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Women with cirrhosis have lower self-rated health than men

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Abstract

Background: Women systematically experience lower rates of liver transplantation (LT) and higher rates of waitlist mortality than men. Self-rated health has been associated with patient outcomes in the global population. We, therefore, assessed gender differences in self-rated and clinician-rated health among LT candidates.

Methods: Ambulatory LT candidates without hepatocellular carcinoma were enrolled from 2012 to 2018. Participants and their hepatologists were asked separately to rate the participant's overall general health on a 6-point scale (0 = "excellent" to 5 = "very poor"). Logistic regression was used to assess the associations between covariates and superior self-assessment, defined as 1 SD above the mean self-assessment score.

Results: Of 855 participants, the median (interquartile range) self-rated health score was 2 (1–3); 156 (18%) were categorized as superior self-rated health. The correlation between self-rated and clinician-rated health was positive (Spearman's rho 0.3, $P < 0.001$). In univariate analysis, being a woman was associated with lower odds of superior self-rated health (OR 0.7, 95% CI 0.5–1.0, $P = 0.04$), which persisted on multivariable analysis (aOR 0.7, 95% CI 0.4–1.0, $P = 0.05$), controlling for race, frailty, work status, comorbidities, Model for End-Stage Liver Disease-Na, hepatic encephalopathy, and ascites.

Conclusion: These findings highlight the need for well-designed quality-based research to determine how our patients perceive health to highlight opportunities to offer more comprehensive, quality-based care.

INTRODUCTION

Women awaiting liver transplantation (LT) experience worse waitlist outcomes than men.^[1–3] Compared with men, women have lower rates of LT referral and

deceased donor liver transplantation, as well as higher death rates on the LT waitlist.^[1–3] Multiple contributors to these gender disparities have been identified, including disproportionately lower priority on the waitlist due to the underestimation of renal dysfunction by

Abbreviations: aOR, adjusted OR; CI, confidence interval; IQR, interquartile range; LT, liver transplantation

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serum creatinine in women compared with men and the lower availability of size-matched livers for women.^[2–5] Several strategies have been proposed to address these specific factors, including optimizing the Model for End-Stage Liver Disease (MELD) score for both women and men and considering alternate deceased donor liver distribution algorithms to prioritize smaller livers to smaller women.^[4,6]

But the process of being selected for and awaiting LT includes not just objective factors (eg, MELD scores, donor-recipient size-concordance) but also subjective factors—which may include a patient's perception of their health status, which we herein refer to as “self-rated health”. Self-rated health is a measure of how an individual perceives their overall general health based on their own values and beliefs of what constitutes health and has traditionally been measured in the literature using a single-item question.^[7,8] Self-rated health has been shown to be a strong predictor of mortality and other health outcomes and remains highly predictive of the outcomes even after considering the objective measure of health or the physicians' perception of patients' health.^[9–13] In 1 study, respondents from 59 countries in the World Health Surveys demonstrated a significant gender gap in self-rated health, with women rating themselves as having substantially poorer health, equivalent to a decade of chronologic aging.^[7,14–16] In addition, gender-concordance between patients and providers (ie, when patients are the same gender as their providers) in different patient populations have found some association between patient perceptions of health and outcomes, but data have been mixed.^[17]

Since this concept of a global assessment of self-rated health using a single-item question has not yet been evaluated in the LT setting, we aimed to examine self-rated health among LT candidates and the clinician assessments of their patients' health in both gender-concordant and gender-non-concordant dyads. We hypothesized that self-rated health, similar to the global population, would differ between women and men and that self-rated health would correlate with the clinicians' assessment of their patients' health status. We also hypothesized that gender discordance between patients and providers would be associated with lower

rates of superior self-rated health compared with gender-concordant dyads.

MATERIALS AND METHODS

Adult patients with cirrhosis seen in the ambulatory setting listed for LT at a single center between 2012 and 2018 were enrolled in this study. Patients with a diagnosis of hepatocellular carcinoma were excluded, as patients with hepatocellular carcinoma who are listed for LT are less sick than those with cirrhosis requiring LT. Self-rated health was assessed using a single question measure “How would you rate your overall general health?”;^[13] participants were asked to respond along a 6-point scale (0 = “excellent” to 5 = “very poor”, [Table 1](#)). During the same clinic visit, the patients' hepatologists were asked, “How would you rate your patient's overall health today as compared with other patients with chronic liver disease?” using the same 6-point scale. Self-rated assessment was dichotomized with a rating greater than 1 SD above the mean self-assessment score for the cohort considered superior. Work or employment was defined as any type of work status excluding patients on disability, retired, or with other self-defined conditions. Gender of the hepatologist was also identified. “Gender-concordance” was defined as a participant-hepatologist dyad with the same gender. Frailty was defined by a previously-established Liver Frailty Index cut-point of ≥ 4.4 .^[18] Median income was defined using median household income by zip code from 2019 United States Census data. Comorbidities were defined using the Modified Charlson Comorbidity Index.^[19] Primary outcomes included delisting, with secondary outcomes including delisting due to social reasons and also due to being too sick. Chi-square analysis and Wilcoxon rank sum tests were used to compare inter-group characteristics. Logistic regression was used to assess the associations between covariates and superior self-assessment. Sociodemographic and clinical variables were defined a priori on univariate analysis with statistically significant variables included in multivariable analysis ($p < 0.05$). Log rank test and multivariable Cox proportional hazard modeling were used to assess the effects of self-rated health and gender

TABLE 1 Self-rated health scores based on gender and frailty

	0 Excellent	1 Very good	2 Good	3 Fair	4 Poor	5 Very poor
Women						
Not Frail n (%)	27 (8)	81 (22)	114 (32)	90 (25)	50 (11)	9 (2)
Frail n (%)	5 (5)	12 (11)	23 (21)	41 (37)	27 (24)	3 (3)
Men						
Not frail n (%)	65 (9)	191 (25)	244 (32)	181 (24)	66 (9)	12 (2)
Frail n (%)	11 (7)	16 (11)	42 (28)	43 (28)	27 (18)	12 (8)

on time on the waitlist. This study was approved by the institutional review board at the University of California, San Francisco.

RESULTS

Our cohort included 855 participants; 354 (41%) were women. [Table 1](#) demonstrates self-rated health scores by gender ($p=0.15$) and frailty ($p<0.001$). Compared with men, fewer women were married (62% vs. 70%, $p=0.02$) and reported actively working at the time of assessment (16% vs. 21%, $p=0.04$). Women also had a lower modified Charlson Comorbidity index ($p=0.04$) than men. Otherwise, women and men were similar by age, race, body mass index, income, frailty, MELD-Na, albumin, dialysis, hepatic encephalopathy, and ascites ([Table 2](#)). Median [interquartile range (IQR)] self-rated health was 2 (1–3); 156 (18%) met the criteria for “superior” self-rated health. Median (IQR) clinician-rated health was 3 (1–3). The correlation (by Spearman) between participant self-rated health and clinician-rated health was 0.3 ($p<0.001$). Participants with superior self-rated health had higher median clinician-rated health than participants without superior self-rated health [2 (IQR 1–3) vs. 3 (2–3), $p<0.001$].

Participants with a self-rating that met the criteria for superior self-rated health differed by % women (33% vs. 43%), % Asian (17% vs. 6%), % working (31% vs. 17%), modified Charlson comorbidity index (Modified Charlson Comorbidity index > 1 : 13% vs. 22%, $= 1$: 24% vs. 18%, $= 0$ 63% vs. 60%), % frailty (15% vs. 27%), % hepatitis C virus cirrhosis (37% vs. 29%) and % with ascites or refractory ascites (Refractory: 16% vs. 25%, Ascites: 50% vs. 53%, No Ascites: 34% vs. 22%) ([Table 3](#)). All other baseline characteristics were similar ([Table 3](#)). In univariate analysis, a superior self-rating was positively associated with Asian race (OR 3.21, 95% CI 1.90–5.43, $p<0.001$), work (OR 2.17, 95% CI 1.46–3.21, $p<0.001$), and hepatitis C virus cirrhosis (vs. alcohol cirrhosis, OR 1.72, 95% CI 1.07–2.78, $p=0.03$) and negatively associated with being a woman (OR 0.68, 95% CI 0.47–0.98, $p=0.04$), modified Charlson Comorbidity index > 1 (vs. 0, OR 0.58, 95% CI 0.34–1.00, $p=0.05$), frailty (OR 0.46, 95% CI 0.29–0.74, $P=0.001$), ascites (vs. no ascites (OR 0.63, 95% CI 0.42–0.94, $p=0.02$) and refractory ascites (vs. no ascites, OR 0.43, 95% CI 0.25–0.73, $p=0.002$) ([Table 4](#)). In multivariable analysis, being a woman remained independently associated with lower odds of superior self-rated health (aOR 0.67, 95% CI 0.44–1.00, $p=0.05$) ([Table 4](#)). There was no significantly detectable difference in gender (HR 1.12, 95% CI 0.97–1.30, $p=0.12$), self-rated health (HR 0.86, 95% CI 0.71–1.03, $p=0.10$), or self-rated health controlling for gender (HR 0.86, 95% CI 0.72–1.04, $p=0.12$) on time on waitlist. Superior self-rated health was not

associated with delisting (HR 0.81, 95% CI 0.61–1.08, $p=0.15$), delisting due to social reasons (HR 0.77, 95% CI 0.54–1.11, $p=0.17$), or delisting due to being too sick (HR 0.89, 95% CI 0.55–1.43, $p=0.62$).

There were 391 (46%) women hepatologists and 391 (46%) men hepatologists, with 73 (9%) missing. Overall, women hepatologists rated their patients as having better health than men hepatologists [2 (1–3) vs. 3 (2–3), $p=0.009$]. When examining patient gender, compared with men hepatologists, women hepatologists rated their men patients as having better health [2 (1–3) vs. 3 (2–3), $p=0.005$] but not their women patients [3 (1–3) vs. 3 (2–3), $p=0.4$]. Among all participants, 411 (48%) had gender-concordant providers at the time of self-assessment. Participants who had gender-concordant providers had similar rates of superior self-rated health compared with those with nonconcordant providers (20 vs. 17%, $p=0.38$). A positive correlation between participant self-rated health and clinician-rated health remained among the participants with gender-concordant providers (Spearman’s rho 0.35, $p<0.001$) and gender-disconcordant providers (Spearman’s rho 0.26, $p<0.001$). For women participants, the correlation between self-rated health and clinician assessment was similar whether their hepatologist was a woman (rho = 0.32; $p<0.001$) or a man (rho = 0.31; $p<0.001$).

DISCUSSION

Poor self-rated health has been shown to be associated with developing chronic disease in the general population.^[20–24] In our study, we found that women with cirrhosis awaiting LT reported lower self-rated health than men, which correlated with the clinician assessments of health regardless of gender-concordance between the participants and providers. This relationship persisted despite controlling for objective measures of health such as MELD-Na, frailty, and history of ascites. Prior studies among variable populations demonstrating gender disparities in self-rated health have attributed to poorer self-rated health among women to a higher health literacy and health consciousness and a greater emphasis placed on disabling symptoms compared with men.^[7,16] Prior studies have also shown that women are less likely to be referred for LT and more likely to be actively delisted than men.^[1] While this study does not demonstrate the effects on LT outcomes, it introduces a new potential source of disparity in health care among LT candidates and suggests that the relationship between clinician assessments of health and poor self-rated health among women should be considered as a possible contributor to these gender disparities in future studies. In hepatology, clinician assessments combine both objective data, such as MELD-Na, with subjective data to

TABLE 2 Characteristics among pre-LT participants among women versus not women

	Women n = 354 (41%)	Not women n = 502 (59%)	p
Self-Perceived assessment*	2 (2–3)	2 (1–3)	0.06
Clinician-perceived assessment*	3 (2–3)	2 (1–3)	0.03
Age, y*	58 (51–63)	56 (48–63)	0.24
Race			0.39
White non-Hispanic	201 (57)	313 (63)	
White Hispanic	110 (31)	127 (25)	
Black	14 (4)	16 (3)	
Asian	26 (7)	41 (8)	
Other	3 (0.9)	4 (0.8)	
BMI*, kg/m ²	27.7 (24.0–32.7)	28.3 (25.2–32.7)	0.18
Work (yes/no)	58 (16)	110 (22)	0.04
Marital Status (Married)	187 (62)	293 (70)	0.02
Income (< \$100,000)	77 (26)	104 (26)	0.98
Modified Charlson Comorbidity Index			0.04
0	208 (65)	259 (58)	
1	63 (20)	84 (10)	
> 1	51 (16)	104 (23)	
Frailty	94 (27)	120 (24)	0.38
Median Liver Frailty Index*	3.9 (3.5–4.5)	3.8 (3.3–4.4)	0.04
Etiology			< 0.001
Alcohol	62 (18)	156 (31)	
HCV	95 (27)	166 (33)	
NAFLD	72 (20)	66 (13)	
Autoimmune	86 (24)	43 (9)	
Other	39 (11)	70 (14)	
MELD-Na*	16 (13–19)	16 (13–19)	0.69
Dialysis	16 (5)	21 (4)	0.81
HE History	245 (70)	327 (68)	0.43
Ascites History			0.23
None	89 (26)	112 (23)	
Yes	187 (54)	246 (51)	
Yes (Refractory)	72 (21)	124 (73)	

*median (IQR).

Abbreviations: HCV, hepatitis C Virus; HE, hepatic encephalopathy; NAFLD; non-alcoholic fatty liver disease.

inform prognostication and clinical decision-making in liver transplantation.^[1,2] This study found that compared with men hepatologists, women hepatologists rated their men patients as having better health but not their women patients. Whether implicit bias among providers contributes to gender disparities in waitlist outcomes requires further examination.

Several possible factors associated with self-rated health should be further evaluated. First, the significance of the history of hepatic encephalopathy trended towards significance in univariate analysis but did not remain significant in multivariate analysis. Hepatic encephalopathy is known to fluctuate and affect

cognition and emotional function and, therefore, may affect self-rated health. Therefore the lack of significance seen in this study may be cohort-related, and further studies should assess the effects of hepatic encephalopathy on self-rated health using hepatic encephalopathy scores, number of hospitalizations for hepatic encephalopathy, and medications to better assess this variable. Second, fewer patients with superior self-rated health had alcohol-associated liver disease compared with patients with non-superior self-rated health. Gender differences among patients with alcohol-associated liver disease^[25] provide attitudes regarding patients with alcohol-associated liver disease

TABLE 3 Characteristics among pre-LT participants with superior (defined as > 1 SD from the cohort mean) versus not superior self-rated health

	Superior n = 156 (18%)	Not superior n = 699 (82%)	p
Self-perceived assessment*	1 (0-1)	3 (2-3)	< 0.001
Clinician-perceived assessment*	2 (1-3)	3 (2-3)	< 0.001
Age, y*	58 (48-63)	57 (49-63)	0.10
Women	53 (34)	301 (43)	0.04
Race			< 0.001
White non-Hispanic	76 (49)	438 (63)	
White Hispanic	46 (29)	191 (27)	
Black	8 (5)	22 (3)	
Asian	26 (17)	41 (6)	
Other	0 (0)	7 (1)	
BMI*, kg/m ²	27.6 (24.5-31.9)	28.2 (25.0-32.9)	0.33
Work (yes/no)	48 (31)	119 (17)	< 0.001
Marital Status (Married)	89 (67)	391 (66)	0.82
Income (< \$100,000)	37 (30)	144 (25)	0.27
Modified Charlson Comorbidity Index			0.04
0	86 (63)	381 (60)	
1	33 (24)	114 (18)	
> 1	18 (13)	137 (22)	
Frailty	23 (15)	191 (27)	0.001
Median Liver Frailty Index*	3.6 (3.1-4.1)	3.9 (3.5-4.5)	< 0.001
Etiology			< 0.001
Alcohol	31 (19.9)	187 (27)	
HCV	58 (37.2)	203 (29)	
NAFLD	13 (8.3)	125 (18)	
Autoimmune	20 (12.8)	109 (16)	
Other	34 (21.8)	75 (11)	
MELD-Na*	15 (12-19)	16 (13-20)	0.08
Dialysis	7 (4.5)	30 (4)	0.91
HE history	96 (63)	476 (70)	0.09
Ascites history			0.004
None	51 (34)	150 (22)	
Yes	76 (50)	356 (53)	
Yes (Refractory)	25 (16)	171 (25)	

*median (IQR).

Abbreviations: HCV, hepatitis C Virus; HE, hepatic encephalopathy; NAFLD, non-alcoholic fatty liver disease.

compared with liver disease from other etiologies,^[26] and psychiatric comorbidities among patients with alcohol-associated liver disease^[27] and may all have implications on gender disparities in self-rated health in this patient population. Third, women are less likely to receive liver transplantation within 3 years on the waitlist compared with men.^[28] This study did not detect a statistically significant difference in self-rated health based on waitlist times; however, additional data examining the effects of waitlist time including larger sample size and changes in self-rated health over time should be considered. This study raises the possibility

of important gender differences that should be further explored in the LT candidate population.

While our study is novel in that it is the first to investigate self-rated health in LT patients, we acknowledge the following limitations. First, we did not assess other sociodemographic variables and social determinants of health that may have been associated with self-rated health in the literature, such as health literacy, number of medications, insurance, homelessness, and urban versus rural neighborhoods. Data, including a number of offers and a number of rejections, were not available in this study to assess the effects of these

TABLE 4 Univariate and multivariate analysis of predictors of superior self-rated health

Factor	OR	Univariate 95% CI	<i>p</i>	aOR	Multivariate 95% CI	<i>p</i>
Female	0.68	0.47–0.98	0.04	0.67	0.44–1.00	0.05
Age	0.99	0.97–1.00	0.10			
Asian Race	3.21	1.90–5.43	<0.001	3.17	1.79–5.62	<0.001
Work	2.17	1.46–3.21	<0.001	1.66	1.05–2.63	0.03
Modified CCI						
0	–	–	–	–	–	–
1	1.28	0.82–2.02	0.28	–	–	–
>1	0.58	0.34–1.00	0.05	0.61	0.35–1.10	0.10
Frailty	0.46	0.29–0.74	0.001	0.63	0.37–1.09	0.10
Etiology						
Alcohol	–	–	–	–	–	–
HCV	1.72	1.07–2.78	0.03			
NAFLD	0.63	0.32–1.25	0.18			
Autoimmune	1.11	0.60–2.04	0.74			
Other	2.73	1.57–4.77	<0.001	–	–	–
MELD-Na (per point)	0.97	0.93–1.00	0.08	0.99	0.95–1.04	0.69
HE History	0.72	0.50–1.05	0.09	1.03	0.66–1.59	0.91
Ascites History						
None	–	–	–	–	–	–
Yes	0.63	0.42–0.94	0.02	0.81	0.51–1.31	0.39
Yes (Refractory)	0.43	0.25–0.73	0.002	0.64	0.34–1.19	0.16

Abbreviations: CCI, Charlson Comorbidity Index; HCV, hepatitis C Virus; HE, hepatic encephalopathy; NAFLD, non-alcoholic fatty liver disease.

covariates on health status, gender, or self-rated health. In addition, mental health diagnoses such as depression and other psychiatric conditions that may impact self-rated health were not available in this study. Particularly, given known gender differences in the prevalence of certain psychiatric conditions and the relationship between frailty and depression among patients with liver disease,^[29] future studies may benefit from examining these possible covariates. In addition, these data came from 1 single center, so it may not be fully representative of the general population of LT patients in the US.

Nevertheless, our study demonstrates poorer self-rated health among women compared with men despite similar clinical characteristics—a provocative finding in light of the persistent disparities that women experience awaiting LT. Whether poor self-rated health among women and clinician-rated health may impact the subjective aspect of clinical assessment leading to reduced rates of referrals for LT and increased rates of delisting should be explored. Our findings highlight the need for well-designed quality-based research to determine how our patients rate their health to highlight opportunities and identify how gender may play a role in this determination to offer more comprehensive, quality-based care.

AUTHOR CONTRIBUTIONS

Melinda Wang: data analysis, manuscript draft, manuscript editing. Chiung-Yu Henson: data analysis, manuscript editing. Giuseppe Cullaro: manuscript editing. Kenneth Covinsky: research design, manuscript editing. Jennifer C. Lai: research design, data analysis, manuscript editing

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CONFLICTS OF INTEREST

Giuseppe Cullaro owns stock in Eli Lilly and Novo Nordisk. The remaining authors [Melinda Wang, Chiung-Yu Henson, Kenneth Covinsky, and Jennifer C. Lai] declare no conflicts of interest.

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