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

Study Outcomes

A. Listings for simultaneous liver and kidney (SLK) transplant: SLK listings (listed for both liver and kidney within 90 days of each other) in the pre-policy era were compared with those listed in the post-policy era for baseline characteristics.

B. 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 was compared between the pre- and post-policy eras and also across UNOS regions. Chi-square and analysis of variance tests were used for comparing categorical and continuous variables. This cohort was examined for 90-d 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-d 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-d follow up for each candidate. Cumulative incidence rates for WL mortality and for receiving LT within 90-d 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.

C. 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 yr. 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-yr. 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-yr. patient survival. Frequency of significant renal dysfunction (eGFR>30 mL/min. or needing dialysis) at six and 12 months was also examined and compared for the two policy eras. Cumulative incidence of 1-yr. listing for and receiving KAL were derived comparing post vs. pre-policy

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 post-policy 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-yr. of listing were included to keep homogeneity with the number of kidneys used within 1-yr. of receiving LT alone. As 2019-2020 data is only included from 08/10/19 to 06/12/20, the number of SLK and for KAL for this period was extrapolated as $(N/10)*12$.

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-yr. of receiving LT alone. Fine and Gray regression models were built to examine the impact of post vs. pre-policy period on receipt of LT within 90-d from listing and on kidney listing or KT within 1-yr. 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. pre-policy period on patient survival at one year after LT. Variables different at baseline and those clinically relevant ones were entered in the model. Results of cox model were expressed as hazard ratio (HR) with 95% CI. Log Rank test used for statistical significance comparing the two policy eras on patient survival at 1-yr. 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 <0.05 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.

RESULTS

A) 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, $P<0.001$. Candidates listed for SLK during the post-policy era vs. those listed during the pre-policy era were older, more likely to be females, listed for ALD, and on dialysis. Although, the MELD score in the two eras were not different, candidates listed during the post-policy era had higher serum creatinine, but lower serum bilirubin and INR values (Table 1). Compared to pre-policy era, odds of SLK listings decreased by 22% during the years after the introduction of OPTN policy, 0.78 (0.72-0.84), $P<0.001$. 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 ($P<0.001$) but not with liver disease etiology ($P=0.33$).

Among 2661 (1302 pre-policy) SLK transplants performed, futile SLK cases (deaths within 15-d) were similar comparing pre- and post-policy periods (2.5 vs. 2.2%, $P=0.663$). Of 2598 SLK transplants with $eGFR<30$ prior to transplant without being on dialysis, there were 4 recipients with delayed graft function (requirement of dialysis within first week of receiving SLK), 1 of 1341 in the pre- and 3 of 1257 in the post-policy period, $P=0.287$.

Impact of UNOS Region on SLK Listings: SLK listings varied from 5.3% in region 6 to 11.9% in region 7 during the pre-policy era, and 5.9% in region 1 to 10% in region 10 during the post-policy era (Figure 2A). Baseline characteristics were different across UNOS regions (Table S1). SLK listings in the post-policy 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 post-policy era for regions 2, 5, and 7 and no difference for other regions (Table 2A).

B. 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 the implementation of OPTN policy, $P < 0.003$. Candidates with renal dysfunction and listed for LT alone during the post-policy era vs. those listed during the pre-policy era were more likely to be listed for ALD and be on dialysis. Although, the MELD score in the two eras were not different, candidates listed during the post-policy era had higher bilirubin values (Table 3). Compared to pre-policy era, odds of renal dysfunction among candidates listed for LT alone were not different in the post vs. pre-policy era, 1.01 (0.96-1.07), $P = 0.67$. 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 interaction of policy era with UNOS region ($P < 0.03$) but not with liver disease etiology ($P = 0.32$).

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).

Liver Transplant and Mortality Within 90-d 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-d from listing. The 90-d probability of receiving LT after the policy was implemented was 64% as compared to 61% before the policy implementation, $P < 0.001$ (Figure 3A). In a Fine and Gray competing risk model, 90-d cumulative probability of receiving LT was 7% higher in the post vs. pre-policy era, 1.07 (1.00-1.15), $P = 0.037$. 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-d from listing, with lower cumulative probability among candidates listed after vs. before implementation of the policy, (14.4 vs. 16% $P < 0.001$), (Figure 3B).

C 1-yr. Outcomes in Recipients of LT Alone With Renal Dysfunction

Patient Survival

Of 3272 recipients of LT alone, 1-yr. patient survival among 1445 recipients during pre-policy era was 91.5% and among 1827 transplanted during post-policy era was 92.2%, $P = 0.67$ (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, $P = 0.26$), female gender (45 vs. 46%, $P = 0.40$), race / ethnicity Caucasians: blacks: Hispanics (67:10:18 vs. 65:9:19, $P = 0.30$), diabetes mellitus (20 vs. 19%, $P = 0.46$), 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. pre-policy period, 0.96 (0.74-1.24), $P = 0.75$. Age at transplant, black race, and ALD vs. HCV liver disease etiology predicted 1-yr. patient survival.

Renal Outcomes

The renal outcomes at 1-yr. 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.

Renal dysfunction: A total of 111 (3.4%) LT recipients (83 after policy introduction) needed dialysis within 1-yr., with higher probability among LT recipients in the post- vs. pre-policy era (5.6 vs. 2.3%, $P<0.001$), Figure S2. In a competing risk model controlling for demographics (age, gender, and race), diabetes mellitus, eGFR, UNOS region, and liver disease etiology, the sub-hazard for requirement of dialysis within 1-yr. of receiving LT alone was higher by 2.5 folds in the post vs. pre-policy era, 2.46 (1.58-3.83), $P<0.001$. None of the other variables predicted need for dialysis. There was no interaction of policy era with region ($P=0.78$) or with liver disease etiology ($P=0.76$).

Frequency of renal dysfunction (eGFR <30 or on dialysis) at six months follow up was higher among recipients in the post-policy (N=1190) vs. pre-policy (N=894) era (14.7 vs. 11.4%, $P=0.028$). The frequency of renal dysfunction at 12 months tended to be higher among recipients in the post-policy (N=1095) vs. pre-policy (N=1009) era (16.4 vs. 13.7%, $P=0.087$).

Listing for and receipt of KAL: A total of 153 (4.7%) recipients (133 in the post-policy era) needed to be listed for KAL within 1-yr, with a higher probability among LT recipients in the post- vs. pre-policy era (11.4 vs. 2.0%, $P<0.001$), Figure S3A. In a competing risk model, the sub-hazard for KAL listing within 1-yr. of receiving LT alone was higher by about 5.3 folds in the post vs. pre-policy era, 5.27 (3.27-8.50), $P<0.001$. There was interaction of policy era with region ($P<0.001$) but not with liver disease etiology ($P=0.38$).

A total of 52 (1.6%) recipients (48 in the post-policy era) received KAL within 1-yr., with a higher probability among LT recipients in the post- vs. pre-policy era (3.7 vs. 0.25%, $P<0.001$), Figure S3B. In a competing risk model, the sub-hazard for KT within 1-yr. was higher by about 15 folds in the post vs. pre-policy era, 14.6 (4.5-47.4), $P<0.001$. There were no other predictors for listing or need for KAL within 1-yr. of receiving LT alone. There was interaction of policy era with region and with liver disease etiology, $P<0.001$ for both.

Impact of OPTN policy on the donor kidney pool

Although, there was interaction between policy era and the UNOS region for KAL listing and for receiving KAL within 1-yr. 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-yr. after receiving LT alone) were calculated. Of 3194 SLK transplants (1785 in pre- and 1409 in post-policy era), 2755 (1282 in post-policy era) were performed within 1 year from the time of SLK listing. After extrapolating 323 SLK transplants and 23 KAL in the post-policy era to until 08/09/20, a total of 2820 SLK (1347 in post-policy era) and 67 KAL (63 in the post-policy era), a total of 67 (2.4%) kidneys were saved in the post-policy era. Across regions, 51 (16.6%) and 46 (18.1%), 11 (4.3%), and 2 (2.9%) kidneys were saved in the post-policy 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 post-policy 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 one 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 post-policy period.

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-yr. 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-yr. listing and KAL within 1-yr. of LT alone) decreased by 2.4% in the post-policy 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 post-policy 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 candidate waiting only for one rather than two simultaneous organs. In our analysis also, 56% of all LT alone were in the post-policy 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 post-policy 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 post-policy 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 to 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 post-policy era within 1-yr. of receiving LT alone are similar to a recently reported study using the UNOS database until 06/12/2019, with increase in kidney listing and KT in the post vs. pre-policy era: 8.8% vs. 2.9% and 4.0% vs. 0.7% 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 post-policy era.

LT alone recipients in the post-policy 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 survival at 1-yr 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-yr. patient survival of 44 patients meeting the new SLK criteria was similar to 302 who did not meet these criteria (95 vs. 94%, $P=0.53$).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-yr. 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 examine patient or graft survival among KAL, 1-yr. 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 judgement 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-yr. among those receiving LT alone to examine 1 year patient survival and renal outcomes. However, our study suffers 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-yr. 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-yr of receiving LT alone under safety net, less number of kidneys were used in the post-policy 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.

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	<0.007
% Females	40	43	<0.02
% C, AA, H	61, 14, 20	60, 13, 21	0.66
% diabetes mellitus	56.4	55.9	0.1
% on dialysis	48	51	<0.03
Serum bilirubin (mean ± SD) mg/dL	5.4 ± 8.8	4.4 ± 7.7	<0.001
INR (mean ± SD)	1.58 ± 0.7	1.51 ± 0.6	<0.001
Serum creatinine (mean ± SD) mg/dL	3.5 ± 2.4	3.7 ± 2.4	<0.001
Serum sodium (mean ± SD) mEq/L	136 ± 4	137 ± 4	<0.08
MELD score (mean ± SD) at listing	23.2 ± 10.2	23 ± 9.3	0.32
% HCV, ALD, NASH etiology	21, 25, 20	13, 28, 24	<0.001

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

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Table 2 Logistic regression models for each UNOS region on odds of **A)** SLK listing in the post vs. pre-policy 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)	0.7	0.18-1.01	0.059
Region 2	430 (4375)	299 (3997)	0.57	0.46-0.70	<0.001
Region 3	467 (4519)	461 (4712)	0.91	0.76-1.09	0.3
Region 4	352 (3603)	352 (3810)	0.87	0.70-1.07	0.18
Region 5	576 (5468)	508 (5541)	0.76	0.64-0.89	<0.001
Region 6	53 (993)	63 (963)	1.08	0.66-1.79	0.76
Region 7	341 (2855)	246 (2746)	0.63	0.50-0.79	<0.001
Region 8	162 (2059)	159 (1868)	0.88	0.66-1.19	0.41
Region 9	166 (1996)	178 (2134)	0.92	0.69-1.23	0.59
Region 10	288 (2726)	302 (3010)	0.9	0.73-1.12	0.33
Region 11	240 (2826)	242 (3025)	0.83	0.64-1.07	0.15

B)

	Pre-policy	Post-policy	OR	95% CI	P
Region 1	158 (1588)	180 (1698)	0.94	0.59-1.51	0.8
Region 2	499 (3945)	546 (3698)	0.98	0.76-1.27	0.9
Region 3	449 (4052)	503 (4251)	1.06	0.81-1.39	0.68
Region 4	391 (3251)	410 (3457)	0.79	0.58-1.08	0.14
Region 5	760 (4892)	765 (5033)	1.14	0.90-1.43	0.28
Region 6	117 (940)	118 (900)	1.13	0.63-2.03	0.69
Region 7	296 (2514)	346 (2480)	1.13	0.82-1.58	0.45
Region 8	173 (1897)	190 (1709)	0.97	0.66-1.43	0.88
Region 9	174 (1830)	260 (1956)	1.32	0.89-1.96	0.17
Region 10	256 (2430)	273 (2708)	0.89	0.64-1.23	0.48
Region 11	268 (2586)	286 (2783)	0.84	0.60-1.18	0.32

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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	0.82
% females	49	48	0.45
% C, AA, H	66, 10, 18	65, 9, 19	0.16
% diabetes mellitus	23	21	0.22
% dialysis	33	37	<0.001
Serum bilirubin (mean ± SD) mg/dL	14.3 ± 13.1	15.1 ± 13.6	<0.02
INR (mean ± SD)	2.3 ± 1.4	2.4 ± 1.5	0.73
Serum creatinine (mean ± SD) mg/dL	2.6 ± 2.0	2.6 ± 2.0	0.25
Serum sodium (mean ± SD) mEq/L	136 ± 6	136 ± 5	0.33
MELD score (mean ± SD)	27.8 ± 14.4	28.3 ± 14.8	0.21
% 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: Non-alcoholic steatohepatitis

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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)*		Net saving of kidneys	% change in post vs. pre-policy era
	SLK transpla nts	KAL after LT alone	SLK transpla nts	KAL after LT alone		
Regi on 1	37	0	32	3	2	2.9
Regi on 2	182	1	125	7	51	16.6
Regi on 3	277	0	276	12	-11	-2.0
Regi on 4	119	0	115	7	-3	-1.3
Regi on 5	238	2	224	13	3	0.6
Regi on 6	28	0	32	0	-4	-6.7
Regi on 7	152	1	102	5	46	18.1
Regi on 8	94	0	103	2	-11	-5.6
Regi on 9	63	0	63	3	-3	-2.4
Regi on 10	147	0	158	3	-14	-4.6
Regi on 11	136	0	117	8	11	4.3
Total	1473	4	1347	63	67	2.4

* As 2019-2020 data is only included from 08/10/19 to 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

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Legends to Figures

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.*

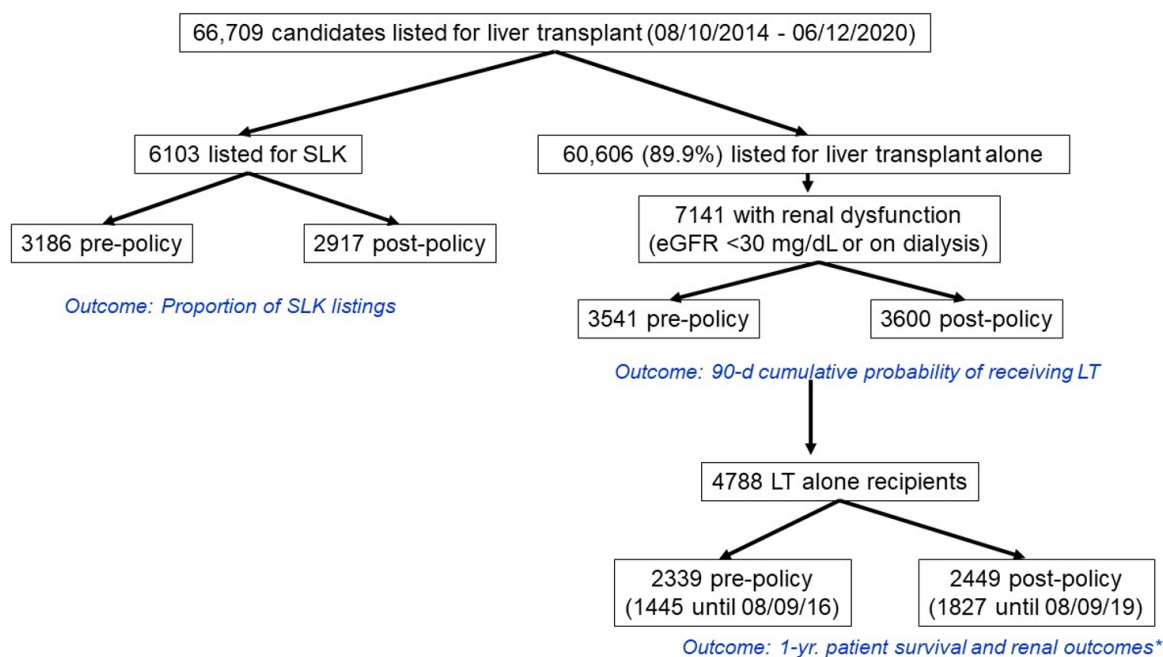


Figure 2 Frequency of listings for simultaneous liver and kidney transplantation across 11 UNOS regions **A**) and of renal dysfunction (estimated glomerular filtration rate <30 or on dialysis within previous week of listing) among listings for liver transplant alone **B**) across 11 UNOS regions during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

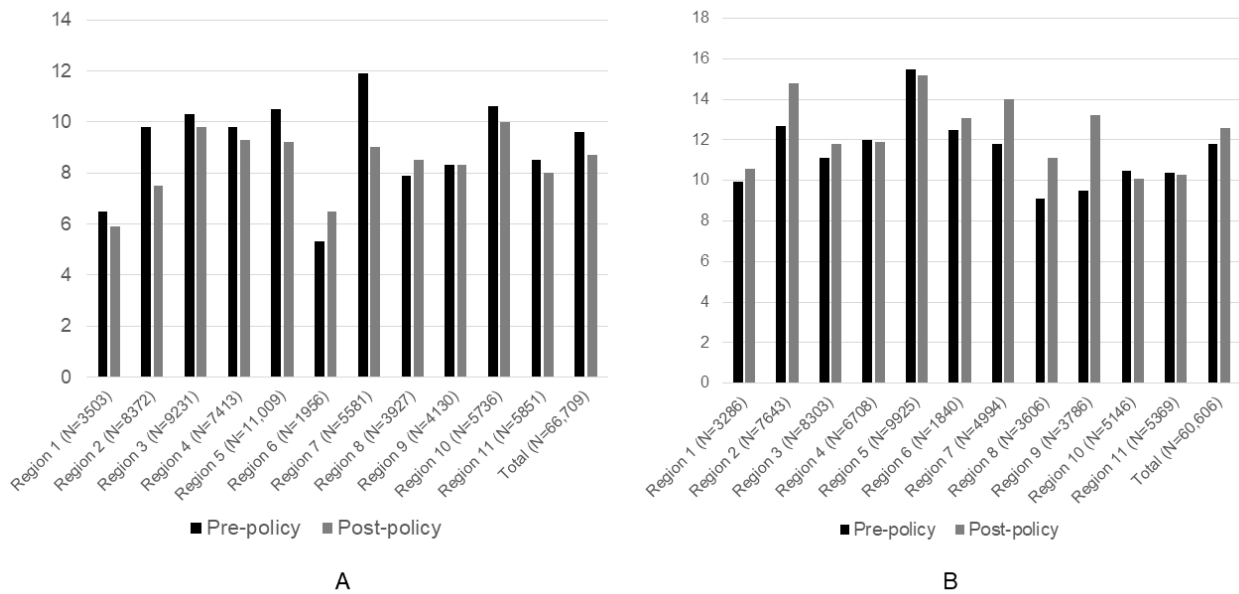


Figure 3 Cumulative 90-d probability of receiving liver transplant **(A)** and of patient mortality while waiting on the list **(B)** among candidates with renal dysfunction (serum creatinine >1.5/dL at or on dialysis within previous week of listing) and listed for liver alone. Comparison for listed 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.

