Sex disparities in waitlisting and liver transplant for acute liver failure
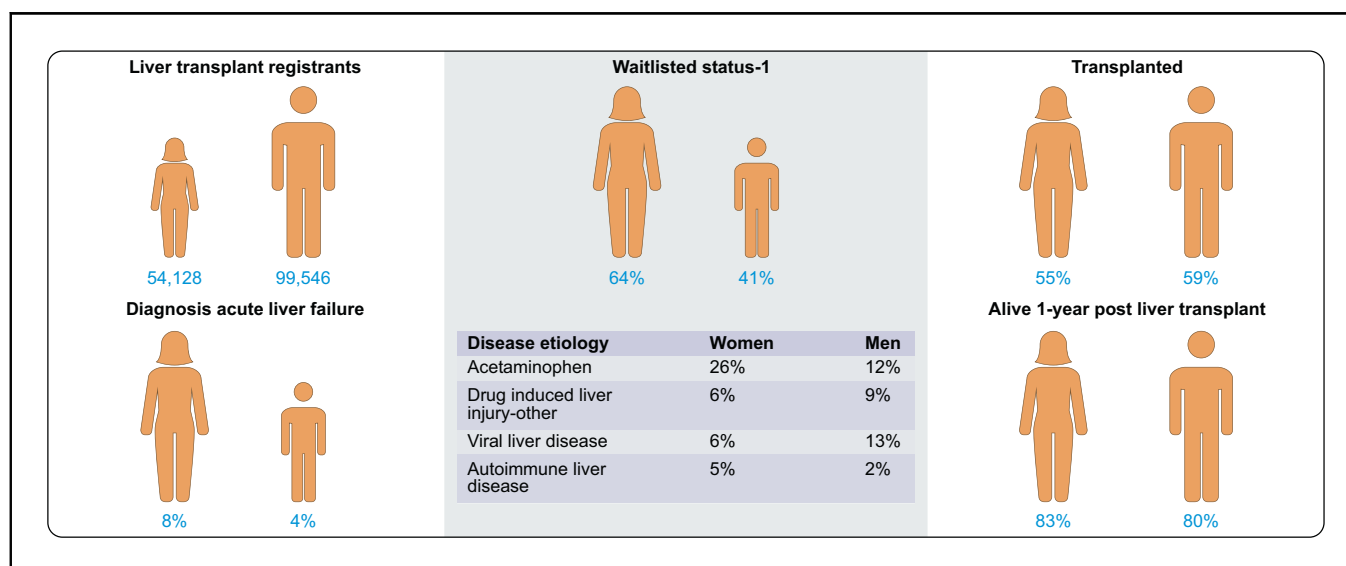
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Graphical abstract

Liver transplant registrants
54,128 — 99,546

Diagnosis acute liver failure
8% — 4%

Waitlisted status-1
64% — 41%

Disease etiology	Women	Men
Acetaminophen	26%	12%
Drug induced liver injury-other	6%	9%
Viral liver disease	6%	13%
Autoimmune liver disease	5%	2%

Transplanted
55% — 59%

Alive 1-year post liver transplant
83% — 80%

Highlights

- Women with ALF more often require urgent Status-1 waitlisting.

- There were no sex-based based disparities in liver transplantation for ALF.

- This is in contrast to chronic liver disease, where sex-based disparities exist.

- Status-1 priority may mitigate sex-based disparities in LT.

Lay summary

Women with acute liver failure appear to be sicker than men and more often require urgent Status-1 waitlisting. There were no sex disparities in waitlist removal because of clinical deterioration or liver transplantation. This is in contrast to chronic liver disease, where sex disparities exist. The Status-1 waitlisting that women with acute liver failure receive may in part mitigate sex disparities in liver transplantation.

Sex disparities in waitlisting and liver transplant for acute liver failure

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Background & Aims: Sex disparities in liver transplantation (LT) for chronic liver disease have been described. It is unclear if similar disparities exist for acute liver failure (ALF).
Methods: Adults waitlisted for LT from 2002 to 2016 with ALF were investigated using the United Network of Organ Sharing database. Clinical characteristics and causative aetiologies were compared between men and women who were waitlisted Status-1. Differences in LT, waitlist removal, and 1-year post-transplant survival were explored.
Results: Of 8,408 patients waitlisted for LT with ALF, 41.3% of men and 63.9% of women were waitlisted Status-1 (p <0.001). Women had significantly higher international normalised ratio, higher frequency of grade 3–4 hepatic encephalopathy, and different aetiologies of ALF than men. On univariable analysis, women were less likely to undergo LT (subdistribution hazard ratio [SHR] 0.90; 95% CI 0.84–0.97) and were more likely to die or be removed from the waitlist as a result of clinical deterioration (SHR 1.14; 95% CI 1.002–1.30) than men. The disparities in LT (HR 0.95; 95% CI 0.87–1.03) and death/clinical deterioration (SHR 1.13; 95% CI 0.99–1.29) were no longer significant on multivariable analysis. On multivariable analysis, there was no difference in 1-year post-transplant survival between men and women.
Conclusions: Women with ALF are more likely to be waitlisted Status-1 than men. There were no clear disparities in LT or waitlist removal. Sex differences in LT and waitlist removal were attenuated on fully adjusted models, suggesting that these disparities may in part be mitigated by Status-1 listing.

Introduction

There are important biologic and behavioural differences between men and women that lead to differences in clinical presentation and natural history of disease.[1] These differences are apparent in liver disease with women being more severely affected by alcohol- and drug-induced liver injury (DILI) and having a higher incidence of acute liver failure (ALF) than men.[2]

Sex differences in the aetiology and the presentation of ALF have been described. Women are more likely to present with acetaminophen-induced ALF with worse encephalopathy.[3] However, less is known about sex differences in the frequency or severity of rarer causes of ALF, such as autoimmune hepatitis (AIH), which in its chronic form is more likely to affect women.

Although the majority of patients with ALF recover with supportive care, approximately 25% require liver transplantation (LT).[4] Sex disparities in LT for chronic liver diseases have been well described, with women being less likely to undergo LT and more

likely to die on the waitlist than men.[5,6] These disparities are thought to be driven by a combination of lower model for end-stage liver disease (MELD) scores in women compared with men because of lower creatinine levels, as well as difficulty finding appropriately sized organs for smaller statured women.[6,7] However, it is unclear if similar sex disparities exist for patients with ALF requiring LT.

Patients with ALF who meet specific criteria for acute and catastrophic liver failure can be waitlisted Status-1 for LT. This increases a candidate's waitlist priority with organs being offered to these patients first, ahead of patients with liver failure caused by chronic liver disease.[8] It is unclear if this increased priority and expanded donor pool is sufficient to negate the sex disparity in LT seen in chronic liver disease.

In this acutely ill population with high morbidity and mortality, recognising any disparity is important for optimising outcomes. In this study we explored sex differences in the presentation, aetiology, Status-1 waitlisting, LT, and waitlist removal in patients with ALF waitlisted Status-1 for LT.

Patients and methods

Study population

A retrospective cohort study of adults (aged 18 years and older) waitlisted for LT in the USA with a diagnosis of ALF between 27

February 2002 and 31 December 2016 was conducted. The United Network of Organ Sharing (UNOS) maintains a database which includes data on all candidates waitlisted for LT and was used for this analysis. This study was deemed exempt by the Indiana University School of Medicine Institutional Review Board, Indianapolis, Indiana.

To determine the number of patients with ALF who required Status-1 waitlisting, all patients with ALF were first identified. ALF was defined by a primary diagnosis code of ALF or an unknown primary diagnosis code coupled with Status-1 waitlisting and a free text diagnosis code consistent with ALF. Our analysis was restricted to patients with ALF waitlisted Status-1 for LT because (a) we were interested in characterising and exploring outcomes in the most acute cases of ALF and (b) Status-1 waitlisting requires strict criteria for ALF be met, thus ensuring our study contained true ALF cases and minimised misclassifications. Patients with codes for re-transplant were excluded from the analysis.

Sex was categorised as male or female. Race or ethnicity was categorised as White, Black, Hispanic, and Asian, based on UNOS classification. Patients coded as American Indian, Alaskan Native, Hawaiian/Pacific Islander, and other were classified as other.

Clinical and demographic characteristics of the recipient including age, height, blood type, laboratory MELD score and its components, grade of hepatic encephalopathy, ventilator status at time of waitlisting, the need for dialysis in the week before waitlisting, and region were compared between groups. Causative aetiologies were divided into 7 categories including: (1) DILI secondary to acetaminophen, (2) DILI from other causes, (3) viral liver disease (hepatitis B virus, hepatitis A virus, hepatitis C virus, varicella zoster virus, herpes simplex virus), (4) AIH, (5) Wilson's disease, (6) other (including, but not limited to, Budd Chiari, ischaemic cholangiopathy, and those coded as other), and (7) unknown. Seventy-five percent of the cases classified as other had a diagnosis code of primary graft non-function or hepatic artery thrombosis; however, these were not re-transplants in the database (patients did not have a transplant date or associated donor). These cases' diagnoses were misclassified in the database and were therefore coded as other in our analysis. We were interested in the number of cases with acute fatty liver disease of pregnancy given this uniquely impacts women. These cases were looked at separately and also classified as other. Causative aetiologies were defined based on primary and secondary diagnosis codes and free text diagnosis fields.

Donor characteristics included in the donor risk index were collected and included: age, race/ethnicity, height, cause of death, donor after cardiac death status, cold ischaemic time, and location of organ based on donor service area.

The primary outcomes were the frequency of LT and waitlist removal as a result of death or clinical deterioration. Waitlist removal because of other reasons such as recovery or inability to be reached were classified as other. These outcomes were identified using UNOS waitlist removal codes. The secondary outcome was 1-year post LT survival.

Statistical analysis

Baseline characteristics were presented as percentages. Means were presented for normally distributed variables and medians for non-normally distributed variables. Chi-square tests were used to compare categorical variables and rank sum and t tests used to compare continuous variables.
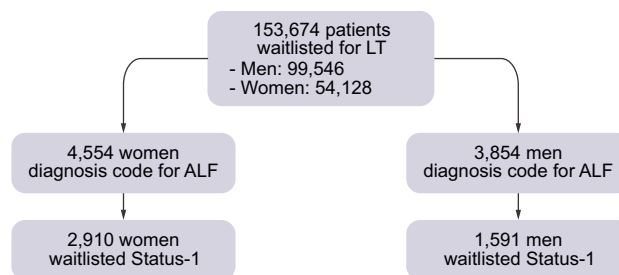

Fig. 1. **Patients with acute liver failure waitlisted Status-1 by sex.**

Trends in waitlisting were explored by plotting the percent of patients waitlisted Status-1 (denominator all patients waitlisted for LT during that year) for ALF annually. Spearman tests for trends were used to quantify the trend over the study period.

The cumulative incidence of death/clinical deterioration and LT were compared with the method of Fine and Gray. In these analysis both death/clinical deterioration and LT were considered in separate analysis as competing events. Unadjusted and adjusted subdistribution hazard ratios and corresponding 95% confidence intervals (CIs) were calculated using univariable and multivariable competing risk analysis. Two approaches were used in multivariable model building: (1) all variables collected were included in the model given their plausible association with the exposure and outcome and (2) only variables with p <0.1 on univariable analysis were included in the model (reduced model).

The Nelson-Aalen cumulative hazard function was used to explore gender differences in 1-year post LT mortality (1-Kaplan Meier estimates). Unadjusted and adjusted hazard ratios and corresponding 95% CIs were calculated using univariable and multivariable Cox regression models. All donor risk index components were included in the multivariable models. Then recipient variables including age and underlying aetiology were then included in the multivariable model. All analyses were performed using STATA version 14 (STATA Corp., College Station, TX, USA).

Results

There were 153,674 patients waitlisted for LT during the study period; 8,408 were waitlisted with ALF (3.9% of men and 8.4% of women, p <0.001). Of the ALF cohort, 4,501 patients were waitlisted Status-1 for LT (41.3% of men and 63.9% of women, p <0.001; Fig. 1). The number of men and women waitlisted Status-1 downtrended significantly over the study period (Spearman men −0.93, p <0.001; Spearman women −0.94, p <0.001; Fig. 2). There were 17 cases of acute fatty liver disease of pregnancy waitlisted.

Women waitlisted Status-1 were younger than men (women 39.8 years and men 43.7 years, p <0.001) and more likely to be Black (19.0% of women and 14.0% of men, p <0.001; Table 1). Women and men had similar MELD scores at waitlisting. However, women had lower creatinine and bilirubin, but higher international normalised ratio (INR) than men (Table 1). Women were more likely to have grade 3–4 hepatic encephalopathy than men (women 69.3% and 52.6% men, p <0.001; Table 1).

Aetiologies of ALF

ALF secondary to acetaminophen (women 26.0% *vs.* men 11.9%) and other causes of DILI (women 9.0% *vs.* men 5.7%) were more
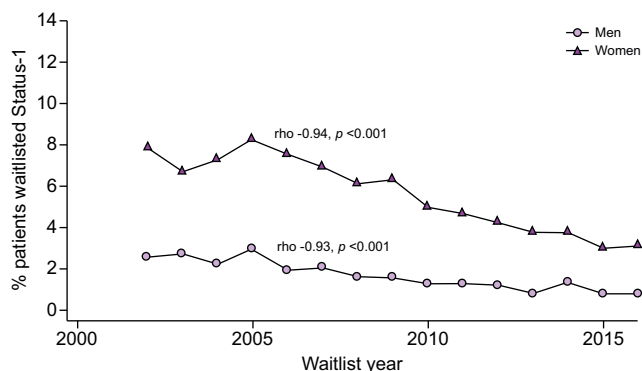
Fig. 2. Trends in acute liver failure in patients waitlisted Status-1 by sex. Spearman test for trend was used to explore trends in waitlisting, by sex, over time.

Fig. 3. Aetiologies of acute liver failure in patients waitlisted Status-1 by sex. Chi-squared testing was used to compare liver disease aetiologies by sex. AIH, autoimmune hepatitis; DILI, drug-induced liver injury.

common in women than men (Fig. 2). Women were more likely to have ALF secondary to AIH, whereas men were more likely to have ALF secondary to viral liver diseases (Fig. 3). There were 17 women with acute fatty liver disease of pregnancy waitlisted Status-1 during the study period.

Waitlist removal because of LT or death/clinical deterioration
Women were more likely than men to be removed from the waitlist because of death or clinical deterioration (women 22.6% and men 20.1%, p = 0.049; Table 2). The median MELD score at removal was 38.5 for men and 38 for women (p = 0.78; Table 2). The median time to removal was 2 days for both men and women (Table 2). On competing risk analysis (competing risk: LT) women were more likely to be removed from the waitlist because of death or clinical deterioration (subdistribution hazard ratio [SHR] 1.14; 95% confidence interval [CI] 1.002–1.30; Table 3). The disparity was no longer significant on multivariable analysis (SHR 1.13; 95% CI 0.99–1.29; reduced model: age, race/ethnicity, blood type, creatinine, INR, bilirubin, grade of hepatic encephalopathy, ventilator status at time of waitlisting, the need for dialysis in the week prior to waitlisting, region, and aetiology; Table 3).
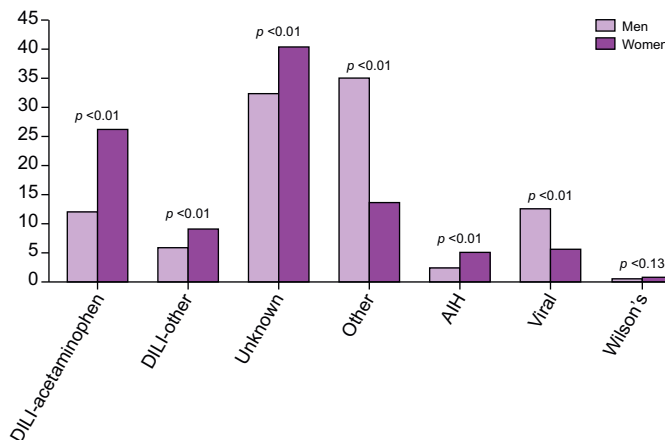
Women were less likely to be transplanted than men (54.6% of women and 59.0% of men, p = 0.01; Table 2). The median MELD score at transplant was 34 for both groups. The median time to LT was 2 days for both men and women (Table 2). On competing risk analysis (competing risk: death or clinical deterioration), women remained less likely to undergo LT than men (SHR 0.90; 95% CI 0.84–0.97; Table 3). The disparity was no longer significant on multivariable analysis (SHR 0.95; 95% CI 0.87–1.03; reduced model: blood type, creatinine, INR, bilirubin, grade of hepatic encephalopathy, ventilator status at time of waitlisting, the need for dialysis in the week prior to waitlisting, region, and aetiology; Table 3).

There were no differences between men and women in the number of patients who were removed from the waitlist because of other reasons including becoming too well for LT (men 20.6% and women 22.6%, p = 0.12; Table 2).

Of the 17 women who were waitlisted Status-1 for acute fatty liver disease of pregnancy, 10 (58%) were transplanted and 7 clinically improved and were removed from the waitlist.

Table 1. Clinical characteristics of patients with ALF waitlisted Status-1 for liver transplantation.

	Men n = 1,591	Women n = 2,910	*p* value
Age (years), mean ± SD	43.7 ± 14.5	39.8 ± 13.9	<0.001
Race/ethnicity (%)			
White	62.7	62.7	<0.001
Black	14.0	19.0	
Hispanic	12.3	10.6	
Asian	9.0	6.2	
Other	1.99	1.6	
Height (cm), mean ± SD	176.4 ± (13.8)	162.0 ± 10.5	<0.001
Listing MELD, median, IQR	35 (28–40)	35 (28–40)	0.96
INR	4.1 ± 4.5	4.8 ± 5.1	0.001
Serum creatinine (mg/dl), mean ± SD	2.3 ± 1.8	1.9 ± 1.5	<0.001
Serum total bilirubin (mg/dl), mean ± SD	14.4 ± 12.3	12.8 ± 10.5	<0.001
Grade 3–4 HE (%)	52.6	69.3	<0.001
Ventilator (%)	50.1	51.5	0.34
Dialysis (%)	14.3	11.5	<0.01

Chi-squared test were used to compare categorical variables and rank sum and *t* test were used to compare continuous variables. ALF, acute liver failure; HE, hepatic encephalopathy; INR, international normalised ratio; MELD, model for end-stage liver disease.

Table 2. Waitlist removal in patients with ALF waitlisted Status-1 for liver transplantation, by sex.

	Men n = 1,591	Women n = 2,910	*p* value
Death or clinical deterioration n (%)	319 (20.1)	657 (22.6)	0.049
Removal MELD (median, IQR)	38.5	38	0.78
Time from waitlisting to removal (median, IQR)	2 (1–5)	2 (1–5)	0.84
Transplanted n (%)	939 (59.0)	1,590 (54.6)	0.01
Transplant MELD (median, IQR)	34	34	0.92
Time from waitlisting to transplant (median, IQR)	2 (1–4)	2 (1–3)	0.38
Removal for clinical improvement n (%)	328 (20.6)	658 (22.6)	0.12
Time from waitlisting to other removal (median, IQR)	6 (3–32)	7 (3–43)	0.36
Remained on waitlist n (%)	5 (0.31)	5 (0.17)	0.33

Chi-squared test were used to compare categorical variables and rank sum and *t* test were used to compare continuous variables. ALF, acute liver failure; MELD, model for end-stage liver disease.

Post-transplant survival

Seventy-nine percent of the deaths that occurred (366/463) in the first year after LT occurred in the first 90 days. Men trended toward lower 90-day post LT survival than women (men 84.3% and women 86.5%, *p* = 0.05) and had significantly lower 1-year survival than women (men 80.0% *vs.* women 83.4%, *p* = 0.009; Fig. 4). On multivariable analysis including donor factors there was a significant difference in 1-year survival between men and women (HR 0.79, 95% CI 0.65–0.97). This was no longer significant when recipient age and underlying aetiology was added to the model (HR 1.01, 95% CI 0.80–1.26).

Discussion

Women are known to have higher rates of ALF than men, however, differences in waitlist outcomes have been less clear.[2] Here we demonstrate that women with ALF are more likely to be waitlisted Status-1 than men, have worse coagulopathy, and more frequently have grade 3–4 encephalopathy. Our competing risk analysis tells a more complex story. On univariable analysis women were less likely to undergo LT and subsequently trended toward being more likely to die on the waitlist than men. These differences, however, were no longer significant on multivariable analysis. This is in contrast to the known sex disparities in LT for chronic liver disease which persists in previously reported multivariable analysis. This suggests that the Status-1 waitlisting

priority that women with ALF receive may mitigate sex disparities in LT.

Women with ALF were significantly more likely to be waitlisted Status-1 than men. Women had higher rates of grade 3–4 hepatic encephalopathy and worse coagulopathy than men. Similarly, in a study from the ALF Study Group, women had higher prevalence of severe encephalopathy, and required more frequent intubation than men.[3] This was hypothesised to be as a result of higher rates of co-ingestion of sedating agents by women compared with men in the cohort.[3] It is possible that co-ingestion contributed to higher Status-1 waitlisting in our cohort or that women have more severe ALF at the time of waitlisting. It is also possible that women are waitlisted later in their course of ALF then men as clinicians make decisions about the likelihood that acetaminophen-DILI or AIH may reverse with time or treatment.

Women waitlisted Status-1 had higher rates of DILI and AIH than men. Women have previously been shown to have worse DILI and were 4 times more likely than men to develop AIH.[9,10] Data on sex difference in the severity of AIH have been mixed. In 1 single-centre study, the progression to cirrhosis, liver failure, and death from liver failure were similar between men and women; however, in a more recent single-centre study women were found to be more likely to die or require LT.[11,12] Sex differences in acute AIH warrant further study.

Fifty-eight percent of women waitlisted with acute fatty liver disease of pregnancy went on to require LT and 42% improved spontaneously. This is comparable to numbers found in a previous Scientific Registry of Transplant Recipients (SRTR) database

Table 3. Competing risk multivariable analysis: Death or clinical deterioration and LT by sex.

	SHR (95% CI)	*p* value
Death or clinical deterioration (competing risk LT)		
Reference men		
Unadjusted	1.14 (1.002–1.30)	0.047
Full model	1.16 (1.00–1.37)	0.06
Reduced model*	1.13 (0.99–1.29)	0.07
Liver transplant (competing risk death or clinical deterioration)		
Reference men		
Unadjusted	0.90 (0.84–0.97)	0.01
Full model	0.92 (0.86–1.01)	0.09
Reduced model†	0.95 (0.87–1.03)	0.18

Covariates in full model include: age, race/ethnicity, blood type, height, creatinine, INR, bilirubin, grade of hepatic encephalopathy, ventilator status at time of waitlisting, the need for dialysis in the week prior to waitlisting, region, and aetiology. Univariable and multivariable competing risk analysis were used to assess the association between sex and death/clinical deterioration and liver transplantation. INR, international normalised ratio; LT, liver transplantation; MELD, model for end-stage liver disease score; SHR, subdistribution hazard ratio.
* Model does not contain height.
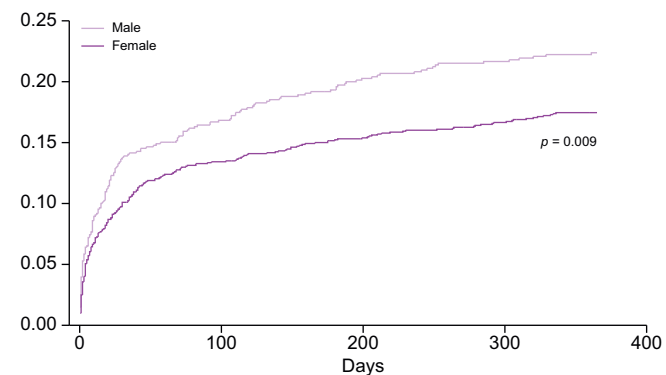† Model does not contain height, ethnicity/race, or age.

Fig. 4. One-year post liver transplant mortality by sex. Kalplan-Meier survival analysis and log-rank testing were used to compare sex differences in 1-year post liver transplant survival.

study exploring waitlist outcomes in acute fatty liver disease of pregnancy that found a LT rate of 46% and spontaneous improvement rate of 46%.[13]

Women, in our unadjusted models, were less likely to undergo LT and trended toward being more likely to die or clinically deteriorate before LT than men. These disparities, however, did not remain significant on multivariable analysis. Status-1 waitlisting increases the priority of patients who are waitlisted for LT, making organs available to these patients ahead of other patients on the waitlist.[8] Because Status-1 patients are the first to receive organ offers, one might hypothesise that this broadened donor pool may eliminate sex disparities in waitlist outcomes. Our data suggest that this could be the case. The broadened donor pool and heightened priority may overcome sex disparities that have largely been shown to be driven by donor-recipient size mismatch and underestimations in severity of liver disease by MELD score.[7]

Women with ALF waitlisted Status-1 had better 1-year post-transplant survival than men on multivariable analysis controlling for donor factors, but similar survival when controlling for both donor and recipient factors. Data on sex differences in post-LT survival have been mixed.[14] In a 20-year follow-up study of 313 LT patients, sex together with indication, age, renal function, and re-transplantation were associated significantly with patient survival.[15] However, in a study using SRTR data there were no differences in graft survival between men and women after adjusting for donor risk indices which were lower in women.[16] There was no sex difference in transplant-free survival in the acetaminophen-induced ALF study at 21 days.[3]

The strength of our study is that it explores a large, diverse, cohort of men and women with ALF from multiple aetiologies. This study has several limitations. First, much of the data on causative aetiologies depend on free text entries. Patients in our cohort were classified as having an unknown cause of ALF at higher rates than prospective studies of ALF. It is unclear if the diagnosis were truly unknown and this represents real-life uncertainty or if the diagnosis were not known to the person entering the data. Furthermore, there were cases coded as primary graft non-function that were not re-transplants. Therefore, it is possible that there were diagnoses that were miscoded. It is unlikely however, that these misclassifications were different by sex. Second, many patients with a diagnosis code for ALF were not waitlisted Status-1 for LT. It is possible that there was some degree of chronicity to the liver diseases in these cases that precluded patients from meeting Status-1 criteria. This led us to focus just on those patients waitlisted Status-1 to be sure we were capturing patients with true ALF. Finally, we excluded patients with a primary diagnosis code of graft failure (re-transplants); however, they made up less than 1% of waitlisted cases.

In summary, we sought to explore sex differences in the natural history and outcomes of patients waitlisted with ALF. Women with ALF were more likely to be waitlisted Status-1 for LT than men. Sex differences in LT and waitlist removal were attenuated on fully adjusted models, suggesting that these disparities may in part be mitigated by Status-1 listing. Although this Status-1 waitlisting is not a solution for sex disparities in chronic liver disease, it does suggest that the drivers of sex disparities can be improved through changes in allocation policy.

References
[1] Regitz-Zagrosek V. Sex and gender differences in health. Science & society series on sex and science. EMBO Rep 2012;13:596–603.

[2] Guy J, Peters MG. Liver disease in women: the influence of gender on epidemiology, natural history, and patient outcomes. Gastroenterol Hepatol 2013;9:633–639.

[3] Rubin JB, Hameed B, Gottfried M, Lee WM, Sarkar M, For the Acute Liver Failure Study Group. Acetaminophen-induced acute liver failure is more common and more severe in women. Clin Gastroenterol Hepatol 2018;16:936–946.

[4] Lee WM, Squires Jr RH, Nyberg SL, Doo E, Hoofnagle JH. Acute liver failure: summary of a workshop. Hepatology 2008;47:1401–1415.

[5] Moylan CA, Brady CW, Johnson JL, Smith AD, Tuttle-Newhall JE, Muir AJ. Disparities in liver transplantation before and after introduction of the MELD score. JAMA 2008;300:2371–2378.

[6] Lai JC, Terrault NA, Vittinghoff E, Biggins SW. Height contributes to the gender difference in wait-list mortality under the MELD-based liver allocation system. Am J Transplant 2010;10:2658–2664.

[7] Nephew LD, Goldberg DS, Lewis JD, Abt P, Bryan M, Forde KA. Exception points and body size contribute to gender disparity in liver transplantation. Clin Gastroenterol Hepatol 2017;15:1286–1293.e2.

[8] Institute of Medicine (US) Committee on Organ Procurement and Transplantation Policy. Organ Procurement and Transplantation: Assessing Current Policies and the Potential Impact of the DHHS Final Rule. Washington (DC): National Academies Press (US); 1999. C, Current Liver Allocation Policies. Available from: https://www.ncbi.nlm.nih.gov/books/NBK224641/ Accessed December 2020.

[9] Manns MP, Czaja AJ, Gorham JD, Krawitt EL, Mieli-Vergani G, Vierling JM, et al. Diagnosis and management of autoimmune hepatitis. Hepatology 2010;51:2193–2213.

[10] Reuben A, Koch DG, Lee WM, Acute Liver Failure Study Group. Drug-induced acute liver failure: results of a U.S. multicenter, prospective study. Hepatology 2010;52:2065–2076.

[11] Czaja AJ, Donaldson PT. Gender effects and synergisms with histocompatibility leukocyte antigens in type 1 autoimmune hepatitis. Am J Gastroenterol 2002;97:2051–2057.

[12] Al-Chalabi T, Underhill JA, Portmann BC, McFarlane IG, Heneghan MA. Impact of gender on the long-term outcome and survival of patients with autoimmune hepatitis. J Hepatol 2008;48:140–147.

[13] Kushner T, Tholey D, Dodge J, Saberi B, Schiano T, Terrault N. Outcomes of liver transplantation for acute fatty liver disease of pregnancy. Am J Transplant 2019;19:2101–2107.

[14] Rodriguez-Castro KI, De Martin E, Gambato M, Lazzaro S, Villa E, Burra P. Female gender in the setting of liver transplantation. World J Transpl 2014;4:229–242.

[15] Schoening WN, Buescher N, Rademacher S, Andreou A, Neuhaus R, Guckelberger O, et al. Twenty-year longitudinal follow-up after orthotopic liver transplantation: a single-center experience of 313 consecutive cases. Am J Transplant 2013;13:2384–2394.

[16] Mathur AK, Schaubel DE, Zhang H, Guidinger MK, Merion RM. Disparities in liver transplantation: the association between donor quality and recipient race/ethnicity and sex. Transplantation 2014;97:862–869.