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Authors

Cullaro, Giuseppe
Verna, Elizabeth C
Lai, Jennifer C

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Association Between Renal Function Pattern and Mortality in Patients with Cirrhosis

Giuseppe Cullaro, MD¹, Elizabeth C. Verna, MD, MS², Jennifer C. Lai, MD, MBA¹

¹Division of Gastroenterology and Hepatology, Department of Medicine, University of California, San Francisco, CA, USA

²Center for Liver Disease and Transplantation, Columbia University, College of Physicians and Surgeons, New York, NY, USA

Abstract

Background & Aims: Renal dysfunction increases risk of death for patients with cirrhosis. We investigated whether mortality differs significantly among patients with acute kidney injury (AKI), chronic kidney disease (CKD), and both.

Methods: We performed a retrospective analysis of all non-status 1 adults on the waitlist for liver transplantation for at least 90 days, collected from the Organ Procurement and Transplantation Network registry from July 1, 2007 through July 1, 2014. We assigned patients to groups of AKI (an increase of 0.3 mg/dL or 50% in serum creatinine in the last 7 days or fewer than 72 days of hemodialysis), CKD (an estimated glomerular filtration rate <60 ml/min/1.73 m² for 90 days with a final rate 30 ml/min/1.73 m² or 72 days of hemodialysis), AKI and CKD (meet both definitions), or normal (meet neither definition). We performed competing risk analyses to associate patterns of renal dysfunction with waitlist mortality, accounting for liver transplantation, with renal pattern as a time-dependent covariate. Logistic regression for 6-month mortality determined the added benefit of including renal function pattern in the assessment.

Results: There were 22,680 patients in the cohort; they spent a median 1.6 years (range, 0.7–3.1 years) on the waitlist and a median 5 years (range, 2–9 years) undergoing assessments of renal function. In competing risk analysis, even after adjusting for confounders including final model for end-stage liver disease sodium (MELD-Na) scores, the pattern of renal function was significantly

Corresponding Author: Jennifer C. Lai, 513 Parnassus Avenue, UCSF Box 0538, San Francisco, CA 94143 USA, Tel: +1 415 476 2777, Fax: +1 415 476 0659, jennifer.lai@ucsf.edu.

Author's Contribution:

Giuseppe Cullaro: Data Acquisition, Statistical Analysis, Interpretation of data, Preparation of Manuscript, including final approval for publication; No conflict of interests.

Elizabeth C. Verna: Interpretation of data, Preparation of Manuscript, including final approval for publication; No conflict of interests.

Jennifer C. Lai: Data Acquisition, Statistical Analysis, Interpretation of data, Preparation of Manuscript, including final approval for publication; No conflict of interests.

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associated with waitlist mortality: AKI and CKD (subhazard ratio [SHR], 2.86; 95% CI, 2.65–3.10), AKI (SHR, 2.42; 95% CI 2.22–2.64), CKD (SHR, 1.56; 95% CI, 1.45–1.67) compared with normal. The area under the curve values, based on MELD-Na score at time of placement on the waitlist, were 0.80 with renal function pattern and 0.71 without ($P<.001$).

Conclusion: In competing risk analysis, even after adjusting for confounders including final MELD-Na score, we found the pattern of renal dysfunction to associate with mortality in patients with cirrhosis. Including information on type of renal dysfunction could improve risk analysis.

Keywords

Renal Dysfunction; Liver Disease; Waitlist Mortality; Liver Transplantation

INTRODUCTION

Renal dysfunction in patients with cirrhosis is common, affecting 20% of patients who are hospitalized and 37% of patients who are followed as outpatients (1,2). Renal dysfunction is also a key determinant of outcomes, with 50% of patients with cirrhosis dying within 30 days of developing renal failure (3,4). However, renal dysfunction in the context of cirrhosis arises from a broad spectrum of pathologies, including *acute kidney injury (AKI)* from alterations in perfusion (e.g., pre-renal, hepatorenal syndrome) to *chronic kidney disease (CKD)* from renal parenchymal damage (e.g., diabetic nephropathy, hypertensive nephrosclerosis). It is not well-established if each of these pathologies impacts survival equally (5,6).

To date, studies evaluating the impact of renal dysfunction on prognosis in patients with cirrhosis have mostly focused on AKI (2, 7, 8). While AKI is a critical determinant of mortality in patients with cirrhosis, the data regarding CKD and AKI on CKD are limited. The one study that focused on the cause of renal failure in patients with cirrhosis and prognosis reported a statistically different association between the etiology of renal dysfunction and survival outcomes. However, this study was limited by subjective definitions of renal failure as well as relatively short follow-up that could not address the long-term natural progression of renal dysfunction in patients with cirrhosis (6).

Herein, we present a study focused on determining the association between the pattern of renal function and mortality in patients with cirrhosis. We hypothesized that the pattern of renal function would have varying impact on survival, specifically that patients with AKI or AKI on CKD are at greater risk than those with CKD or normal renal function.

METHODS

Patients

All patients listed for liver transplantation in the UNOS/OPTN registry from July 1st 2007 through July 1st 2014, which represents a time frame of relatively stable liver allocation policy, were evaluated for inclusion in this study. Patients who were less than 18 years old or listed as Status 1, including those with fulminant hepatic failure were excluded. Those who received exceptions points or underwent a living donor liver transplantation were also

excluded, as these patients have a likelihood of receiving a liver transplant that is independent of their liver function. Because we could not know whether patients listed for < 90 days had acute or chronic kidney disease, we excluded those who spent < 90 days on the waitlist.

Covariates

Data were obtained from the UNOS/OPTN registry as of June 17th, 2016. Demographic data and transplant date 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 (9). Observations with implausible values or missing data were censored - this represented <3% of the cohort. The Model for End-Stage Liver Disease including Serum Sodium (MELDNa) score (10) was calculated and capped at 6 and 40, per current liver allocation policy. Listing diagnoses were grouped into the following common diagnostic categories: hepatitis C virus (HCV), nonalcoholic fatty liver disease (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 etiologies of cirrhosis (any other listing code that met inclusion criteria). Listing and receipt of a simultaneous-liver kidney transplant (SLKT) was determined at the time of last follow up, as outlined in UNOS protocol these patients received no prioritization for liver transplantation.

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. Observations with missing creatinine values were excluded. For the assessment of AKI, each serum creatinine was compared to the serum creatinine from 7 or more days earlier; a cut-off of ≥ 0.3 mg/dL or $\geq 50\%$ from previous value was chosen as outlined by the International Club of Ascites (11). When the testing interval was > 48 hours we assumed that the increase in sCr happened in the 48 hours prior to testing. We defined CKD as outlined by the UNOS/OPTN: an eGFR < 60 ml/min/1.73 m² for ≥ 90 days with a current eGFR of ≥ 30 ml/min/1.73 m² (12). We calculated eGFR using the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) creatinine based equation (13). We chose this equation, because understanding the limitations of the GFR calculators that can be used with the data available in the UNOS/OPTN registry, the CKD-EPI creatinine based equation most closely estimates GFR relative to GFR as measured by iothalamate clearance in patients with cirrhosis (14–16). Those on hemodialysis were treated as having an eGFR < 15 ml/min/1.73 m² and were not included in the descriptive statistics for serum creatinine and eGFR. Based on current UNOS/OPTN criteria for CKD if patients received hemodialysis during follow-up, we defined this as AKI if they were on hemodialysis for < 72 days and CKD if they were on hemodialysis for ≥ 72 days (12). Patients with two or fewer observations of renal function

were treated as having normal renal function, unless they were on hemodialysis, which was treated as AKI or CKD, as above.

Renal Function Pattern Definitions

We defined renal function patterns as follows (Figure 1):

- **AKI**: an increase in serum creatinine by ≥ 0.3 mg/dL or $\geq 50\%$ in the last 7 days or < 72 days of hemodialysis
- **CKD**: an eGFR < 60 ml/min/1.73 m² for 90 days with a final eGFR of ≤ 30 ml/min/1.73 m² or ≤ 72 days of hemodialysis
- **AKI on CKD**: meeting both AKI and CKD definitions
- **Normal Renal Function**: meeting neither definition

Outcomes

The primary outcome was waitlist mortality defined as death or removal from the waitlist for sickness. Patient follow-up began on the date of listing for liver transplantation and ended at the time of death, removal from the waitlist, or transplant. Patients removed from the waitlist for adequate hepatic reserve or social reasons were censored at the time of their removal.

Statistical analysis

Continuous variables were compared between groups by Wilcoxon rank-sum or Kruskal-Wallis. Categorical variables were compared between groups by chi-squared test.

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 $p < 0.05$.

For the analysis of waitlist mortality, competing risk was used in assessing the association between the pattern of renal function with the primary outcome. In this analysis using the Fine-Gray model, removal from the waitlist for transplantation was treated as a competing risk (17). Further, renal function pattern was treated as a time-dependent covariate to allow the pattern of renal function to vary over time. For example, if a patient had normal renal function, then developed AKI that progressed to CKD, this patient would contribute time to the normal, AKI, and CKD groups during follow-up. Postestimation analysis of the final multivariate model included determining the adjusted mean subhazard ratio (SHR) for each pattern of function pattern at 2 MELDNa point intervals from a MELDNa of 6 to 40 (Figure 1).

To determine the added benefit of including renal function pattern in the prediction of waitlist mortality, but not overall mortality risk, bivariate logistic regression was completed. In this analysis, the MELDNa at listing and the renal function pattern at day 90 (the earliest timepoint where patients could have developed CKD or AKI on CKD) were used as predictors to estimate odds ratios and assess the independent association of renal function pattern and waitlist mortality at 6 months. The timepoint of 6 months was specifically

chosen to assess the 3-month mortality from the earliest timepoint where renal function pattern can be assessed. The c-statistics for listing laboratory MELDNa score with and without renal function pattern were compared using nonparametric methods (18).

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.

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

Patient Characteristics

From July 1st 2007 through July 1st 2014, 74,771 patients were listed for liver transplantation. A total of 52,091 patients were excluded from this study: 25,372 who received exception points, 1,337 who received a living donor liver transplant, 46 who were listed in error, 2,929 who were less than 18 years old, 2,114 who were listed with fulminant hepatic failure, 20,293 who were listed for less than 90 days. After excluding these patients, a total of 22,680 patients formed the study cohort (Figure 1).

Of the 22,680 patients in the cohort, patients spent a median of 1.6 (IQR 0.7 – 3.1) years on the waitlist, with a median of 5 (IQR 2 – 9) assessments of renal function. The study cohort had a median age of 57 (IQR 51 – 63) years and was comprised of 8,805 (39%) women, 16,572 (73%) Caucasians, and 5,665 (25%) patients with diabetes mellitus. The etiology of cirrhosis was HCV in 8,762 (39%), nonalcoholic steatohepatitis (NASH) in 4,840 (21%), ALD in 4,613 (20%), autoimmune-related in 3,142 (14%), and other in 1,323 (6%) patients. The median MELDNa score at listing was 16 (IQR 13 – 20), with a final or most recent median MELDNa score of 20 (IQR 14 – 29). There were 19,816 episodes of AKI (13% of total follow-up visits). There were 6,965 (31%) patients who met the criteria for CKD at the end of follow up. A total of 2,522 (11%) patients received any hemodialysis during follow up and 2,333 (10%) of patients were listed for SLKT. These patients received a median of 50 (IQR 0 – 259) days of hemodialysis. At the end of follow up, 8,582 (38%) were still waiting for liver transplantation, 7,460 (33%) received a liver transplant and 6,638 (29%) either died on the waitlist or were removed for sickness (Table 1).

Time-Dependent Competing Risk Survival Analysis for Waitlist Mortality

In univariable analysis, the pattern of renal function was significantly associated with waitlist mortality: CKD compared to normal (SHR 1.82, 95CI 1.70 – 1.95); AKI compared to normal (SHR 3.25, 95CI 3.00 – 3.52); AKI on CKD compared to normal (SHR 4.03, 95CI 3.75 – 4.34). Further, even when treating CKD as the reference group, there remained a significant association with waitlist mortality: Normal compared to CKD (SHR 0.55, 95CI 0.51 – 0.59); AKI compared to CKD (SHR 1.78, 95CI 1.63 – 1.95); AKI on CKD compared to CKD (SHR 2.21, 95CI 2.03 – 2.41).

The other factors that were significantly associated with waitlist mortality in univariable analysis after accounting for liver transplantation were: final age (SHR 1.02, 95CI 1.02 – 1.03); female sex (SHR 1.09, 95CI 1.04 – 1.15); HCV compared to ALD (SHR 1.22, 95CI 1.14 – 1.31); NASH compared to ALD (SHR 1.17, 95CI 1.09 – 1.27); autoimmune-related compared to ALD (SHR 0.88, 95CI 0.81 – 0.97); Caucasian race (SHR 0.94, 95CI 0.89 – 0.99); presence of ascites (SHR 1.56, 95CI 1.48 – 1.63); presence of HE (SHR 2.80, 95CI 2.65 – 2.96); presence of diabetes mellitus (SHR 1.30, 95CI 1.23 – 1.37); final MELDNa (SHR 1.05 per 1 point, 95CI 1.05 – 1.06); and final albumin (0.63 per 1 g/dL, 95CI 0.61 – 0.66). In the final multivariate model even after adjusting for confounders, including final MELDNa, final albumin, age, female sex, etiology of cirrhosis, BMI, presence of ascites, presence of HE, presence of diabetes mellitus, region, and blood type the pattern of renal function was significantly associated with waitlist mortality: AKI compared to normal (SHR 2.42, 95CI 2.22 – 2.64), CKD compared to normal (SHR 1.56, 95CI 1.45 – 1.67); AKI on CKD compared to normal (SHR 2.86, 95CI 2.65 – 3.10) (Table 2). Further even after adjustment, both the AKI (SHR 1.56, 95CI 1.43 – 1.72) and the AKI on CKD (SHR 1.85, 95CI 1.70 – 2.02) groups had significantly higher rates of waitlist mortality when compared to the CKD group. The cumulative incidence of waitlist mortality by pattern of renal function is demonstrated in Figure 2.

Next, we wanted to explore if this association was present at all levels of the final MELDNa score. We plotted the mean difference of the adjusted SHR between each of the patterns of renal function and CKD (e.g., Normal *minus* CKD; AKI *minus* CKD; AKI on CKD *minus* CKD). This was completed at 2-point intervals from a final MELDNa score of 6 to 40. As highlighted by the confidence intervals, the AKI and AKI on CKD groups had statistically greater adjusted SHR, while the normal group had statistically lower adjusted SHR. Further, as the MELDNa increases the difference between each of the patterns of renal function (AKI, AKI on CKD and normal) and CKD increases (Figure 3).

Logistic Regression Models of Renal Function Pattern and Final MELDNa For Waitlist Mortality

In bivariate logistic regression models of patients in our cohort, odds ratios for 6-month (at listing to 180d) waitlist mortality were calculated using MELDNa at listing with and without renal function pattern at day 90 (Table 3). In the univariate models, there was a statistically significant increase in the odds of waitlist mortality for MELDNa at listing (OR 1.14, 95CI 1.13 – 1.16), AKI compared to normal renal function (OR 7.01, 95CI 5.89 – 8.35) and AKI on CKD compared to normal renal function (OR 4.74, 95CI 3.38 – 6.67). In the bivariate model, these same variables remained significant: MELDNa at listing (OR 1.14, 95CI 1.12 – 1.16), AKI compared to normal renal function (OR 6.23, 95CI 5.19 – 7.45), and AKI on CKD compared to normal renal function (OR 3.65, 95CI 2.56 – 5.22). Patients with CKD had an odds of waitlist mortality that was similar to those with normal renal function (OR 0.82, 95CI 0.58 – 1.16). When we examined the ROC curves generated from the logistic regression models to predict 6-month waitlist mortality, the addition of the pattern of renal function to MELDNa at listing increased the accuracy of the model from an AUC of 0.71 to an AUC of 0.80 ($p < 0.001$) (Table 3).

DISCUSSION

In this study evaluating objectively-defined patterns of renal function, we aimed to describe the impact of patterns of renal function on survival in patients with cirrhosis. Confirming prior reports (6), we observed that each pattern of renal function has a varying effect on survival. More specifically, we demonstrated that those with an acute worsening of their renal function (i.e. AKI or AKI on CKD) were at significantly higher risk of waitlist mortality than both those with stable CKD and normal renal function, even after controlling for final MELDNa score. Further, we demonstrated that this effect increased as MELDNa score increased. This suggests that incorporating the pattern of renal function could provide an opportunity to better prognosticate risk of mortality in the patients with cirrhosis who are the sickest. In fact, we observed that a model including the renal function pattern *and* MELDNa score was more accurate at predicting mortality at 6-months than the model including MELDNa score alone, improving the C-statistic from 0.71 to 0.80.

We hypothesize that the mechanism by which renal function patterns have a varying impact on survival in patients with decompensated cirrhosis is related to the etiology of the renal dysfunction. We suspect that those patients who experience AKI and AKI on CKD in our cohort, likely had a triggering event – infection, bleeding, hypovolemia – that put these patients at greater risk for waitlist mortality. These events inherently carry more risk than stable non-liver related elevations in serum creatinine that are seen in patients with CKD. Given this heterogeneity of etiology in renal dysfunction in patients with cirrhosis, it is perhaps not surprising that unique renal function patterns variably impact mortality. As we have shown in our models, a simple, objective categorization of renal function patterns that we developed in this study may serve as an additive marker in the prediction of waitlist mortality and future studies should focus on the best way to incorporate the pattern of renal function into the MELDNa score in an attempt to maximize its accuracy.

We acknowledge the following limitations to this study. First, there was no standardized protocol for measuring serum creatinine levels. As such, there may be certain patients who are misclassified by renal function pattern in our cohort because of either insufficient data or more frequent assessments. However, the use of UNOS/OPTN dataset provided the power and follow up (median 1.6 years) necessary to overcome this shortcoming and reflects the information that is currently available in clinical practice, enhancing the applicability of our findings. That being said, it was not possible to determine the specific precipitants or etiologies of AKI or CKD from this national data registry, supporting the need for prospective cohorts to inform the natural history of renal dysfunction in patients with cirrhosis. Second, as with any analysis of UNOS registry data, our results are limited by the accuracy of the registry inputs. We minimized any impact input errors may have had in our results by focusing on objective data, such as change in serum creatinine. Third, the definitions of renal function patterns chosen require that patients be followed for a minimum of 90 days. Statistically, the possibility of introducing bias, particularly “immortal time bias” was addressed by treating renal function pattern as a time-dependent covariate (19). However, clinically, it means that our findings are only applicable to those patients who have been followed at a minimum of 90 days and are decompensated enough to require liver transplantation.

Despite these limitations, this is one of the first studies to demonstrate that the pattern of renal function has a significant impact on survival in patients with cirrhosis. Our finding that patients with AKI and AKI on CKD have nearly twice the risk of waitlist mortality compared to those with CKD even after adjusting for MELDNa score has important implications for clinical practice. Specifically, it highlights an opportunity to enhance mortality prediction in patients with cirrhosis. Our data demonstrate that not only can the inclusion of the renal function pattern improve the accuracy of the MELDNa score, it appears that this effect will have a greater impact in patients who are at greatest risk of mortality. The mechanism of this impact and whether these patterns can be identified at the time of listing for liver transplant warrants further study in cohorts with more granular data. Nevertheless, our data, focusing on the impact of the pattern of renal function on mortality in patients with cirrhosis, demonstrate an opportunity to enhance prognostication of mortality and provide the framework for further study of renal dysfunction in all patients with cirrhosis.

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Abbreviations:

AKI	Acute Kidney Injury
CKD	Chronic Kidney Disease
AKI on CKD	Acute on Chronic Kidney Disease
MELD	Model for End-Stage Liver Disease
HCC	Hepatocellular Carcinoma

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What You Need to Know

Background:

Renal dysfunction increases risk of death for patients with cirrhosis. We investigated whether the risk is the same for patients with acute kidney injury (AKI), chronic kidney disease (CKD), or both.

Findings:

In an analysis of adults on the waitlist for liver transplantation, we found that even after adjusting for confounders including final MELD-Na score, there is a significant association between type of renal dysfunction and mortality in patients with cirrhosis. AKI and CKD increased risk of death almost 3-fold, followed by AKI or CKD alone.

Implications for patient care:

Including information on type of renal dysfunction could improve risk analysis for patients with cirrhosis.

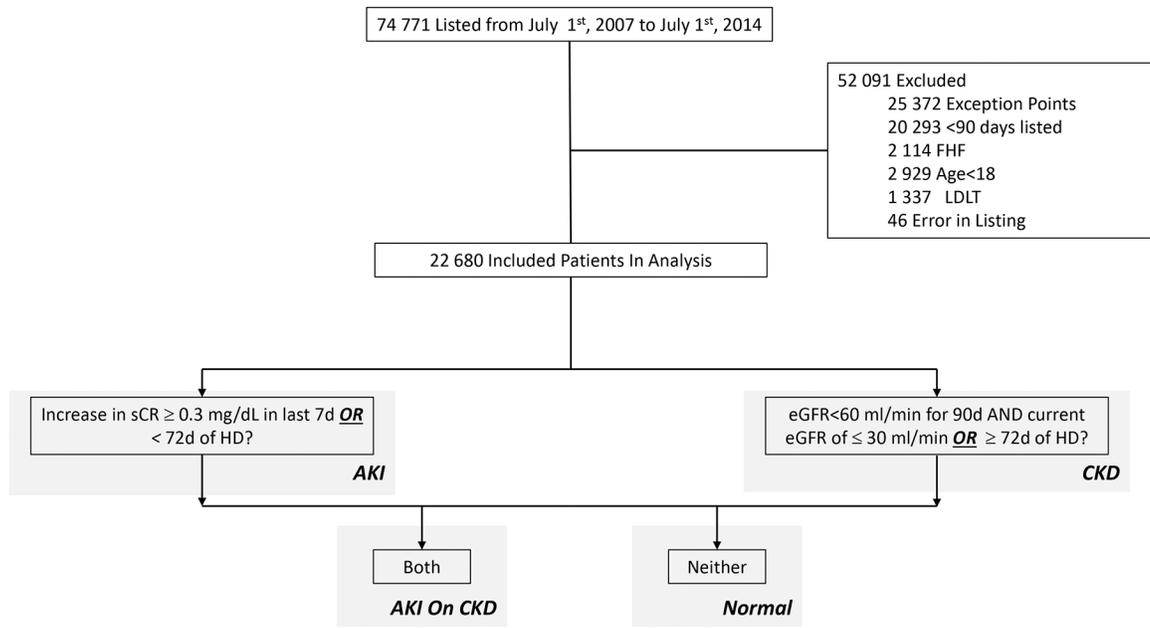


Figure 1.
Flow Diagram with Definitions of Renal Patterns

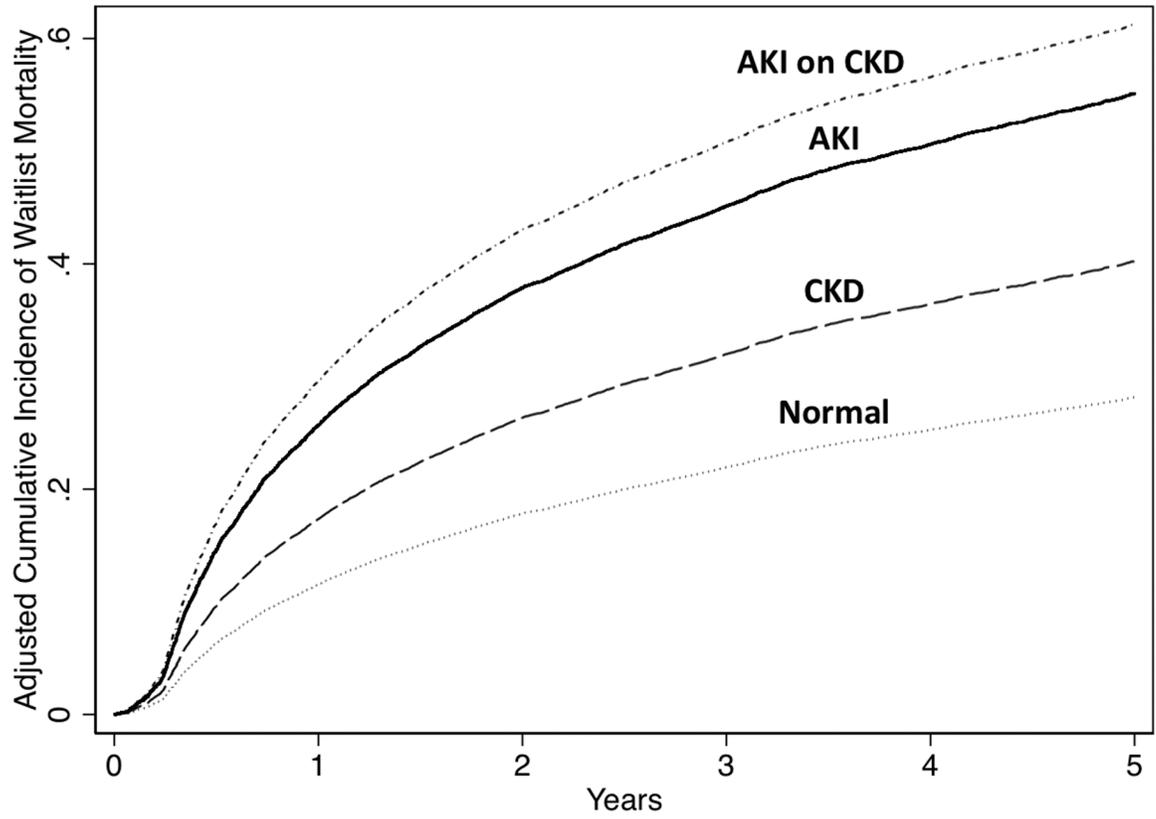


Figure 2. Cumulative Incidence Curve for Waitlist Mortality by Renal Function Pattern

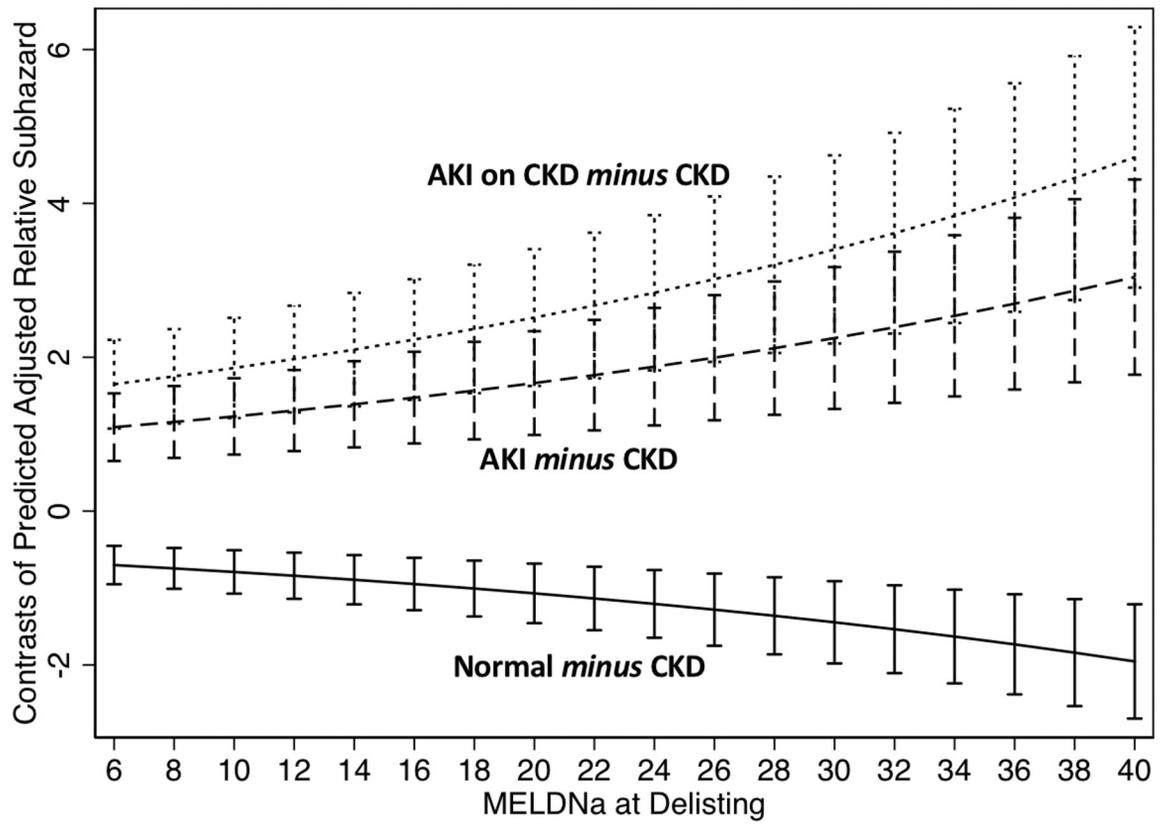


Figure 3. Contrasts of Adjusted Mean Subhazard Ratio in Reference to CKD at Varying Final MELDNa Scores

Error bars represent 95% Confidence Intervals

Table 1.

Baseline Demographics

Characteristic	Entire Cohort (n = 22 680)
Years on waitlist, m(IQR)	1.6 (0.7 – 3.1)
Age at delisting, m(IQR)	57 (51 – 63)
Female sex, no (%)	8805 (39)
Listing diagnosis, no. (%)	
Alcohol	4613 (20)
HCV	8762 (39)
NAFLD/NASH	4840 (21)
Autoimmune ^I	3142 (13)
Other	1323 (6)
Non-Hispanic white, no. (%)	16572 (73)
Ascites, no. (%)	7302 (32)
Hepatic encephalopathy, no. (%)	2997 (13)
Diabetes Mellitus, no. (%)	5665 (25)
MELDNa at listing, m(IQR)	16 (13 – 20)
MELDNa at delisting, m(IQR)	20 (14 – 29)
Met CKD, no. (%)	6965 (31)
Hemodialysis during follow-up, no. (%)	2522 (11)
Listed for SLKT, no. (%)	2333 (10)
Waitlist Outcome, no. (%)	
Still Waiting	8582 (38)
“Too Sick” or Death	7460 (33)
DDLT	6638 (29)

^I Combined Autoimmune Hepatitis, Primary Sclerosing Cholangitis, and Primary Biliary Cholangitis; Hepatitis C (HCV); Non-Alcoholic Steatohepatitis (NASH); Model for End-Stage Liver Disease with Serum Sodium (MELDNa)

Table 2.

Time-Dependent Competing Risk Regression Analysis for Waitlist Mortality

	Univariable			Multivariable*		
	SHR	95% CI	p-value	SHR	95% CI	p-value
Renal Group						
Normal	-	-	-	-	-	-
AKI	3.25	3.00 – 3.52	<0.001	2.42	2.22 – 2.64	<0.001
CKD	1.82	1.70 – 1.95	<0.001	1.56	1.45 – 1.67	<0.001
AKI on CKD	4.03	3.75 – 4.34	<0.001	2.86	2.65 – 3.10	<0.001
Age per Year	1.02	1.02 – 1.03	<0.001	1.02	1.02 – 1.03	<0.001
Female Sex	1.09	1.04 – 1.15	<0.001	1.11	1.05 – 1.18	<0.001
Etiology						
Alcohol	-	-	-	-	-	-
HCV	1.22	1.14 – 1.31	<0.001	1.03	0.95 – 1.11	0.48
NASH	1.17	1.09 – 1.27	<0.001	0.93	0.85 – 1.02	0.13
Autoimmune ^I	0.88	0.81 – 0.97	0.006	0.85	0.76 – 0.94	0.002
Other	0.96	0.85 – 1.08	0.48	1.01	0.88 – 1.16	0.85
Non-Hispanic White	0.94	0.89 – 0.99	0.02			
BMI per 1 kg/m ²	1.00	1.00 – 1.01	0.08	0.99	0.98 – 0.99	<0.001
Ascites	1.56	1.48 – 1.63	<0.001	0.86	0.81 – 0.92	<0.001
HE	2.80	2.65 – 2.96	<0.001	1.91	1.79 – 2.05	<0.001
Diabetes Mellitus	1.30	1.23 – 1.37	<0.001	1.09	1.02 – 1.17	0.007
KPS at last follow-up per 10 points	0.94	0.93 – 0.95	<0.001			
Ventilator Use at Last Follow-Up	0.96	0.55 – 1.67	0.88			
Final MELDNa per point	1.05	1.05 – 1.06	<0.001	1.03	1.02 – 1.04	<0.001
Final Albumin per 1g/dL	0.63	0.61 – 0.66	<0.001	0.68	0.65 – 0.70	<0.001

^I Combined Autoimmune Hepatitis, Primary Sclerosing Cholangitis, and Primary Biliary Cholangitis; Hepatitis C (HCV); Non-Alcoholic Steatohepatitis (NASH); Body Mass Index (BMI); Hepatic Encephalopathy (HE); Karnofsky Performance Score (KPS); Model for End-Stage Liver Disease with Serum Sodium (MELDNa);

* adjusted for region and blood type

Table 3.

Odds of Waitlist Mortality at 6 Months Based on Pattern of Renal Function, Controlling for MELDNa

Models and Variables	6-Month Waitlist Mortality			AUC
	OR	95% CI	P	
<i>1</i>				
MELDNa at Listing	1.14	1.13 – 1.16	<0.001	0.71*
<i>2</i>				
MELDNa at Listing	1.14	1.12 – 1.16	<0.001	
Renal Group				
Normal	-	-	-	0.80*
AKI	6.23	5.19 – 7.48	<0.001	
CKD	0.82	0.58 – 1.16	0.27	
AKI on CKD	3.65	2.56 – 5.22	<0.001	

* Indicates that AUCs are statistically different at the p<0.05 level

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