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Chronic Kidney Disease in Liver Transplant Candidates: A Rising Burden Impacting Post-Liver Transplant Outcomes

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Abstract

The burden of CKD is rising among patients with cirrhosis – it is not known what impact this has had on post-LT outcomes. All patients listed for LT in the U.S. between 2002–17 were analyzed, excluding those listed with MELD exceptions. The primary outcome was post-LT mortality. We defined CKD pre-LT as an eGFR<60 ml/min for 90 days OR ≥72 days of hemodialysis. Cox-regression determined the association between pre-LT CKD and post-LT mortality. Results: Of 78,640 LT candidates, the proportion with CKD among LT recipients increased from 7.8% in 2002 to 14.6% in 2017 (test for trend, p<0.001). Among the 39,719 LT recipients, pre-LT CKD was significantly associated with post-LT mortality (HR:1.16,p<0.001) even after adjusting for DRI, age, MELD, etiology, HE, SLKT, and diabetes. There was no mediating influence of SLKT on the effect of pre-LT CKD on post-LT survival (p>0.05). Therefore, pre-LT CKD has a deleterious impact on post-LT outcomes – an impact that is not mediated through SLKT. These findings highlight the need for the identification of CKD when preventative measures are possible.

Keywords

Acute Kidney Injury; Chronic Kidney Disease; Liver Transplantation; Diabetes Mellitus; NASH

INTRODUCTION

Chronic kidney disease (CKD) is the end manifestation of persistent intrinsic renal damage, a pathology distinct from the reversible acute kidney injury (AKI) typically seen in patients with cirrhosis (e.g., hepatorenal syndrome). This distinction is critical because a single measure of creatinine, as included within the MELD score, does not differentiate between AKI and CKD, and these entities significantly differ in how they impact short- and long-term risk in patients with cirrhosis (1). Despite this important distinction, little is known of not only the burden of CKD among patients with cirrhosis, but also the impact of pre-liver transplant CKD on post-liver transplant outcomes.

In fact, studies evaluating the prevalence of CKD among patients with cirrhosis have largely focused on the increased utilization of simultaneous liver kidney transplant (SLKT) (2–5). However, utilization of SLKT is highly variable, so this may not be the best metric to describe changes in the prevalence of CKD (2,6,7). This is critical because it is becoming more evident that pre-LT CKD impacts the risk of both pre-LT AKI and waitlist mortality (8,9). That being said, although studies have investigated the impact of pre-liver transplant renal function on post-liver transplant survival, these studies were limited by subjective definitions of renal failure that did not distinguish between AKI and CKD (10–12). Consequently, it is not established if pre-LT renal function patterns differentially impact post-LT outcomes.

Herein, we aimed to determine the prevalence CKD among patients with cirrhosis on the liver transplant wait list and determine the impact of CKD, as opposed to AKI, on post-liver transplant mortality.

METHODS

Patients

All patients listed for liver transplantation in the UNOS/OPTN registry between January 1st 2002 through December 31st 2017 were included in this study. Patients who were less than 18 years old, listed as Status 1, who received exceptions points or underwent a living donor liver transplantation were excluded. We excluded those listed with exceptions because we believe they are intrinsically different than those without exceptions with different natural history of disease and therefore risk for CKD.

Renal Function

Serum creatinine and estimated glomerular filtration rate (eGFR) were determined longitudinally from the time of listing for liver transplantation to removal from the liver transplant waitlist. Renal function was assessed every 7 days or longer. When a patient had more than one serum creatinine for the same 7-day period, the first test result was used. We calculated eGFR using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine based equation (13). We chose this equation, because of the GFR calculators that can be used with the data available in the UNOS/OPTN registry, the CKD-EPI equation most closely estimates GFR relative to GFR as measured by iothalamate clearance in

patients with cirrhosis (14–17). Those on hemodialysis were treated as having an eGFR <15 ml/min.

Based on guidelines from Kidney Disease Outcomes Quality Initiative, International Club of Ascites and UNOS, along with previously published work (1,5,18–20), we categorized the renal function pattern at time of DDLT in this study as follows:

- **AKI**: A rise of serum creatinine 0.3 mg/dL or by greater than 50% on the assessment prior to DDLT **OR** < 42 days of hemodialysis at DDLT

- **CKD**: An eGFR < 60 ml/min for 90 days OR 42 days of hemodialysis including at DDLT

- **AKI on CKD**: Meeting both criteria

- **Normal**: Not meeting any of the above criteria

Because of the nature of the UNOS database, we compared measurements for AKI within 7 days, and not 48 hours as used in current definitions (20).

Similarly based on KDOQI guidelines, we defined stages of CKD among only patients with an eGFR < 60 mL/min for 90 days or 42 days of hemodialysis as follows(18):

- **Stage 3**: an eGFR at transplant <60 mL/min but 30 mL/min

- **Stage 4**: an eGFR at transplant <30 ml/min but 15 ml/min

- **Stage 5**: an eGFR at transplant <15 ml/min or on HD

Renal Function Pattern in Those Listed < 90 Days

Because we could not know whether patients listed for <90 days had CKD, no patient listed for <90 days was considered to have CKD, unless they were on hemodialysis for 42 days. That being said, those patients listed for <90 days were eligible to meet the criteria for AKI.

Covariates

Data were obtained from the UNOS/OPTN registry as of April 6th, 2018. Demographic data were collected at listing. The following data were collected at listing and at the end of follow-up: total bilirubin, international normalized ratio (INR), presence of hepatic encephalopathy (HE), and presence of ascites. Cutoffs deemed to be implausible were as follows: total bilirubin 0 mg/dL, INR 0, and creatinine 0 mg/dL (21). Observations with implausible values were set as missing for that specific value. The Model for End-Stage Liver Disease including Serum Sodium (MELDNa) score (22) was calculated and capped at 6 and 40, per current liver allocation policy. Because MELD*Na* score was not implemented until 2016, the MELD score was utilized in the descriptive statistics and analysis of the development of CKD (23,24). Listing diagnoses were grouped into the following common diagnostic categories: hepatitis C virus (HCV), NAFLD (including cryptogenic cirrhosis and nonalcoholic steatohepatitis), alcohol-related cirrhosis (ALD), autoimmune etiologies (including primary biliary cirrhosis, primary sclerosing cholangitis and autoimmune hepatitis), and other. As has been done in previous studies (21,25), regions were grouped according to median MELD score at time of liver transplant into low (regions 3, 6, 10, and

11), medium (regions 2, 4 and 8), and high (regions 1, 5, 7, and 9) MELD regions. Donor characteristics included those used to calculate the donor risk index (DRI) (26). The data were categorized into 4-year increments (2002 – 2005, 2006 – 2009, 2010 – 2013, 2014 – 2017) based on year of last follow up to allow for an adequate sample size by year and to address changes in transplant policy (e.g., implementation of MELDNa, "Share 35"). The year of last follow up was chosen to best determine the incidence of CKD at the time point closest to transplant.

Outcomes

The primary independent variable was the presence of CKD at time of LT. A primary outcome of post-liver transplant mortality was used to determine the impact of pre-liver transplant CKD on post-liver transplant survival; for this analysis, follow-up began on the date of liver transplantation and ended at the time of death or last update to the UNOS/OPTN registry.

Statistical analysis

Descriptive Data Analysis—Continuous variables were compared between groups by Wilcoxon rank-sum or Kruskall-Wallis. Categorical variables were compared between groups by chi-squared test. To test for statistical trends over time, non-parametric tests for trend were used to evaluate significant changes in percentage of patients by pre-liver transplant year of last follow-up.

Cox-Regression Analysis—Post-transplant patient survival was assessed using cox-regression analysis. For this analysis patient follow up began on the date of liver transplantation and ended at the time of death, with those alive after transplant being censored at the time of last update of the UNOS Registry (i.e., March 6th, 2019). To evaluate factors associated with post-liver transplant mortality, Cox proportional hazard models were used. Unadjusted models were used to assess the association of covariates with the outcomes of interest. All covariates with a p<0.2 in univariate analysis were considered for inclusion in multivariate models. Sequential backward selection was used to eliminate those not reaching significance of p<0.05. Kaplan-Meier failure plots were generated to visualize the impact of the pre-LT final renal function pattern on post-liver transplant survival. To highlight the importance of the distinction between AKI and CKD, we completed post-estimation analyses of the final multivariable model to determine the average risk difference for post-liver transplant mortality between the final pre-LT renal function patterns.

Mediation Analysis—We suspected that receiving a SLKT was a mediator in the effect of CKD on post-liver transplant mortality. To explore this effect, we generated cox-regression multivariable models for overall post-liver transplant survival. We determined the proportion of the adjusted effect of meeting the SLKT criteria on post-liver transplant survival that was attributable to receiving a SLKT by comparing coefficient estimates of the two different models, one not including the SLKT variable and the other including the SLKT variable. The 95% confidence intervals for the proportion of this effect were calculated using the bias-corrected percentile bootstrap method with 1000 bootstrap samples (27). Meeting the SLKT

criteria was defined as: an eGFR < 60 ml/min for 90 days with an eGFR at LT of < 30 ml/min OR 42 days of hemodialysis including at DDLT.

Significance—Two-sided p-values <0.05 were considered statistically significant. Analyses were performed using Stata 15.0 statistical software (College Station, TX). This study was approved by the institutional review board at the University of California, San Francisco.

UNOS Policy—The data reported here have been supplied by the United Network for Organ Sharing as the contractor for the Organ Procurement and Transplantation Network. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the OPTN or the U.S. Government.

RESULTS

Population Characteristics

A total of 78,640 patients listed for liver transplantation met study inclusion criteria (Figure 1). Of the 78,640 patients listed for liver transplantation, 39,719 (51%) received a deceased donor liver transplantation, 20,791 (26%) either died on or were removed from the waitlist for "sickness", and 18,130 (23%) were still waiting on the waitlist. Overall, the cohort consisted of 29,846 women (38%), 57,609 (73%) Caucasians, 18,589 (24%) patients with ALD, 27,289 (35%) patients with HCV, 16,974 (22%) patients with NASH. The median age of the cohort at listing was 55 years (interquartile range [IQR], 48 – 60), the median listing eGFR was 72 (IQR 43 – 98) ml/min, the median final eGFR was 57 (IQR 23 – 91) ml/min, the median listing MELD was 18 (IQR 13 – 25), and the median final MELD was 23 (16 – 32).

Among 39,719 LT recipients, 6,269 (16%) patients met the CKD criteria at the time of last transplant. Patients who developed CKD prior to LT were significantly older (58 v. 54y, p<0.001), more likely to be female (43 v. 34%, p<0.001), have a listing diagnosis of NASH (31 v. 21%, p<0.001), ascites (55 v. 53%, p<0.001), and diabetes mellitus (33 v. 20%, p<0.001). They were also more likely to be from a high-MELD region (37 v. 32%, p<0.001). Those who developed CKD had a significantly lower eGFR at listing (52 v. 72 ml/min, p<0.001) (Table 1). During the study period there were significant changes in the characteristics of patients undergoing liver transplantation. The proportion of patients meeting CKD criteria at the time of last follow-up increased from 7.8% in 2002 to 14.6% in 2017 (test for trend, p<0.001) (Figure 2).

Cox Regression Analysis for Post-Liver Transplant Survival

Of the 39,719 patients who underwent liver transplantation during the study period, 10,830 (27%) died post-liver transplant at a median of 2.3 (IQR 0.4 – 6.0) years. There was a significant decrease in both 1-year and 5-year post-liver transplant mortality by year of transplant during the study period: 1-year: 12.4% in 2002 to 6.9% in 2016; 5-year 23.9% in 2002 to 18.3% in 2012 (p<0.001 for both by test for trend). As compared to those without

CKD, those with CKD prior to liver transplantation were significantly more likely to die post-liver transplant: 1-year: (11.9 v. 9.0%, p<0.001); 5-year: (21.5 v. 17.5%, p<0.001).

In univariable analysis for post-liver transplant mortality, CKD at transplant was significantly associated with post-liver transplant mortality (as compared to no CKD, Stage 3 CKD: HR 1.16 [95CI 1.08 – 1.25]; Stage 4 CKD: HR 1.42 [95CI 1.28 – 1.58]; Stage 5 CKD: HR 1.42 [95CI 1.31 – 1.54]) **(Table 3).** In the final multivariable model CKD at transplant was associated with a 16% higher risk of mortality post-liver transplant (HR 1.16, 95CI 1.10 – 1.22), even after adjusting for the following: age at transplant (HR 1.02 per 1 year, 95CI 1.01 – 1.02); etiology of cirrhosis compared to ALD (HCV: HR 1.19, 95CI 1.13 – 1.26; NASH: HR 0.94, 95CI 0.88 – 1.01; Autoimmune-related: HR 0.82, 95CI 0.76 – 0.88; Other: HR 0.91, 95CI 0.83 – 1.00); ethnicity compared to non-Hispanic white (African American: HR 1.18, 95CI 1.11 – 1.27; Hispanic: HR 0.80, 95CI 0.75 – 0.85; Asian: HR 0.76, 95CI 0.65 – 0.88); presence of hepatic encephalopathy (HR 1.16, 95CI 1.11 – 1.22), MELD at transplant (HR 1.02 per 1 point, 95CI 1.01 – 1.02), era of transplant compared to 2002 – 2005 (2006 – 2009: HR 0.98, 95CI 0.92 – 1.03; 2010 – 2013: HR 0.82, 95CI 0.76 – 0.87; 2014 – 2016: HR 0.73, 95CI 0.68 – 0.79), presence of diabetes mellitus (HR 1.32, 95CI 1.26 – 1.40) and donor risk index (HR 1.03 per 0.1 point, 95CI 1.03 – 1.04) **(Table 3)**.

Using this model we found a number of additional findings. First, we found that any stage of CKD was associated with higher post-LT mortality, with the HR to increase at higher stages (as compared to no CKD, Stage 3 CKD: HR 1.11 (95CI 1.03 – 1.20); Stage 4 CKD: HR 1.19 (95CI 1.06 – 1.33); Stage 5 CKD: HR 1.21 (95CI 1.11 – 1.32). Second, if instead of the diagnosis of CKD, the total days with an eGFR<60 ml/min was incorporated into the final adjusted model, we found that for every 90 days with CKD, the risk of post-liver transplant mortality increased by 2.7% (aHR 1.03, 95CI 1.02 – 1.04). Third despite the significant improvement in liver transplant outcomes by era, there was no significant interaction between the effect of pre-liver transplant CKD on post-liver transplant survival by era (p>0.05 for all eras), meaning that we have not decreased the impact of pre-liver transplant CKD on post-liver transplant outcomes.

Mediating Influence of Receiving a SLKT on Post-Liver Transplant Mortality in those with CKD

Next, we wanted to better understand the impact of receiving a SLKT on post-liver transplant outcomes, particularly in the 3 736 (9%) with CKD who met the SLKT criteria. 48.6% of those with CKD pre-liver transplant received an SLKT vs. 6.4% of those without (p<0.001). There were significant differences between those who did and did not receive a SLKT (Supplemental Table 1). The Kaplan-Meier failure plot demonstrates that those with any chronic renal dysfunction (e.g., met SLKT without SLKT, SLKT without meeting SLKT, or met SLKT and underwent SLKT) had significantly higher rates of post-liver transplant mortality (p<0.001 by log-rank test) (Figure 3). Additional multivariable models then demonstrated that there was no significant mediating influence of SLKT on the effect of pre-liver transplant CKD on post-liver transplant survival: 1-year proportion of the attributable effect of SLKT (4.0%, Bias Corrected 95CI –41.1 – 49.1%); 5-year proportion of the attributable effect of SLKT (6.0%, Bias Corrected –9.7 – 23.1%).

Impact of Renal Function Pattern on Post-LT Survival

Of the 39,719 DDLT recipients, 5,739 (14%) patients had AKI, 5,188 (13%) patients had CKD, and 1,019 (3%) patients had AKI on CKD at the time of their transplant. There was a significant trend for all renal dysfunction patterns (i.e., AKI, CKD, AKI on CKD) to increase during the study period (test for trend, p<0.001). As compared to those with normal renal function, the rates of post-LT mortality were significantly higher in those with CKD (31 v. 26%, p<0.001), AKI (29 v. 26%, p<0.001) and AKI on CKD (31 v. 26%, p<0.001).

In univariable analysis as compared to those with normal renal function at the time of LT, CKD (HR 1.33, 95CI 1.26 – 1.41), AKI (HR 1.35, 95CI 1.27 – 1.42), and AKI on CKD (HR 1.54, 95CI 1.37 – 1.73) had significantly higher risk of post-LT mortality. Similarly, in the final multivariable model after adjustment for age, MELD at transplant, etiology of cirrhosis, encephalopathy, diabetes at transplant, race, and era of transplant, each of the renal dysfunction patterns had greater post-LT mortality as compared to normal: *AKI*: aHR 1.21, 95CI 1.13 – 1.27; *CKD*: aHR 1.19 95CI 1.12 – 1.27; *AKI on CKD*: aHR 1.28, 95CI 1.13 – 1.45). That being said, there was no significant difference between the *AKI* or *AKI on CKD* groups and CKD group (p>0.05 for both comparisons).

DISCUSSION

In this national study of more than 78,000 adult liver transplant candidates in the United States, we aimed to describe and determine the impact of CKD among patients with cirrhosis undergoing liver transplantation. We first quantify the rise in the prevalence of CKD among liver transplant recipients, demonstrating a 187% increase in the proportion of patients with cirrhosis who had CKD at the time of liver transplant. Our data suggest that this rise has had a detrimental impact on post-liver transplant outcomes, with those with CKD at the time of transplant having an adjusted 16% increase risk of death post-liver transplant – an effect that was independent of receiving a SLKT and equivalent to the impact of AKI on post-liver transplant outcomes.

What might explain the rising prevalence of CKD? We offer two main reasons based on our results. First, we suspect that the emergence of NASH as a leading indication for liver transplantation has led to a greater proportion of patients with manifestations of the metabolic syndrome being considered for transplant. As a result, these patients are more likely to have intrinsic renal damage (e.g., diabetic nephropathy or hypertensive nephrosclerosis). They are therefore more susceptible to episodes of AKI and less likely to have the renal reserve to recover from these episodes. This is supported by previous studies that demonstrated that those with a higher baseline creatinine are more susceptible to AKI and less likely to recover from those episodes of AKI (8,9). Second, this increased susceptibility is potentiated by factors that lead to longer wait times, whereby patients who spend more time at risk for renal injury are most vulnerable to CKD. This not only leads to progression of renal disease in those with intrinsic renal damage, but also leaves the patient with decompensated cirrhosis exposed to hemodynamic abnormalities for a longer period putting them at greater risk for the development of type 2 hepatorenal syndrome.

The rising prevalence of CKD is all the more important given the association that we observed between CKD and mortality *after* liver transplantation. Although overall post-liver transplant outcomes have improved over time (28), patients with CKD continued to have significantly higher rates of post-liver transplant mortality in all eras – an impact that, based on our data, was neither mitigated nor potentiated by SLKT. Moreover, we demonstrate that the deleterious impact of CKD on post-liver transplant outcomes is directly correlated with the degree and duration of CKD: 1. The longer a patient has CKD in the pre-liver transplant setting, the greater the impact of CKD on post-liver transplant outcomes; the greater the CKD stage at transplant the worse the post-liver transplant survival. These findings suggest that the burden of CKD on the overall health of the liver transplant recipient increases as renal function declines.

We acknowledge the following limitations to this study. First, we fully acknowledge that accurate ascertainment of all episodes of AKI would require serial measurements of creatinine at frequent and specific time points in all subjects. However, our data reflect what is available in real-life clinical practice – and demonstrate that AKI as defined by what can be measured in this clinical setting has prognostic value. Although the use of UNOS/OPTN dataset reflects the information that is currently available in clinical practice and thus enhances the generalizability of our findings to the real-life setting, our inability to determine those with CKD at the time of listing and the reliance on serum creatinine, which overestimates eGFR, means that we are likely underreporting the burden of CKD on the liver transplant waitlist. Second, as with any analysis of UNOS registry data, our results are limited by the accuracy of the registry. We minimized any impact clinical inaccuracy may have had in our results by focusing on objective data, such as serum creatinine. Third, because previous data suggest that patients listed with exception points (e.g. HCC) have different causes of post-liver transplant mortality, we excluded these patients from our analysis (29,30). That being said, investigation if pre-liver transplant CKD equally affects this group is warranted. Finally, there may be differences in patients with and without CKD that are not captured using national registry data – such as unmeasured comorbidities. This highlights the need for prospective cohorts to better study renal disease among patients with cirrhosis.

Despite these limitations, our findings that CKD is rising among and having a greater burden on liver transplant recipients has important implications for clinical practice. Specifically, these findings demonstrate the increasing importance of the appropriate management of CKD-associated medical co-morbidities and the necessity to prevent the development and progression of CKD among LT candidates.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

(T32 DK060414; Cullaro), both of which played no role in the analysis of the data or the preparation of this manuscript

Abbreviations:

AKI	Acute Kidney Injury
CKD	Chronic Kidney Disease
NASH	Non-alcoholic Steatohepatitis
MELD	Model for End-Stage Liver Disease
HCC	Hepatocellular Carcinoma
SLKT	Simultaneous Liver-Kidney Transplant

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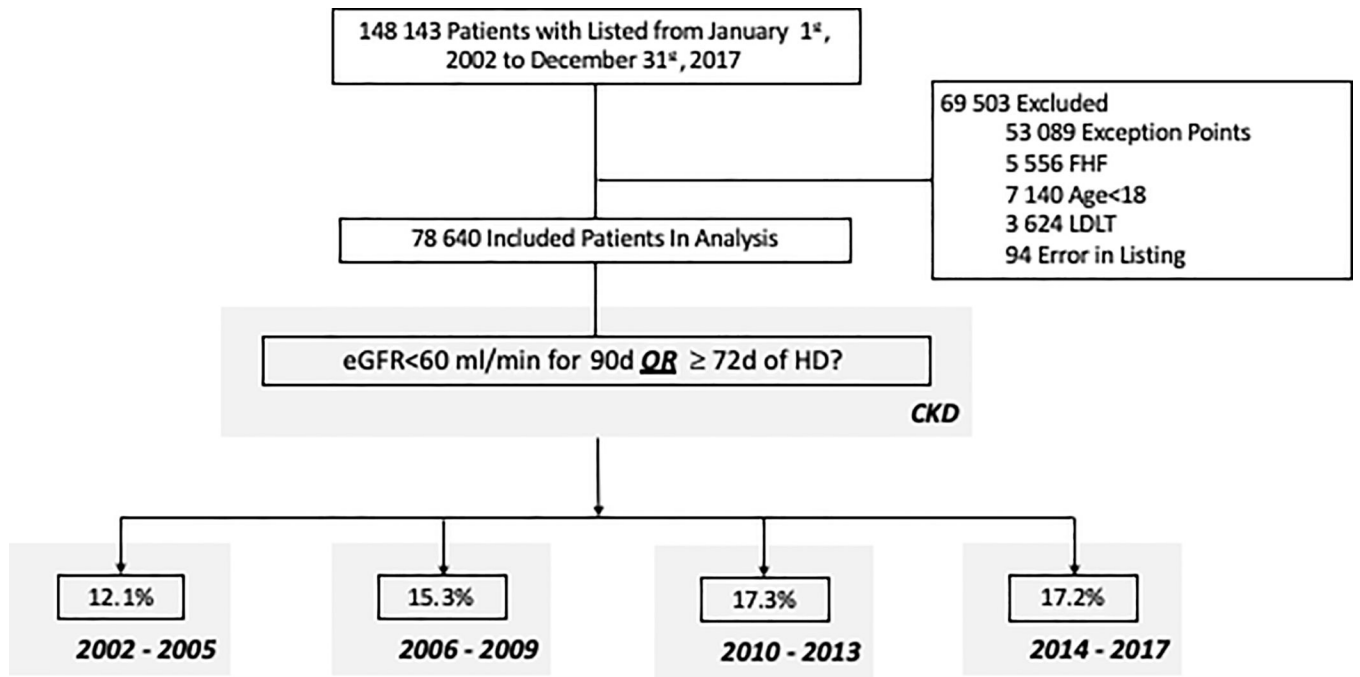
Figure 1. Flow Diagram with Definitions of CKD
estimated glomerular filtration rate (eGFR); days (d); hemodialysis (HD); chronic kidney disease (CKD); fulminant hepatic failure (FHF); living donor liver transplant (LDLT)
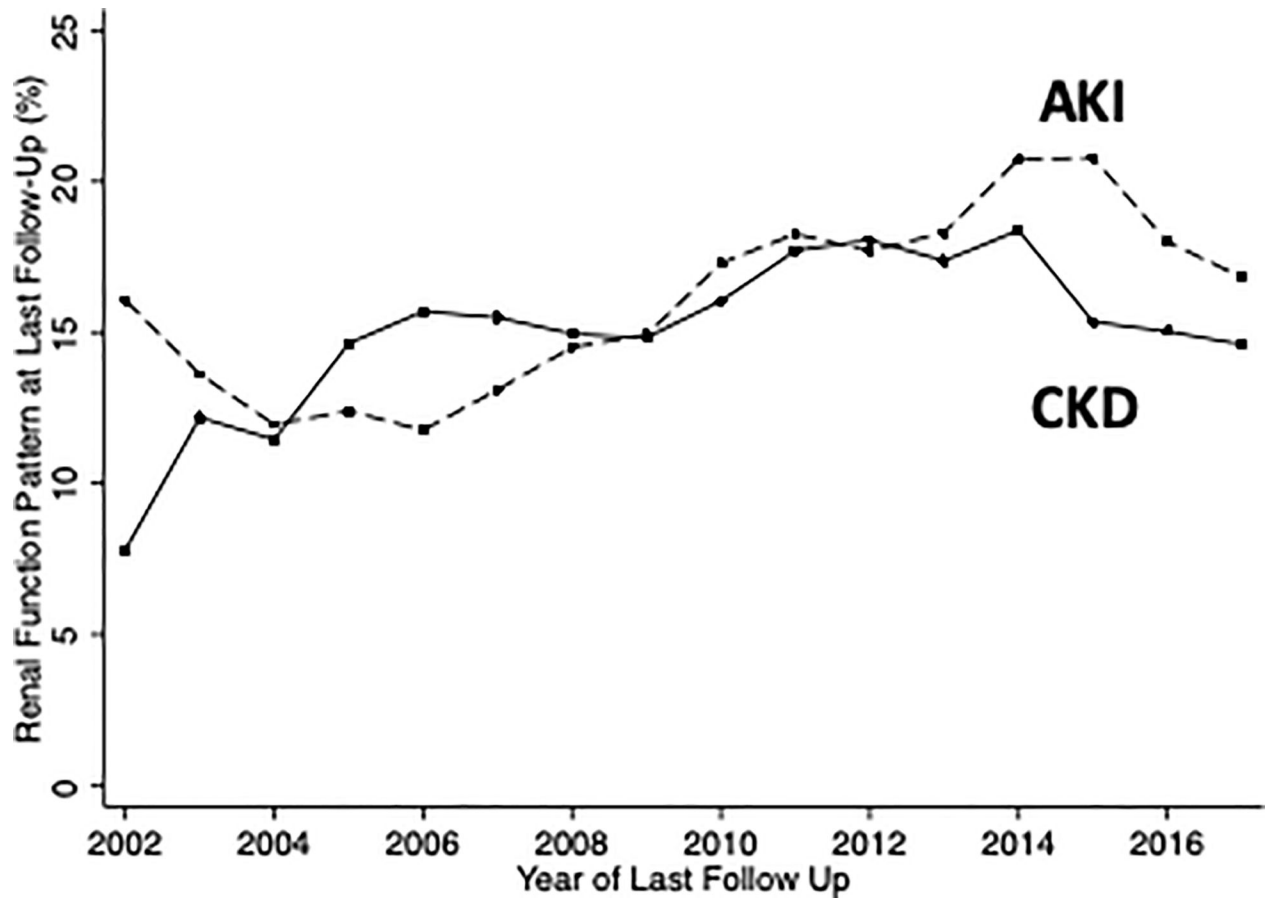
Figure 2. Temporal Changes in Percentage of Patients Listed for Liver Transplantation with CKD at Last Follow-Up
acute kidney injury (AKI); chronic kidney disease (CKD)
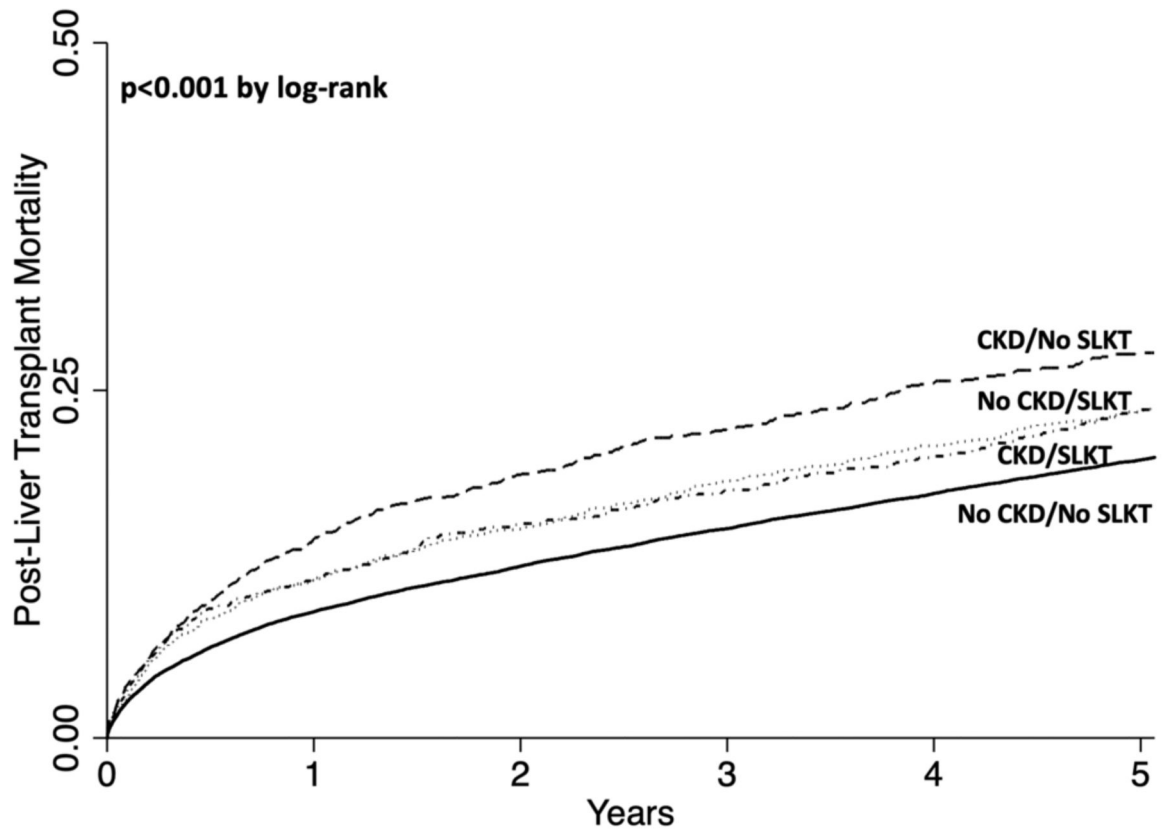
Figure 3. Kaplan-Meier Failure Plot for Post-Liver Transplant Mortality by Pre-Liver Transplant CKD and SLKT Status
chronic kidney disease (CKD); simultaneous-liver kidney transplant (SLKT)

Table 1.

Baseline Demographics of the 39 719 Patients Liver Transplantation Recipients by CKD Status

	No CKD (n = 33 450)	CKD (n = 6 269)	p
Age at last follow-up, years	54 (47 – 60)	58 (53 – 63)	<0.001
Female sex	11 228 (34)	2 700 (43)	<0.001
Ethnicity			
Non-Hispanic White	24 891 (74)	4 624 (74)	
African American	3 039 (9)	492 (8)	
Hispanic	4 319 (13)	829 (15)	<0.001
Asian	790 (2)	129 (2)	
Other	411 (1)	104 (2)	
Listing diagnosis			
Alcohol	7 762 (23)	1 088 (17)	
HCV	11 016 (33)	2 190 (35)	
NAFLD/NASH	7 139 (21)	1 970 (31)	<0.001
Autoimmune[1]	5 207 (16)	670 (11)	
Other	2 326 (7)	351 (6)	
Region MELD			
Low	14 080 (42)	2 190 (35)	
Medium	8 815 (26)	1 771 (28)	<0.001
High	10 555 (32)	2 308 (37)	
Ascites	17 697 (53)	3 466 (55)	<0.001
Hepatic encephalopathy	7 920 (24)	1 410 (23)	<0.001
Diabetes Mellitus	6 319 (20)	1 928 (33)	<0.001
MELD at listing	21 (16 – 29)	17 (14 – 21)	<0.001
eGFR at Listing	72 (39 – 99)	52 (35 – 72)	<0.001
MELD at transplant	25 (19 – 33)	25 (20 – 32)	0.001
Received a SLKT	2 440 (7)	1 666 (27)	<0.001
Donor Risk Index per 0.1 point	1.4 (1.2 – 1.8)	1.4 (1.2 – 1.8)	0.56
Era of Transplant			
2002 – 2005	6 552 (20)	903 (14)	
2006 – 2009	8 345 (25)	1 503 (24)	<0.001
2010 – 2013	7 802 (23)	1 632 (28)	
2014 – 2017	10 751 (32)	2 231 (36)	

Hepatitis C (HCV); Donor Risk Index (DRI); Non-Alcoholic Steatohepatitis (NASH); Model for End-Stage Liver Disease with Serum Sodium (MELDNa); *indicates a non-parametric test for trend

[*]
All Data either: Median [IQR] or Number (%)

Table 2.

Cox Regression Analysis for Post-Liver Transplant Mortality

	Univariable			Multivariable*		
	HR	95% CI	p-value	HR	95% CI	p-value
CKD at Transplant	1.29	1.23 – 1.36	<0.001	1.16	1.10 – 1.22	<0.001
Age per Year	1.02	1.02 – 1.03	<0.001	1.02	1.01 – 1.02	<0.001
Female Sex	0.97	0.93 – 1.02	0.22	-	-	-
Etiology						
Alcohol	-	-	-	-	-	-
HCV	1.21	1.15 – 1.28	<0.001	1.19	1.13 – 1.26	<0.001
NASH	1.08	1.02 – 1.15	0.01	0.94	0.88 – 1.01	0.09
Autoimmune[1]	0.79	0.74 – 0.85	<0.001	0.82	0.76 – 0.88	<0.001
Other	0.87	0.79 – 0.95	0.002	0.91	0.83 – 1.00	0.06
Ethnicity						
Non-Hispanic White	-	-	-	-	-	-
African American	1.18	1.10 – 1.26	<0.001	1.18	1.10 – 1.27	<0.001
Hispanic	0.86	0.81 – 0.91	<0.001	0.80	0.74 – 0.85	<0.001
Asian	0.77	0.67 – 0.89	0.001	0.76	0.65 – 0.88	<0.001
Other	1.03	0.86 – 1.22	0.78	1.01	0.84 – 1.22	0.91
Ascites	1.15	1.10 – 1.19	<0.001	-	-	-
Hepatic Encephalopathy	1.24	1.19 – 1.29	<0.001	1.16	1.11 – 1.22	<0.001
Diabetes Mellitus	1.35	1.29 – 1.42	<0.001	1.33	1.26 – 1.40	<0.001
MELD at transplant per point	1.01	1.01 – 1.02	<0.001	1.02	1.01 – 1.02	<0.001
Received a SLKT	1.23	1.16 – 1.31	<0.001	-	-	-
Era of Transplant						
2002 – 2005	-	-	-	-	-	-
2006 – 2009	0.99	0.95 – 1.05	0.84	0.98	0.92 – 1.03	0.44
2010 – 2013	0.88	0.83 – 0.94	<0.001	0.81	0.76 – 0.87	<0.001
2014 – 2017	0.80	0.74 – 0.86	<0.001	0.74	0.68 – 0.79	<0.001
Donor Risk Index per 0.1 point	1.03	1.02 – 1.03	<0.001	1.03	1.03 – 1.04	<0.001

Hepatitis C (HCV); Donor Risk Index (DRI); Non-Alcoholic Steatohepatitis (NASH); Model for End-Stage Liver Disease with Serum Sodium (MELDNa);