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Waitlisted candidates with polycystic liver disease are more likely to be transplanted than those with chronic liver failure

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Abstract

Background—Polycystic liver disease (PCLD) is characterized by cystic replacement of the hepatic parenchyma, leading to hepatic dysfunction, portal hypertension, and hepatomegaly. Patients with liver dysfunction and/or symptomatic disease are eligible for liver transplantation. However, little is known about these patients' waitlist outcomes relative to others with chronic liver disease.

Methods—We used OPTN/UNOS data from February 27, 2002 to December 31, 2015 to compare waitlist outcomes of adult patients with PCLD to those with chronic liver failure (CLF) and hepatocellular carcinoma (HCC).

Results—The study cohort included 620 patients with PCLD, 18 240 patients with HCC, and 98 567 patients with CLF. Compared to CLF patients, PCLD patients had significantly lower bilirubin and INR at waitlisting, and less ascites and encephalopathy. However, they were significantly more likely to have severe chronic kidney disease. Moreover, patients with PCLD were more than 70% more likely to be transplanted compared to patients with CLF (OR: 1.72, 95% CI: 1.46–2.02) and had significantly longer posttransplant survival ($p < 0.001$). PCLD patients with exceptions were 5.7 times more likely to be transplanted than those without (OR: 5.67, 95% CI: 3.95–8.15).

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Authorship Page

Sahil D Doshi – Conception and design of the work, analysis and interpretation of data, and drafting of the work.

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and measures of hepatic/renal dysfunction were inversely associated with the receipt of exceptions.

Conclusions—Despite having more preserved liver synthetic function than patients with CLF on the waitlist, patients with PCLD are preferentially transplanted because they frequently receive exception points in an unstandardized fashion.

Introduction

Polycystic liver disease (PCLD) is a genetic disorder characterized by cystic replacement of the hepatic parenchyma. This disease has 2 forms: a) autosomal dominant polycystic liver disease (ADPLD), in which cysts are isolated in the liver; and 2) autosomal dominant polycystic kidney disease (ADPKD), in which cysts occur in the liver and the kidney ¹. Mutations in 2 genes, PRKCSH and SEC63, are found in 20% of patients with ADPLD, while mutations in 2 other genes, PKD1 and PKD2, are associated with 85–90% and 10–15% of ADPKD cases, respectively ^{1–3}. Both forms are rare overall and, ADPLD only affects 1/100 000 patients in the U.S. ^{1,4,5}.

In over 95% of patients, PCLD is asymptomatic. However, in approximately 3% it can become clinically significant due to increasing cyst number and/or volume, which can lead to hepatic dysfunction, portal hypertension, and hepatomegaly ¹. Because of a lack of effective medical therapies for PCLD, patients with symptomatic disease may be eligible for liver transplantation (LT) ⁶. Though patients with ADPLD often have larger and more numerous liver cysts than those with ADPKD, they typically undergo LT less often, perhaps due to the absence of kidney dysfunction ⁵.

Long-term posttransplantation outcomes for PCLD patients are favorable, though reported survival estimates are highly variable due to limited large volume studies ^{6,7}. Due to the presence of disease-associated renal insufficiency, up to 40% of patients transplanted for PCLD undergo simultaneous liver-kidney transplantation (SLK) ⁸. Because patients with PCLD have a relative absence of hepatic dysfunction and are commonly transplanted for uncontrolled symptoms related to hepatomegaly, they frequently have low biologic MELD scores at transplantation or MELD scores primarily driven by their creatinine ^{8,9}.

In 2015, the Organ Procurement and Transplantation Network (OPTN) published a guidance document to standardize the submission and allocation of exception points in candidates with PCLD to encourage transplantation within 1 year and to prioritize patients thought to have an increased risk of waitlist mortality from liver related comorbidities. These recommendations require the presence of severe diffuse cystic disease with at least 2 of the following: hepatic decompensation, hemodialysis, and “compensated comorbidities” ¹⁰. However, “compensated comorbidities” has not been defined, nor is this terminology used elsewhere in OPTN policies. Moreover, these recommendations are not evidence-based, as no study has specifically evaluated the use of exception points in the PCLD patient population, especially in context of the OPTN/UNOS Liver and Intestinal Organ Transplantation Committee statement that exception points should be based on risk of waitlist mortality and not quality-of-life.¹¹ In an era of organ shortage and other competing

LT indications with high waitlist mortality, an understanding of whether candidates with PCLD are being appropriately prioritized for LT is required.

Materials and Methods

Study participants

This was a retrospective cohort study using OPTN/UNOS data that included all adults (≥ 18 years of age) waitlisted for LT between February 27, 2002 and December 31, 2015, with follow-up until March 4, 2016. We excluded patients listed for re-transplantation, multi-organ waitlist candidates (other than those waitlisted for an SLK), and those waitlisted as Status 1.

We identified the etiology of liver disease using diagnostic codes and/or free text. Patients were categorized as: 1) PCLD if they had a diagnostic code of PCLD and/or had free text diagnoses of PCLD and/or cystic liver disease in the setting of polycystic kidney disease; (2) chronic liver failure (CLF) which included all other patients waitlisted for LT without exception points; and 3) hepatocellular carcinoma (HCC) based on receipt of standardized MELD exception points for HCC within Milan criteria. We included patients with standardized MELD exception points for HCC within Milan criteria to help contextualize exception point allocation in PCLD patients¹².

Outcomes

The primary outcome was LT among waitlisted patients, as the goal of the study was to evaluate differences in transplant rates for patients with PCLD and CLF. Secondary outcomes included receipt of exception points, waitlist removal for death or clinical deterioration, and posttransplant patient survival. Furthermore, we categorized PCLD patients according to whether they met the current OPTN recommendations for exception point allocation and compared outcomes based on this. Because all of the data to define those meeting the OPTN criteria are not available in the OPTN/UNOS dataset, we defined patients meeting OPTN guidelines if the patient had both a hepatic decompensation (ascites and/or encephalopathy at listing or transplant if transplanted) and was on dialysis (those on dialysis at listing or transplant if transplanted). In doing so, we assumed all waitlisted PCLD patients had severe diffuse cystic disease. Since the term “compensated comorbidities” has not been defined, we were not able to include this criterion in the categorization.

Statistical Analysis

Chi-square tests were used for categorical variables, while Kruskal-Wallis tests were used to evaluate continuous variables among the 3 groups. Multivariable logistic regression models were used to compare the odds of transplantation for patients with PCLD, CLF, and HCC. Logistic regression using a binary outcome was used to assess waitlist outcomes, as the outcome of interest for waitlisted patients is death/delisting for being too sick or transplantation. The end date for inclusion and the follow-up period ensured a minimum of nearly 3 months follow-up for all patients, which is appropriate as the MELD score is a validated predictor of 3 month waitlist outcomes. Covariates that could potentially confound the relationship between disease category and transplant were first tested in univariable

models, and variables with a $p < 0.1$ in univariable models were included in potential multivariable models; only variables with a $p < 0.05$ were retained in the final model. Covariates included gender, race/ethnicity, and age. Since we only included covariates that could confound the odds of transplantation, receipt of MELD exception points was not tested in these models, as it would be in the causal pathway for PCLD and HCC patients. Waitlist data on severity of ascites and hepatic encephalopathy at waitlisting, bilirubin and INR, and chronic kidney disease (CKD) stage were not tested either, as they would be in the causal pathway for LT candidates.

Secondary models evaluated factors associated with transplantation in patients with PCLD (exception points included in this model), as well as factors associated with receiving exception points among patients with PCLD (CKD stage included in this model). CKD stage was defined according to Kidney Disease Outcomes Quality Initiative guidelines and determined by the estimated glomerular filtration rate (eGFR) using the Modification of Diet in Renal Disease-4 formula¹³.

We evaluated unadjusted posttransplant patient survival probability using Kaplan-Meier analysis and compared all 3 groups using the log-rank test. We only evaluated unadjusted survival in order to report actual outcomes of patients based on indication for transplantation. Such data served to place posttransplant outcomes in perspective, without adjusting for factors that may have influenced outcomes, as the goal of the study was not to compare and/or assess factors with posttransplant survival.

All statistics and calculations were performed using SPSS Statistics Version 23 (IBM, Armonk, NY) and Stata Version 14.0 (StataCorp, College Station, TX). This study received an exempt status from the Institutional Review Board of the University of Pennsylvania.

Results

Characteristics at waitlisting

The final cohort included 620 patients with PCLD, 18 240 patients with HCC, and 98 567 patients with CLF waitlisted for LT during the study period. All HCC patients included in the final cohort received exception points. Of the 98 567 CLF patients, 36 673 (37.2%) had Hepatitis C, 19 969 (20.3%) had alcoholic liver disease, 2557 (2.6%) had Hepatitis B, 17 029 (17.3%) had nonalcoholic fatty liver disease, 4644 (4.7%) had primary sclerosing cholangitis, 3662 (3.7%) had an autoimmune liver disease, 3639 (3.7%) had primary biliary cirrhosis, and 10 394 (10.6%) were classified as other.

Clinical and demographic characteristics are listed in Table 1. PCLD patients were significantly more likely to be female (71.5% vs 22.8% and 36.1%, respectively; $p < 0.001$) and had lower median bilirubin and INR levels compared to HCC and CLF patients ($p < 0.001$). Patients with PCLD and HCC were significantly less likely to have decompensated liver disease as manifested by ascites and/or encephalopathy compared to CLF patients ($p < 0.001$; Figures 1a–1b), and there were significant differences in baseline CKD stage among the 3 groups ($p < 0.001$; Figure 1c). Although a similar proportion of patients with PCLD and HCC had ascites, a greater proportion of PCLD patients had

moderate-severe, rather than mild ascites (Figure 1a). In the PCLD patients with mild and moderate-severe ascites, the serum albumin at waitlisting was higher than the serum albumin in patients with HCC and CLF with mild and moderate-severe ascites.

Among the 3 groups, patients with PCLD were least likely to have a history of hepatic encephalopathy (23.0%), compared to patients with HCC (39.5%) and CLF (63.9%; $p<0.001$ comparing PCLD vs HCC and PCLD vs CLF; Figure 1b). However, a significantly greater proportion of patients with PCLD had CKD stage 4 or 5 (50.3% vs 1.6% for HCC and 13.4% for CLF; $p<0.001$ for all among-group comparisons; Figure 1c). Of the PCLD patients that underwent LT, 34.5% of patients were on dialysis prior to transplant as compared to 0.9% of HCC patients and 16.2% of CLF patients ($p<0.001$). There was not a clinically meaningful difference in the median serum sodium levels at waitlisting among the 3 groups (139 mEq/L for PCLD patients; 138 mEq/L for HCC patients; 136 mEq/L for CLF patients). Body mass index values that classify an individual as underweight ($<18.5\text{kg/m}^2$) were characterized among the 3 groups as a clinical surrogate marker since PCLD patients can be listed for LT for reasons relating to severe body weight loss, cachexia, and sarcopenia. The proportion of transplant recipients that were underweight (calculated body mass index $<18.5\text{kg/m}^2$ at transplant) was not clinically significant across the 3 groups (3.9% for PCLD patients; 0.7% for HCC patients; 3.5% for CLF patients).

Unadjusted and adjusted waitlist and posttransplant outcomes

Unadjusted waitlist outcomes differed significantly among the 3 groups ($p<0.001$, Figure 2). Among the 620 PCLD patients, 351 (56.6%) were transplanted while 81 (13.1%) died or became too sick for transplantation. Of the 169 PCLD patients that met OPTN guidelines for exceptions, 100 (59.2%) were transplanted. Of the 351 total LT recipients, 183 (52.1%) had an SLK. Of the 183 SLK recipients, 90 (49.2%) met OPTN guidelines for exceptions, while of the 168 LT-only recipients, only 10 (6.0%) met OPTN guidelines ($p<0.001$ comparing SLK vs LT-only for meeting OPTN guidelines). Patients meeting OPTN guidelines for PCLD exceptions were significantly more likely to be removed from the waitlist due to death or clinical deterioration than the patients who did not meet guidelines (17.8% vs 11.3%, $p=0.034$), but had no differences in the probability of being transplanted (59.2% vs 55.7%, $p=0.43$).

To put these outcomes in context, 15 444 (84.7%) patients with HCC were transplanted while 941 (5.2%) were removed after dying or becoming too sick to transplant, as compared to 43 545 (44.2%) CLF patients who were transplanted and 26 472 (26.9%) who died or became too sick to transplant.

Of the 351 PCLD patients that were transplanted, 16 (4.6%) received a living donor graft, which was comparable to the 5.1% of CLF patients that received livers from living donors, but significantly higher than the 1.2% of HCC patients ($p<0.001$). Among transplant recipients in the 3 groups, the median (IQR) waiting time for PCLD patients was significantly higher than it was for transplant recipients with HCC or CLF (PCLD: 196 days (77–480); HCC: 130 days (47–294); CLF: 58 days (13–206); $p<0.001$). For PCLD patients that received exception points and underwent LT, the median difference between the exception MELD score and the calculated MELD score at transplantation was 11, compared

to a median difference score of 13 for HCC patients that received exception points and underwent LT.

The severity of ascites was associated with survival in different patterns in the 3 groups of patients. Of the 270 patients with PCLD who had no ascites, 16 (5.9%) were removed from the waitlist after dying or becoming too sick, compared to 15.7% and 23.3% in those with mild ascites and moderate-severe ascites, respectively. By contrast, the proportion removed from the waitlist for death or clinical deterioration among HCC patients was 4.1%, 5.7%, and 9.2% in those with no, mild, and moderate-severe ascites, and 24.5%, 27.0%, and 28.5%, respectively, in CLF patients.

These differences in transplantation rates persisted after covariate adjustment in multivariable models (Table 2). After adjusting for factors that may confound the relationship between PCLD and transplantation, it was found that patients with PCLD were more than 70% more likely to be transplanted when compared to CLF patients (OR: 1.72, 95% CI: 1.46–2.02).

There were significant differences in unadjusted posttransplant survival across the 3 groups. While 1-year survival probability was clinically similar across all 3 groups (90.9% for PCLD vs 90.8% for HCC vs 88.4% for CLF; Table 3), Kaplan-Meier analysis revealed significantly longer posttransplant survival probability in patients with PCLD as compared to HCC and CLF ($p < 0.001$; Figure 3). Estimates of 3- and 5-year survival probability for LT recipients with PCLD were 88.8% and 85.1% compared to 79.3% and 70.8% with HCC, and 80.5% and 74.2% with CLF, respectively (Table 3).

Factors associated with transplantation and exception points in patients with PCLD

The only factor significantly associated with increased transplantation among PCLD patients was receipt of exception points. Severity of ascites at waitlisting, severity of hepatic encephalopathy at waitlisting, bilirubin and INR levels at waitlisting, CKD stage, age, gender, and ethnicity were all not significantly associated with increased odds of transplantation. Of the 620 patients with PCLD, 269 (43.4%) received exception points while 351 (56.6%) did not, with significantly different waitlist outcomes based on receipt of exception points ($p < 0.001$): 78.8% vs 39.6% were transplanted while 2.2% vs 21.4% died or became too sick for transplantation for those receiving vs not receiving exception points, respectively. In univariable logistic regression models, patients with PCLD who received exception points were more than 5 times more likely to be transplanted than those without (univariable unadjusted OR: 5.67, 95% CI: 3.95–8.15). Severity of hepatic and/or renal dysfunction, as indicated by INR, bilirubin, and CKD stages, was inversely associated with the receipt of exception points in PCLD patients (Table 4).

There was significant geographic variability in the proportion of waitlisted patients with PCLD who were transplanted ($p < 0.001$, Supplementary Figure 1a). Despite UNOS regions 1, 5, and 9 having the overall highest median allocation MELD scores at transplantation, there was a numerical, albeit not statistically significant, difference in the proportion of PCLD patients transplanted in those 3 regions ($p = 0.3$)¹⁵. Similarly, there was a numerical but not statistically significant difference in the proportion of patients with PCLD in regions

1, 5, and 9 who received exception points (Supplementary Figure 1b, $p=0.2$). There were no among-region differences in the risk of waitlist mortality in PCLD patients who did not receive exception points ($p=0.09$). The median total bilirubin and INR and CKD stage distribution were not different among waitlisted patients with PCLD in these 3 regions ($p>0.1$ for each comparison; Supplementary Table 1). Overall, the OPTN/UNOS region of residency compared to region of transplantation for PCLD patients was similar to that of the overall LT population.

Discussion

This analysis of national transplant data demonstrates that patients with PCLD are significantly more likely to be transplanted than patients with CLF despite having less evidence of liver synthetic dysfunction and/or portal hypertension. Moreover, PCLD patients with less evidence of liver synthetic dysfunction had significantly lower waitlist mortality. However, this subset was more likely to receive exception points, as markers of liver dysfunction (and MELD overall) were inversely associated with receipt of exceptions. The major driver of biologic MELD score in PCLD patients is baseline CKD, presumably due to the presence of associated polycystic kidney disease. In addition, exception points significantly increase the match MELD score of candidates listed with PCLD. For both reasons, PCLD patients are much more likely to be transplanted and less likely to die on the waitlist or become too sick for transplant when compared to CLF patients. As there are proposals to consider national review boards and/or evidence-based guidelines for awarding exception points, the low waitlist mortality rates combined with high transplant rates for PCLD need to be considered when refining the system intended to offer priority for transplant to the sickest patients in greatest need.

While a few studies have described exception point allocation in PCLD patients that are transplanted, this is the first study to explain the clinical presentation of PCLD patients that are waitlisted for LT, and to compare their outcomes with and without exception points⁸. This study not only contributes to the present knowledge of MELD exception point allocation in PCLD patients over the last 13 years, but also compares these outcomes relative to waitlisted CLF patients without exception points and HCC patients with standardized exceptions.

The 2 forms of PCLD, ADPLD and ADPKD, share a similar natural history: there is an increase in size and number of cysts found in the liver, resulting in a continuous increase in volume of the affected liver over time^{16,17}. While both men and women can develop cysts, the disease presentation is significantly more severe in women^{5,17,18}. Prior studies have also shown that symptomatic ADPLD patients are mainly female¹⁹. This may explain why a significantly greater proportion of PCLD patients on the LT waitlist in this study were women, as compared to HCC and CLF patients. However, in both men and women, liver function and hepatic parenchymal volume are mostly preserved²⁰. In fact, polycystic livers have been previously used for emergent transplantation, as advanced fibrosis and portal hypertension are rare^{21–23}. In addition, when these complications are present, they are often due to hepatic venous outflow obstruction or compression of the portal vein²⁴. Furthermore, PCLD livers do not become cirrhotic and are not at an increased risk of developing

malignancy¹. In ADPKD patients, the most detrimental component is the underlying renal cystic disease, which may lead to loss of renal function. This loss of renal function may explain why PCLD patients had a greater proportion of moderate-severe ascites levels than HCC patients in this study, as their serum albumin levels were higher than patients with CLF or HCC who had ascites.

When kidney dysfunction is modest or absent, the intact liver function found in PCLD patients often results in biologic MELD scores that are insufficient for transplantation. These patients frequently receive exception points, which are awarded in an unstandardized fashion. A recent OPTN/UNOS guidance document has suggested recommendations for awarding MELD exception points to PCLD patients. However, due to the scarcity of studies specifically evaluating exception point allocation in PCLD patients, these recommendations are not evidence-based. In most patients, PCLD does not affect survival and liver function is preserved even in severe cases. As demonstrated in this study, patients with PCLD were less likely to die or become too sick for transplant while waitlisted and had an overall waitlist mortality that was half that of CLF patients. Therefore, the MELD allocation system needs a better definition of which PCLD patients are truly at risk for waitlist mortality and most likely to benefit from LT.

From a policy standpoint, it may be argued that the 351 transplants for PLCD over the last 13 years is not that significant of a problem, considering the 70 000–80 000 LTs overall during the same time period. However, these 30 transplants per year are being performed in patients who have significantly lower waitlist mortality rates as a group, which is the intended basis for MELD score prioritization, and could be allocated to other waitlisted candidates with greater synthetic liver dysfunction and a higher risk of dying on the waitlist. While from a utility-perspective it is reassuring that transplanted PCLD patients have significantly longer post-LT survival, the current MELD system is an urgency-based system meant to reflect waitlist mortality.

These results highlight the need for continued revision of the OPTN recommendations for exception point allocation among candidates waitlisted with PCLD, in addition to continued monitoring of the impact of the same guidance document that included PCLD on exception points for other disease states (eg, primary sclerosing cholangitis). One potential provision includes adding a clinically elevated INR (INR>1.5) and/or bilirubin (bilirubin >2.5) at waitlisting to the current recommended OPTN exception criteria (ascites and/or encephalopathy and dialysis). In our sample of 169 patients who met the current OPTN exception criteria, the 38 patients with abnormal laboratory values as above had a waitlist mortality of 26.3%, which is comparable to the CLF group's waitlist mortality of 26.9%. This additional provision may yield a system that is more equitable with respect to waitlist mortality, which is the intended basis for MELD score prioritization.

There were notable differences in the rates of living donor liver transplantation in the PCLD, CLF, and HCC groups. This is likely explained by the fact that HCC patients receive standardized exception points if their biologic MELD scores are not sufficient for LT, and therefore with sufficient waiting time will achieve a MELD score high enough to be transplanted.

There were several limitations to this study. First, clinical phenotypes of PCLD patients, such as whether they had sepsis related to infected cysts or pain from hepatomegaly, were not available so rationale for exception point allocation was not entirely known. However, markers of liver synthetic function were available, which were used to guide the clinical status of patients. Also, patient data was obtained from the OPTN/UNOS database and had already been coded into demographics, clinical variables, and outcomes. Therefore, subjective estimates of ascites and encephalopathy may be variable both within and among transplant centers. In addition, a breakdown of PCLD patients that had ADPKD versus ADPLD was not available. Therefore, the previously reported finding that patients with ADPKD undergo LT more frequently could not be confirmed in this study. Only data from PCLD patients that were listed for LT was available; thus the characteristics and outcomes of all PCLD patients were not evaluated. However, it is reasonable to believe that the more clinically affected PCLD patients were listed for LT, and given that the goal of this study was to understand the severity of liver disease in PCLD patients as compared to CLF patients, this level of data was deemed sufficient.

The central problem in the field of LT is the scarcity of donor organs, which necessitates an equitable and efficient allocation system. In the case of PCLD, exception points are allocated in a nonstandardized manner and vary regionally. Whether exception point allocation for LT remains up to Regional Review Boards or becomes a national system, a more standardized set of criteria are required for exception point allocation in PCLD patients that are on the LT waitlist. In addition, a better understanding of which patients experience liver decompensation and are most likely to benefit from LT is needed. Furthermore, the possibility of using living donors for PCLD patients should be considered with greater frequency, as this would not disadvantage waitlisted candidates with CLF. Ultimately, the current guidelines do not appropriately prioritize PCLD patients as compared to other waitlisted patients, resulting in a process that is incongruent with its intention.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Abbreviations Page

ADPKD	autosomal dominant polycystic kidney disease
ADPLD	autosomal dominant polycystic liver disease
CKD	chronic kidney disease
CLF	chronic liver failure

eGFR	estimated glomerular filtration rate
HCC	hepatocellular carcinoma
INR	international normalized ratio
LT	liver transplantation
OPTN	Organ Procurement and Transplantation Network
PCLD	polycystic liver disease
SLK	simultaneous liver-kidney transplantation
UNOS	United Network for Organ Sharing

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Figure 1.

(3 panels)

a: Severity of ascites at waitlisting in liver transplant candidates in the U.S. between 2002–2015*

- i. Footnote: $p < 0.001$
- ii. Footnote: *Ascites at waitlisting data missing for 5 patients with HCC and 15 patients with CLF. Ascites categories based on coding in UNOS STAR file.

b: Severity of hepatic encephalopathy at waitlisting in liver transplant candidates in the U.S. between 2002–2015*

- i. Footnote: $p < 0.001$
- ii. Footnote: *Encephalopathy at waitlisting data missing for 5 patients with HCC and 15 patients with CLF. Encephalopathy categories based on coding in UNOS STAR file.

c: Chronic kidney disease stage at waitlisting in liver transplant candidates in the U.S. between 2002–2015*

- i. Footnote: $p < 0.001$
- ii. Footnote: *Chronic kidney disease stage based on Kidney Disease Outcome Quality Initiative guidelines using creatinine at time of waitlisting

Figure 2.
Outcomes of patients waitlisted for liver transplantation in the U.S. between 2002–2015

i. Footnote: $p < 0.001$

Figure 3.
Unadjusted posttransplant survival probability of liver transplant recipients in the U.S.
between 2002–2015

Table 1

Demographic and clinical characteristics of patients waitlisted for liver transplantation in the U.S. between 2002–2015

Variable	PCLD N=620	HCC N=18 240	CLF N=98 567	P-value
Age at listing, median (IQR)	54 (48–60)	58 (53–63)	55 (48–60)	<0.001
Female gender, N (%)	443 (71.5)	4158 (22.8)	35 631 (36.1)	<0.001
Race/ethnicity, N (%)				<0.001
White	428 (69.0)	12 114 (66.4)	70 877 (71.9)	
Black	91 (14.7)	1701 (9.3)	8339 (8.5)	
Hispanic	60 (9.7)	2626 (14.4)	14 699 (14.9)	
Asian	32 (5.2)	1552 (8.5)	3441 (3.5)	
Other	9 (1.5)	247 (1.4)	1211 (1.2)	
Bilirubin at listing, median (IQR)	0.6 (0.4–0.9)	1.3 (0.9–2.1)	2.7 (1.5–5.7)	<0.001
INR at listing, median (IQR)	1.1 (1.0–1.2)	1.2 (1.1–1.4)	1.4 (1.2–1.8)	<0.001

Abbreviations: PCLD=Polycystic liver disease; HCC=Hepatocellular carcinoma; CLF=Chronic liver failure; INR=International normalized ratio

Table 2

Multivariable logistic regression model evaluating factors associated with receiving a liver transplant for patients in the U.S. between 2002–2015

Variable	Multivariable OR, 95% CI	P-value
Category		<0.001
CLF	Reference	
PCLD	1.72 (1.46–2.02)	
HCC	7.54 (7.22–7.87)	
Female gender	0.86 (0.84–0.88)	<0.001
Age	0.99 (0.98–0.99)	<0.001
Race/Ethnicity		<0.001
White	Reference	
Black	1.15 (1.10–1.20)	
Hispanic	0.75 (0.72–0.78)	
Asian	0.66 (0.62–0.70)	
Other	0.86 (0.77–0.96)	

Abbreviations: CLF=Chronic liver failure; PCLD= Polycystic liver disease; HCC= Hepatocellular carcinoma

Table 3

Unadjusted posttransplant survival data for liver transplant patients in the U.S. between 2002–2015

Category	Unadjusted posttransplant survival, % (95% CI)		
	1-year	3-year	5-year
PCLD	90.9 (87.2–93.6)	88.8 (84.6–91.9)	85.1 (80.1–88.9)
HCC	90.8 (90.4–91.3)	79.3 (78.6–80.0)	70.8 (69.9–71.7)
CLF	88.4 (88.0–88.7)	80.5 (80.1–80.9)	74.2 (73.7–74.6)

Abbreviations: PCLD=Polycystic liver disease; HCC=Hepatocellular carcinoma; CLF=Chronic liver failure

Table 4

Multivariable logistic regression model evaluating factors associated with receiving exception points among waitlisted patients with PCLD in the U.S. between 2002–2015, N=620

Variable	Multivariable OR, 95% CI	P-value
Bilirubin at waitlisting	0.78 (0.66–0.92)	0.004
INR at waitlisting	0.44 (0.22–0.88)	0.02
CKD stage at waitlisting		<0.001
Stage 1	Reference	
Stage 2	0.89 (0.44–1.78)	
Stage 3	0.76 (0.39–1.51)	
Stage 4	0.44 (0.22–0.91)	
Stage 5	0.38 (0.20–0.74)	

Abbreviations: INR= International normalized ratio; CKD= Chronic kidney disease