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ORIGINAL ARTICLE

The impact of race and comorbid conditions on adult liver transplant outcomes in obese recipients

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SUMMARY

Many prior studies comparing liver transplant outcomes between obese and nonobese recipients found no significant differences in survival. However, obesity is intrinsically associated with demographic factors such as race and comorbidities. Thus, this work aimed to analyze the effects of obesity, in conjunction with these factors, on liver transplant outcomes. OPTN data was analyzed to identify adult-only, first-time liver transplants between 1995 and 2019. Obesity was defined by the CDC obesity classification. Race, insurance status, age, and comorbidities were analyzed together with patient survival and graft survival using a multivariable Cox Proportional-Hazards model and long-term survival with Kaplan–Meier curves. The multivariable models found that being black, older than 50 years, having diabetes, or having nonprivate insurance were all risk factors for both patient survival and graft survival after liver transplant. Adjusting for obesity class, black recipients had a 20% lower patient survival and 23% lower graft survival compared with nonblack recipients. Survival curves verified that obese black liver transplant recipients had poorer long-term patient survival and graft survival compared with both obese nonblack and nonobese recipients. In conclusion, obesity compounds known factors associated with poor outcomes after liver transplantation. Further work is critical to understand why these discrepancies persist.

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Key words
comorbidities, graft survival, liver transplant, obesity, patient survival, race

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Introduction

The obesity epidemic persists in the United States, with 42.4% of American adults having a body mass index (BMI) of greater than 30 kg/m^2 [1]. Similarly, more liver transplant candidates are obese [2], influencing pretransplant selection [3]. This obesity trend is reflected in the rise of nonalcoholic steatohepatitis (NASH) cirrhosis as the soon-to-be leading indication for liver transplantation, recently surpassing hepatitis C virus (HCV), in the United States [2]. Since 2004, the number of liver transplant candidates with NASH has tripled. Studies have shown that patients with NASH experience a higher 90-day waitlist mortality compared with patients with HCV or alcoholic liver disease [4]. With the changing transplant waitlist, a greater understanding of outcomes of

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these patients by the transplant community will permit better pre- and posttransplant care.

Obese patients incur worse health outcomes and increased stigma [5]. Similarly, racial, age, and socioeconomic disparities also impact health [6]. In transplantation, racial and age disparities have been associated with decreased access to transplantation and compromised posttransplant outcomes [7]. To better understand the potentially negative impact of multiple health disparities on transplant outcomes, we assessed the trends of obesity in liver transplant, and the interplay of obesity with other comorbidities and demographic factors on liver transplant outcomes.

Multiple prior single-center studies have compared liver transplant outcomes between obese and nonobese recipients. Fujikawa *et al*. studied 700 adult liver transplants stratified by BMI < 25, 25–30 and >30 kg/m^2 at a single US center and, and found no differences in cost, length of stay, surgical complications, graft survival, or patient survival [8]. Comparably, Nair *et al*. stratified their single center cohort of 193 liver transplants by the Centers for Disease Control and Prevention (CDC) obesity classification (class 1 BMI 30–35 kg/m^2, class 2 BMI 35–40 kg/m^2, and class 3 with a BMI greater than or equal to 40 kg/m^2) [9] and also found no differences in resource utilization, surgical complications, patient survival, or graft survival [10]. Agopian *et al*. analyzed a cohort of 1235 liver transplants by the CDC obesity classification and found that obesity was associated with increased operating room time, longer length of stay, but no difference in patient or graft survival [11].

While these studies yielded consistent results, they do not directly address that obesity is also associated with multiple comorbidities. Thus, the effects of obesity may be magnified by other demographic factors that require a more detailed approach. Adams *et al*. were the first to study the impact of preliver transplant metabolic comorbidities (specifically diabetes, hypertension, and dyslipidemia) on liver transplant patient and graft survival and found that diabetes with obesity was associated with reduced survival at 5 years [12]. Obesity within the liver transplant patient population in the United States is associated with race [13,14], insurance status, and other obesity-related comorbidities such as diabetes. It is imperative to gain a deeper understanding of the obese liver transplant candidate patient population to overcome barriers to access and improve outcomes. Thus, the aims of this study were first to describe the trends in obese liver transplant recipients from 1995 to 2019. The second aim was to analyze the effect of demographic factors (race, age, insurance status), and obesity-related comorbid conditions (diabetes, nonalcoholic steatohepatitis, and alcoholic cirrhosis) on long-term liver transplant outcomes in obese recipients.

Methods

Data source

This study analyzed data from the Organ Procurement and Transplantation Network (OPTN) STAR file released on June 2020 based on data collected through June 12, 2020. The content of this paper is the responsibility of the authors alone and does not necessarily reflect the views or policies of the Department of Health and Human Services. Mentions of trade names, commercial products, or organizations do not imply endorsement. The institutional review board at MGH determined that the study met criteria for exempt status.

Study population

For liver transplant recipient distribution analyses, 152,185 first-time, liver only, liver transplants from deceased donors from January 1995 to December 2019 were included. Pediatric recipients below 18 years were excluded. Obesity prior to transplant, defined by BMI (kg/m^2), was subdivided into categories according to CDC guidelines: nonobese BMI < 30 kg/m^2, class I obesity with BMI 30–35 kg/m^2, class II obesity with 35–40 kg/m^2, and class III obesity as BMI ≥ 40 kg/m^2 [9].

Outcome classifications

Primary outcomes were patient survival and graft survival. Graft survival was defined as time until either retransplantation or patient death with a functioning graft, and patient survival was defined as time until patient death. Other secondary outcomes and demographics of interest stratified by obesity class included annual number of deceased donor liver transplants, mean lab model for end-stage liver disease (MELD) score at transplant, mean wait time for liver transplant, waitlist mortality, mean length of stay after liver transplant, and readmission rate after liver transplant.

Statistical analysis

Comparisons between obesity classes were made using two-way analysis of variance testing. Patient and graft survival were analyzed with a multivariable Cox Proportional-Hazards model. The model included race (black vs. nonblack), diabetes, NASH, alcoholic cirrhosis, age (continuous), obesity class, health insurance status (private vs. nonprivate), and transplant year. The recipients with missing values for BMI (572 patients) were excluded. All of the covariates included in the Cox model were examined for adherence to the proportional hazard assumption [15].

Survival rates were presented in Kaplan–Meier curves and analyzed by log-rank tests. Time to the outcome was defined as the time from the date of transplant to the date of outcome (death or graft failure) and censored for loss to follow-up or end of the study period (December 31, 2019).

Pairwise comparisons of the three obesity classes were conducted with the Bonferroni correction method [16]. All analyses were performed using RStudio software, version 1.1.456 (R. RStudio, Inc., Boston, MA, USA). A *P*-value <0.05 identified statistical significance, and all confidence intervals (CI) used a 95% threshold.

Results

Trends in obese liver transplant recipients

The study included 115 250 adult, liver transplant recipients from 1995 to 2019 in the United States. The percentage of nonobese liver transplant recipients decreased from 1995 to 2019 by 15% while the percentage of obesity class I, II, and III recipients increased by 7%, 6%, and 2% respectively, during the same time period ($P < 0.001$) (Fig. 1a). Weight, physiologically distinct from BMI, also showed similar trends, with the percentage of liver transplant recipients over 100 kg increasing by 8% from 1995

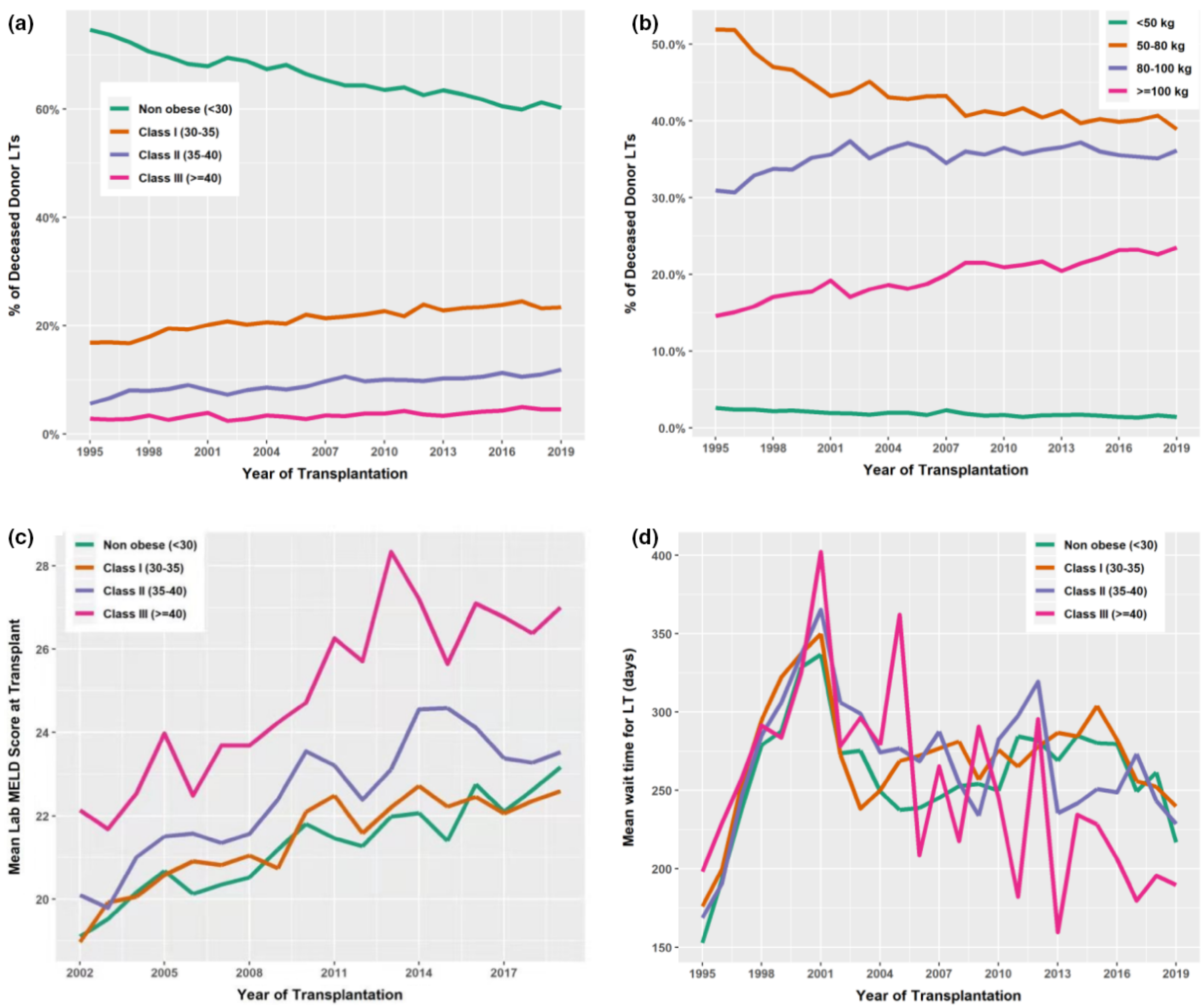

Figure 1 Trends in obese liver transplant recipients prior from 1995 to 2019. Percent of total deceased donor liver transplant recipients by (a) obesity classification and (b) weight in kg. Mean lab MELD score at liver transplant (c) and mean wait time (in days) for liver transplant (d) stratified by BMI.

to 2019 ($P < 0.001$) (Fig. 1b). Regarding severity of disease at time of transplant, in 2019, obesity class III recipients had higher mean lab MELD scores at time of transplant (27.0), compared with obesity class II (23.5), obesity class I (22.5), and nonobese recipients (23.0) ($P < 0.001$). Overall, the mean lab MELD score at transplant increased over time in all obesity classes (Fig. 1c). Finally, obesity class III recipients had lower mean wait time for liver transplant (190 days), compared with obesity class II (230 days), obesity class I (240 days), and nonobese recipients (220 days) ($P < 0.001$) (Fig. 1d).

Trends in outcomes of obese liver transplant recipients

The retransplant rate of all obesity classes decreased from 1995 to 2019, with no significant differences in recent years. Notably, since 2018, the retransplant rate in obesity class III liver transplant recipients decreased from the highest among the obesity classes at 3.7% to the lowest in 2019 at 1.3%, among all obesity classes ($P < 0.001$) (Fig. 2a). The waitlist mortality rate of obesity class III liver transplant candidates has historically been higher than obesity class II recipients, but this difference decreased over the past decade. In 2019, the mortality rate of obesity class III recipients was 11.3%, compared with 11.0% for obesity class II recipients. Obesity class I and nonobese liver transplant recipients still had a lower mortality rate on the waitlist at 8.5% and 8.8%, respectively ($P < 0.001$) (Fig. 2b). In 2004, the mean length of stay after liver transplant of obesity class III recipients was 24.6 days compared with less than 17 days in the other obesity classes. By 2019 the postoperative length of stays were more comparable

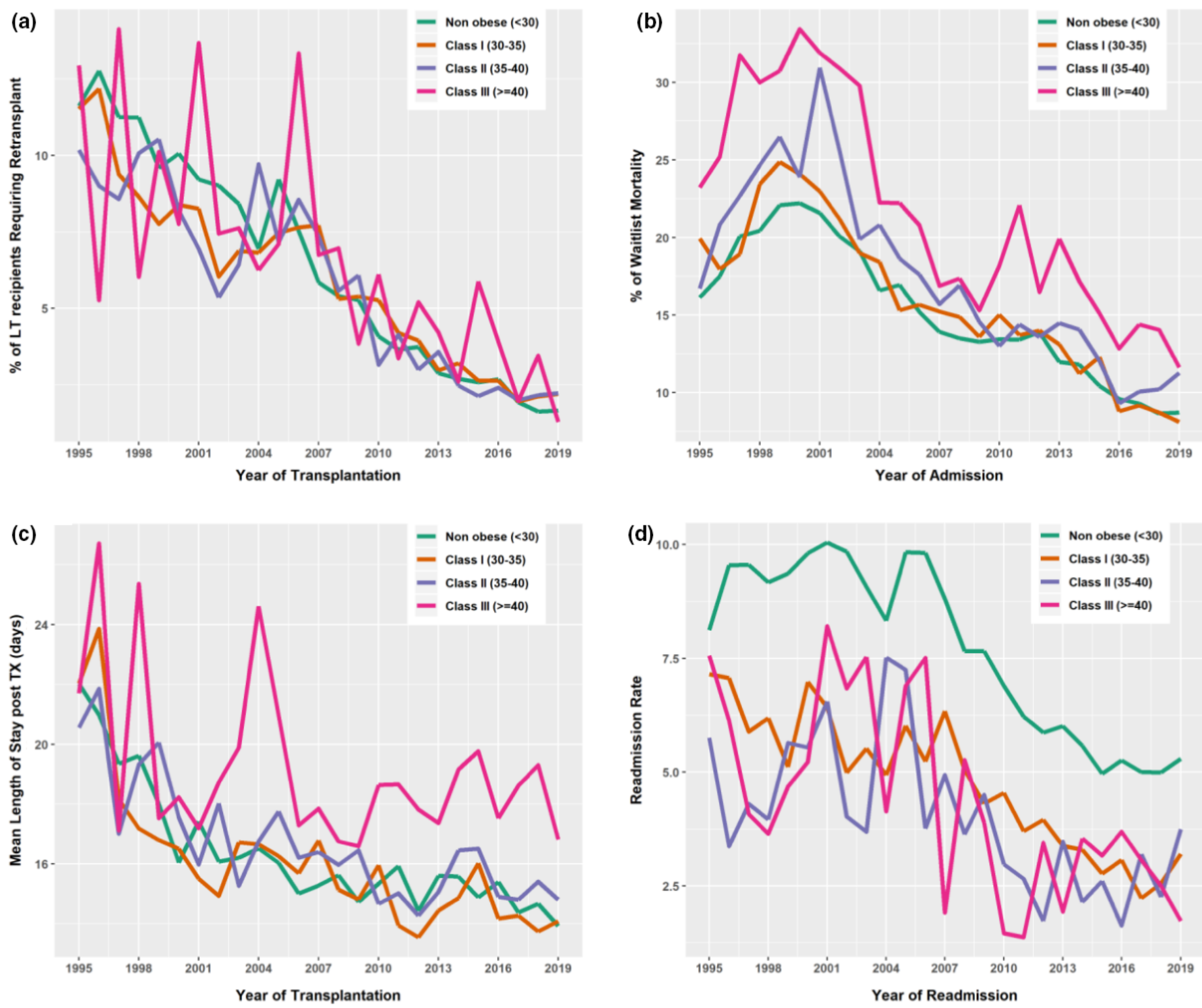

Figure 2 Trends in outcomes after liver transplant in obese recipients. (a) Retransplant rate, (b) waitlist mortality, (c) mean length of stay in days, and (d) readmission rate, all stratified by BMI.

although obesity class III at 16.8 days was still slightly higher compared with obesity class II (14.9 days), obesity class I (14.1 days), and nonobese recipients (13.9 days) ($P < 0.001$) (Fig. 2c). Finally, readmission rates for all obesity classes have been decreasing since 2006 but have paradoxically been persistently higher for nonobese recipients. In 2019, nonobese liver transplant recipients have a readmission rate after liver transplant of 5.25% while recipients in all obesity classes had readmission rates less than 3.75% ($P < 0.001$) (Fig. 2d).

Obesity class III liver transplant recipients had lower unadjusted patient survival after liver transplant compared with class II recipients ($P = 0.03$), class I recipients ($P < 0.001$), and nonobese recipients ($P < 0.001$). There was no difference in long-term patient survival after liver transplant between class I and class II recipients ($P = 0.62$) or between class I and nonobese recipients ($P = 1.0$) (Fig. 3a). Obesity class III liver transplant recipients had lower graft survival after liver transplant compared with class II recipients ($P = 0.03$), class I recipients ($P < 0.001$), and nonobese recipients ($P < 0.001$). However, there was no difference in long-term unadjusted graft survival after liver transplant between class I and class II recipients ($P = 0.77$)

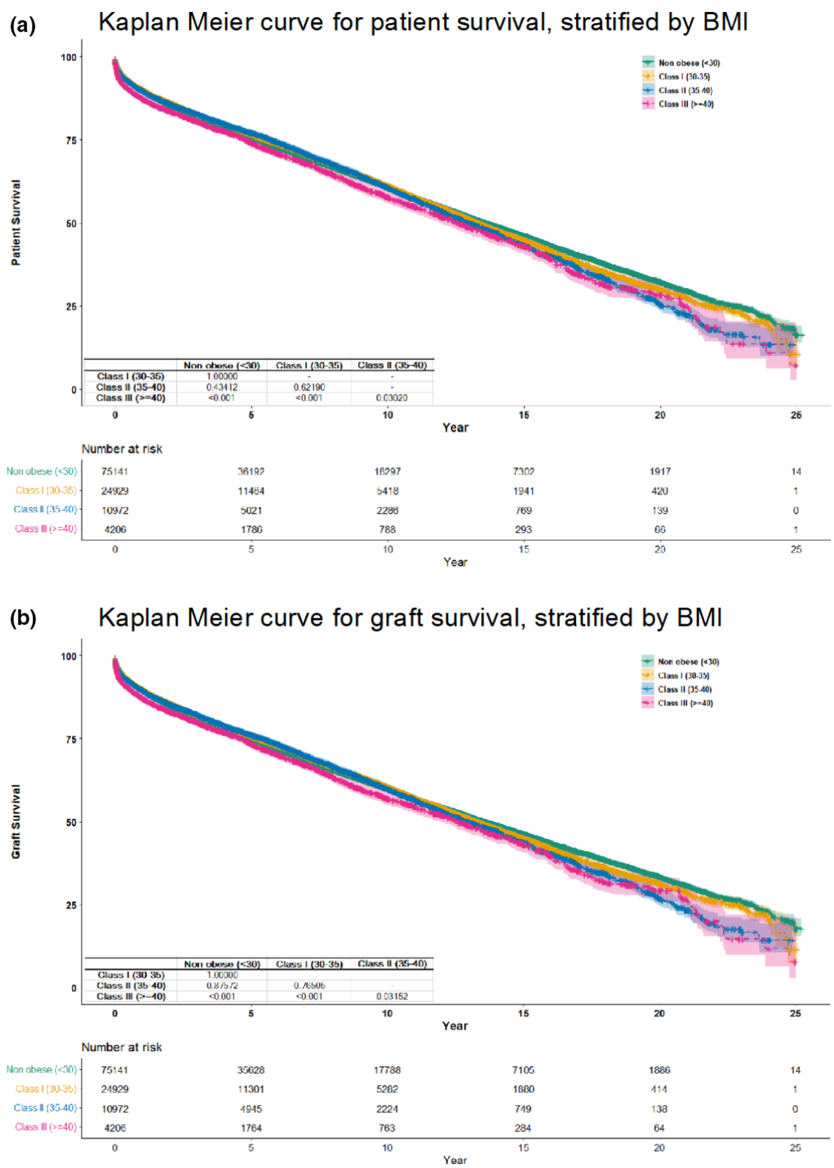

Figure 3 Kaplan–Meier curves of crude (a) patient survival and (b) graft survival stratified by BMI (<30 in green, 30–35 in yellow, 35–40 in blue, and >40 kg/m^2 in pink). Pairwise comparison with p-values comparing the three obesity groups shown in table; significance level: $P < 0.05$. Shaded areas represent 95% confidence intervals.

or between class I and nonobese recipients ($P = 0.71$) (Fig. 3b).

Multivariable Cox Proportional-Hazards model for survival after liver transplant

A multivariable hazards model was conducted to assess the association of obesity, demographic factors (race, age, insurance status), and obesity-related comorbidities (alcoholic cirrhosis, diabetes, NASH) with patient survival after liver transplant. Black liver transplant recipients had a patient mortality hazard ratio (HR) of 1.20 (95% CI 1.15–1.26, $P < 0.001$) compared with nonblack liver transplant recipients. Compared with liver transplant recipients without diabetes, liver transplant recipients with type I diabetes [HR 1.59 (95% CI 1.45–1.77, $P < 0.001$)] or type 2 diabetes [HR 1.35 (95% CI 1.30–1.41, $P < 0.001$)] experienced significantly lower patient survival posttransplant. Alcoholic cirrhosis [HR 1.08 (95% CI 1.05–1.11, $P < 0.001$)], recipient age greater than 50 years [HR 1.47 (95% CI 1.43–1.51, $P < 0.001$)], and nonprivate insurance [HR 1.27 (95% CI 1.24–1.29, $P < 0.001$)] were risk factors for decreased patient survival after liver transplant. NASH cirrhosis and obesity class were not significant risk factors for patient survival after liver transplant in our model (Fig. 4).

The same multivariable hazards model was conducted for graft failure after liver transplant. The relative risk of graft failure after liver transplant for black recipients in the United States was 23% higher than nonblack recipients [HR 1.23 (95% CI 1.18–1.28, $P < 0.001$)]. Having type I diabetes (HR 1.51, 95% CI 1.36–1.68, $P < 0.001$), type II diabetes (HR 1.27, 95% CI 1.22–1.33, $P < 0.001$), recipient age greater than 50 years (HR 1.24, 95% CI 1.21–1.27, $P < 0.001$), and nonprivate insurance (HR 1.20, 95% CI 1.18–1.22, $P < 0.001$) were also risk factors for graft failure after liver transplant in our model while the presence of NASH and obesity class were not significant (Fig. 5). The argument can be raised that death competes with graft failure, so this analysis was done again with death-censored graft survival (DCGS) with similar results. Black race was shown to be an even greater risk factor for graft failure after liver transplant [HR 1.55 (95% CI 1.46–1.65, $P < 0.001$) while obesity class was still not significant (Fig. S1).

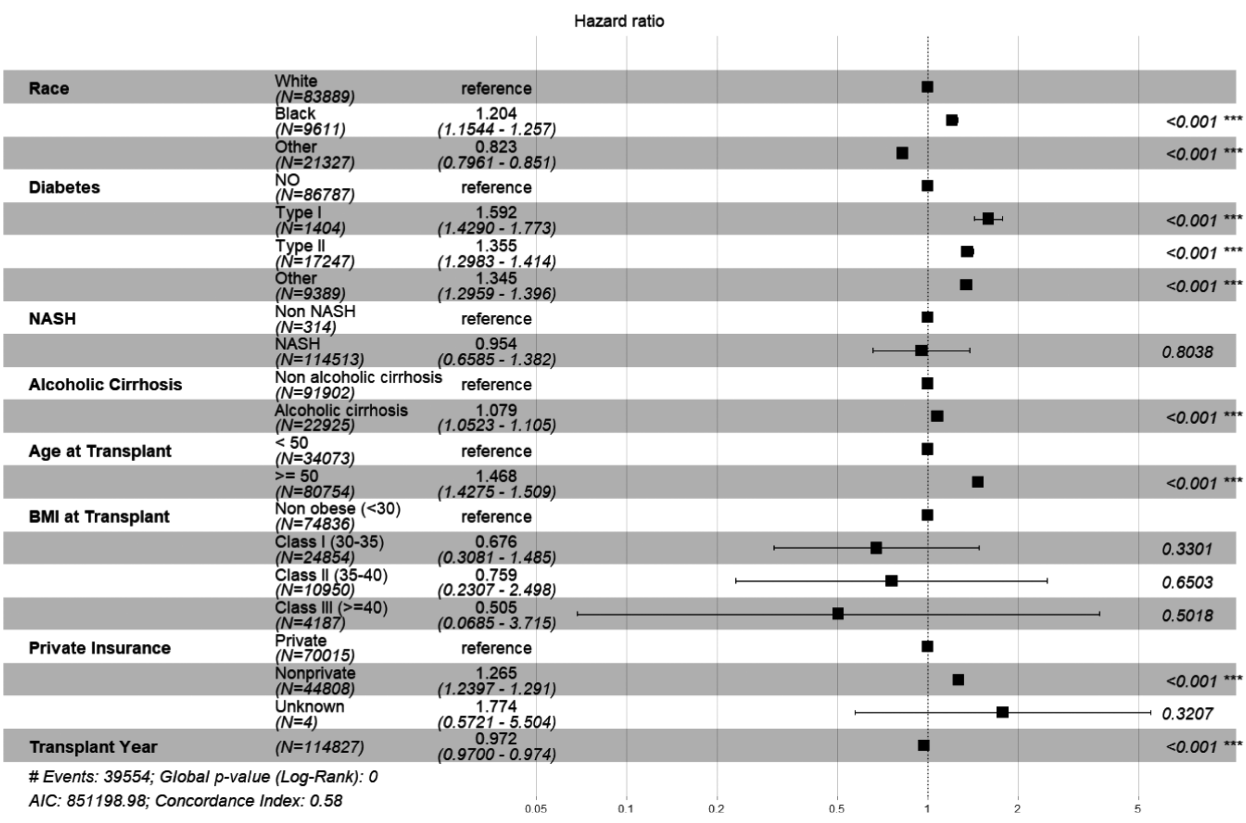

Figure 4 Patient survival after liver transplant; multivariable Cox Proportional-Hazards model assessing race, diabetes (none vs. type I vs. type II), presence of Nonalcoholic Steatohepatitis (NASH), presence of alcoholic cirrhosis, age less than 50 years versus greater than 50 years, BMI, and private versus nonprivate insurance. Significant differences: *$P < 0.05$, **$P < 0.01$, ***$P < 0.0001$.

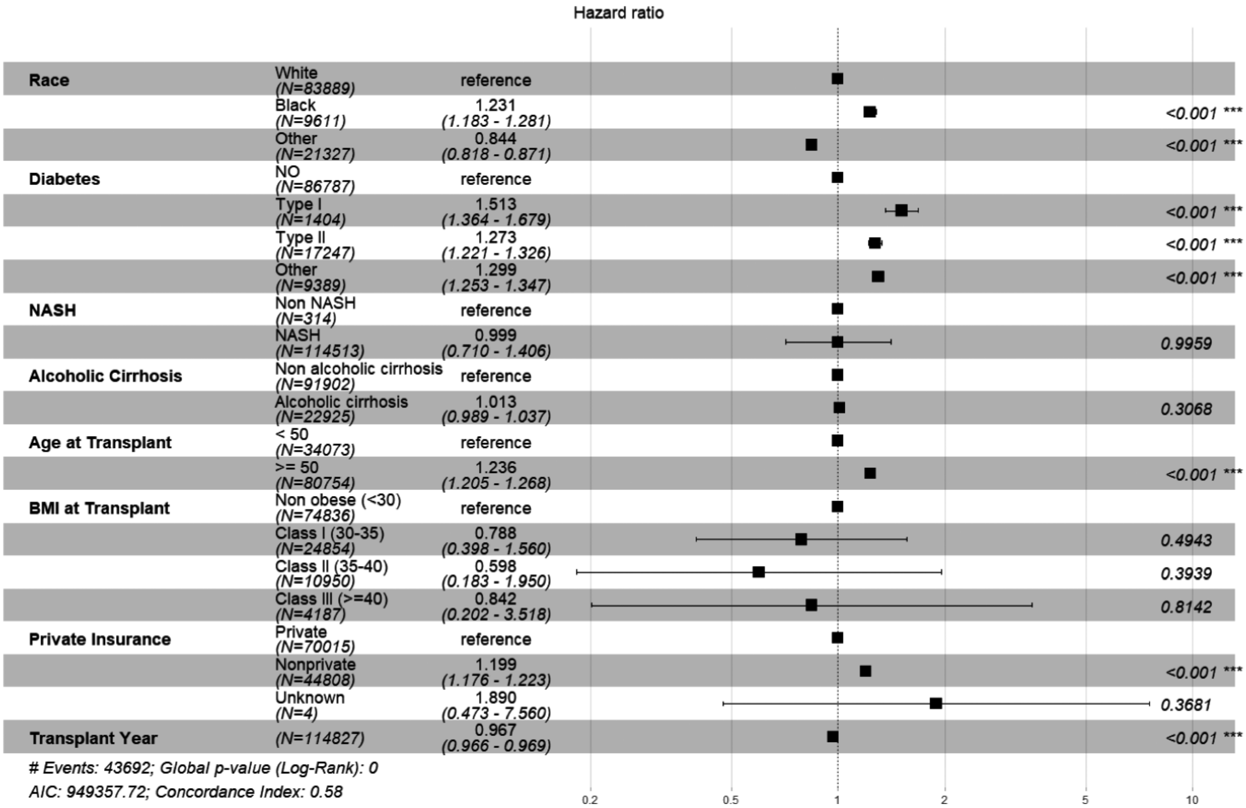

Figure 5 Graft survival after liver transplant; multivariable Cox Proportional-Hazards model assessing race, diabetes (none vs. type I vs. type II), presence of Nonalcoholic Steatohepatitis (NASH), presence of alcoholic cirrhosis, age less than 50 years versus greater than 50 years, BMI, and private versus nonprivate insurance. Significant differences: **P* < 0.05, ***P* < 0.01, ****P* < 0.0001.

Effect of obesity combined with pertinent demographic factors and comorbidities on survival after liver transplant

Based on our significant results in the patient and graft survival multivariable Cox model, we studied the impact of obesity combined with: age, insurance status, diabetes, alcoholic cirrhosis, and race and using Kaplan–Meier survival curves. The results are summarized in Table 1. Recipient age (>50 years) and obesity (BMI > 30 kg/m^2) had a negative synergistic association with survival outcomes after liver transplant. Obese liver transplant patients older than 50 years had significantly worse patient survival ($P = 0.003$) and graft survival ($P = 0.049$) after transplant compared with both younger (< 50 years) and nonobese recipients (BMI < 30 kg/m^2). Of note, the borderline significant p-values (e.g., 0.049) may represent weak signals that are significant because of the large sample size. Next, obese liver transplant recipients with nonprivate insurance (Medicare and Medicaid) had significantly worse patient survival ($P < 0.001$) and graft survival ($P < 0.001$) after transplant compared with both obese recipients with private insurance and nonobese recipients.

The presence of type II diabetes in recipients also conferred a negative synergetic association with obesity on survival, with obese diabetics having significantly worse patient survival ($P = 0.038$) and graft survival ($P = 0.022$) after liver transplant compared with both nondiabetics and nonobese recipients. The presence of alcoholic cirrhosis in recipients did not have a significant association with obesity on survival, with obese alcoholic cirrhotics having similar patient survival ($P = 1.0$) and graft survival ($P = 0.11$) compared with obese nonalcoholic cirrhotics. Finally, Kaplan–Meier patient survival curves showed that through 15 years after liver transplant, obese black liver transplant recipients had worse patient survival compared with obese nonblack recipients ($P < 0.001$), and nonobese black recipients also had worse patient survival compared with nonobese nonblack recipients ($P < 0.001$) (Fig. 6a). With regard to graft survival, obese black liver transplant recipients had worse survival compared with obese nonblack recipients ($P < 0.001$), and nonobese black recipients also had worse graft survival compared with nonobese nonblack recipients ($P < 0.001$) (Fig. 6b). The effects of race on patient and graft

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Table 1. Association of obesity combined with demographic factors and comorbidities and survival after liver transplant in recipients from 1995 to 2019.

Obesity (BMI > 30) combined with:	Patient survival *P*-value	Graft survival *P*-value	Patient & Graft Survival Outcome comparison
(i) Age (>50 or <50 years)	$P = 0.003$*	$P = 0.049$*	Older obese recipients had worse patient and graft survival compared with younger obese recipients
(ii) Insurance status (private vs. nonprivate)	$P < 0.001$*	$P < 0.001$*	Obese recipients with nonprivate insurance had worse patient and graft survival compared with obese recipients with private insurance.
(iii) Presence of type II diabetes	$P = 0.038$*	$P = 0.022$*	Obese diabetics had worse patient and graft survival compared with obese nondiabetics
(iv) Presence of alcoholic cirrhosis	$P = 1.0$	$P = 0.11$	Obese alcoholic cirrhotics had similar patient and graft survival compared with obese nonalcoholics
(v) Race (black vs. nonblack)	$P < 0.001$*	$P < 0.001$*	Obese black recipients had worse patient and graft survival compared with obese nonblack recipients

*Significance level $P < 0.05$.

survival were immediate and persistent for at least 15 years after liver transplant.

Further analysis of this group revealed that demographic factors and common comorbidities did not explain the differences in survival between black and nonblack liver transplant recipients. Results showed that black liver transplant recipients were on average younger than nonblack recipients (50.92 vs. 54.09 years, $P < 0.001$), had a lower BMI (28.34 vs. 28.44 kg/m^2, $P = 0.093$), and were less likely to have a history of diabetes (15.4% vs. 16.9%, $P < 0.001$), myocardial infarction (0.40% vs. 0.70%, $P = 0.018$), or alcoholic cirrhosis (11.40% vs. 20.80%, $P < 0.001$). Black liver transplant recipients also received livers with lower mean cold ischemic times (6.9 vs. 7.05 hours, $P < 0.001$) (Table 2).

A major confounder for black compared with nonblack recipients was having nonprivate insurance. From 1995 to 2019, a smaller percentage of black recipients had private insurance at year of admission for transplant compared with nonblack recipients (55.40% vs. 61.30%, $P < 0.001$) (Table 2). In 2007, the percent of black versus nonblack liver transplant recipients with private insurance was similar at 63%. However, in the decade that followed, the difference in private insurance rates between black and nonblack recipients widened. By 2019, 55% of nonblack liver transplant recipients had private insurance compared with only 45% of black liver transplant recipients (Fig. S2). The relative risk of patient death or graft failure after liver transplant in recipients with nonprivate insurance was 24% and 17% higher, respectively, compared with recipients with private insurance (Figs 4 and 5).

Discussion

Our analysis exposed significant differences in liver transplant clinical practice when stratified by obesity class, with the most obese patients (class III, BMI ≥ 40 kg/m^2) having higher MELD scores at time of transplant and higher mean length of stay after liver transplant. When liver transplant recipients were stratified by obesity class, we found that black race, nonprivate insurance, the presence of diabetes, and age >50 years were independently associated with worse patient and graft survival in obese patients.

The global obesity epidemic, which has affected more than 650 million people (~ 10% of the world's population) [17], has naturally affected the liver transplant patient population as well. In 1995, obese, deceased donor liver transplant patients comprised only 25% of the liver transplant recipient population. However by 2019, 37% of liver transplant patients were obese. Because of the life-saving nature of liver transplantation, most liver transplant centers in the United States do not have a strict BMI limit for transplantation [18,19]. Obese liver transplant recipients pose clinical challenges for transplantation with regard to wound healing [20], more difficult exposure, increased surgical complexity, and longer operative time [21], but these challenges have not directly led to compromised patient and graft survival. Our results indicated that both patient and graft survival stratified by obesity class were comparable through 15 years, and in the multivariable Cox Proportional-Hazards model, BMI alone was not a significant risk factor for patient survival or graft survival at any obesity class.

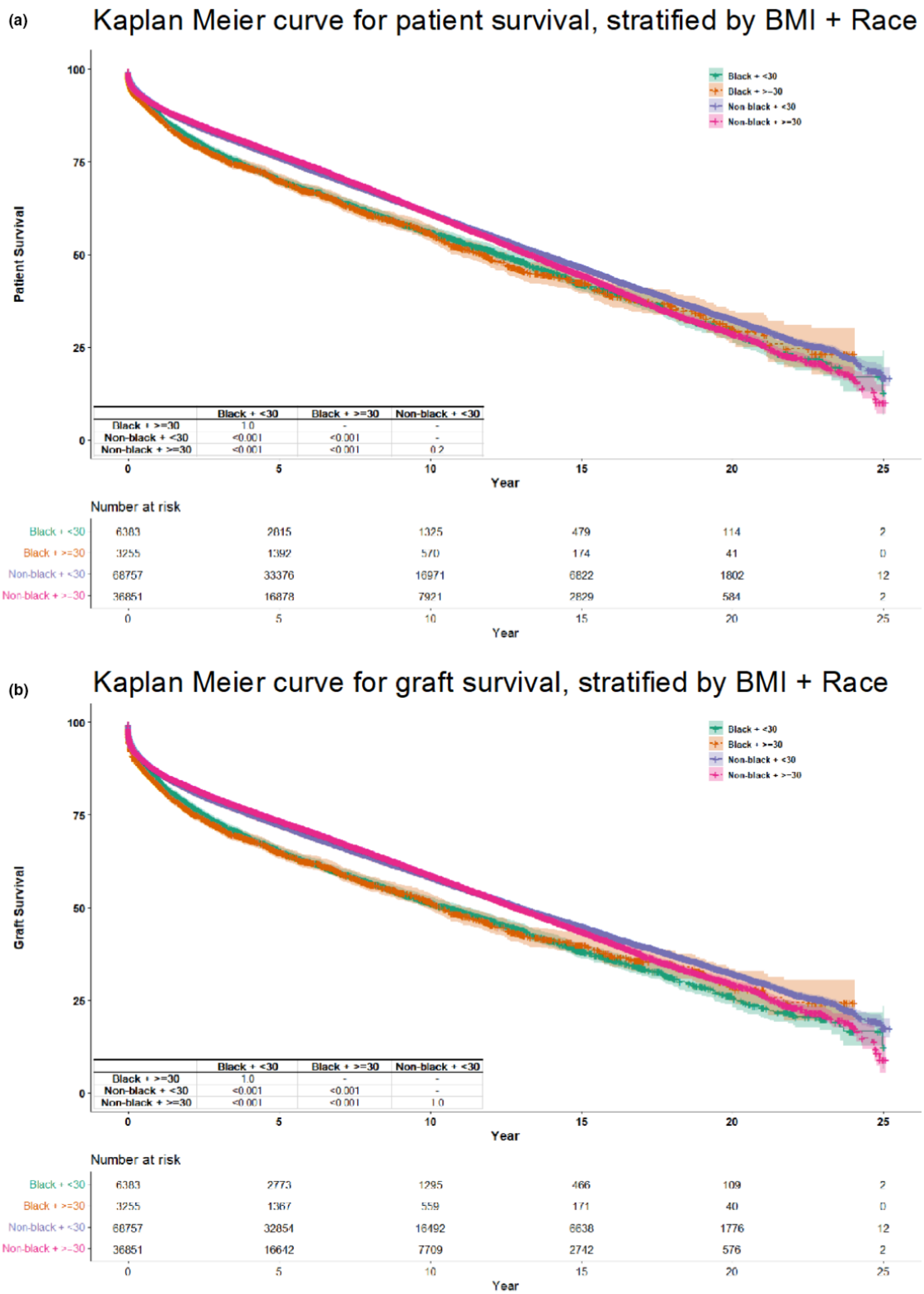

Figure 6 Kaplan–Meier curves of (a) patient survival and (b) graft survival after liver transplant, stratified by BMI and race. Green: nonobese black recipients. Orange: obese black recipients. Purple: nonobese nonblack recipients. Pink: obese nonblack recipients. Pairwise comparison with p-values comparing groups shown in tables; significance level: $P < 0.05$. Shaded areas represent 95% confidence intervals.

Table 2. Comparison of relevant demographic factors and comorbidities of black versus nonblack liver transplant recipients from 1995 to 2019.

Demographic factor/comorbidity	Black recipients	Nonblack recipients	*P*-value
Mean age at transplant (years)	50.92	54.09	<0.001*
Mean BMI (kg/m^2)	28.34	28.44	0.093
History of diabetes (% of total recipients)	15.40%	16.90%	<0.001*
History of myocardial infarction (% of total recipients)	0.40%	0.70%	0.018*
History of alcoholic cirrhosis	11.40%	20.80%	<0.001*
Mean CIT (hours)	6.9	7.05	<0.001*
% of recipients with private insurance	55.40%	61.30%	<0.001*

*Significance level $P < 0.05$.

Prior generalizations about liver transplant outcomes in obese patients from single-center studies have reported comparable survival outcomes [8,10,11]. However, obesity is intrinsically linked to many clinical and demographic factors [22], and therefore cannot be analyzed as an isolated disease process. Our results show that obese patients below 50 years without type I or type II diabetes have better patient and graft survival following liver transplant. These findings are critical for the risk stratification of obese liver transplant recipients. Programs to optimize obese diabetic patients prior to transplant should be implemented.

Compared with nonobese recipients, severely obese patients are more likely to have a multitude of comorbidities such as hypertension, diabetes, cardiovascular disease, and heart failure, making them higher risk for liver transplant [23,24]. These occurrences were evident in our results, with obesity class II and III liver transplant recipients having 2.5% higher waitlist mortality compared with obesity class I and nonobese recipients. Following liver transplant, obese liver transplant recipients had lower hospital readmission rates compared with nonobese liver transplant recipients. This is perhaps caused by more cautious initial recipient selection of obese candidates and conservative postoperative hospital course with a longer initial length of stay. Finally, our results show that both type I and type II diabetes are independent risk factors in obese liver transplant recipients with respect to patient survival and graft survival, similar to previously reported survival analysis results [12]. Recipient age less than 50 years was associated with improved survival after liver transplant regardless of obesity class.

Recipient race was associated with decreased long-term patient survival and graft survival after liver transplant. Historically, it has been felt that inferior outcomes in transplantation for black patients center around access to care. Julapalli *et al.* showed that black veterans were 85% less likely than white veterans to be referred for liver transplantation [25]. Eckhoff *et al.* found in a single-center study that blacks represented only 14% of liver transplant referrals while comprising 25% of the population served by the hospital [6]. Moylan *et al.* reported that out of a cohort of 45 000 black and white patients, blacks had a 25% lower transplant rate than whites in the pre-MELD era that did not persist in the MELD era. While their results showed these disparities did not persist in the MELD era, it is premature to stipulate that pretransplant racial disparities have been eliminated in the United States based on this study because of truncated follow-up time [26].

Our study affirmed that racial and demographic disparities are appreciated posttransplant as well. Adjusting for obesity class, we found that black recipients had a 20% lower patient survival and 23% lower graft survival compared with nonblack transplant recipients. Black obese liver transplant recipients had worse patient and graft survival immediately after liver transplant compared with obese nonblack recipients. These differences persisted for 15 years posttransplant. Having nonprivate insurance was also shown to be a significant risk factor for patient and graft survival after liver transplant. Our results indicate that black liver transplant recipients currently are covered by private insurance 10% less compared to nonblack recipients. Prior studies verify that liver transplant candidates covered by Medicare or Medicaid have both poorer waitlist outcomes and (in concordance with our results) worse posttransplant survival [27,28].

The etiology of the difference in outcome for obese black patients is likely multifactorial. Possible reasons include disparities in access to transplantation, available resources, waiting time, and disease severity. Other factors that have yet to be explored or quantified could also be impacting this difference in survival. Further work is needed to understand the possible reasons for the difference in outcomes for obese patients between racial groups and address these disparities. Specifically, there may be opportunity for improvement in optimizing care for obese black liver transplant recipients. While pretransplant factors exacerbating racial disparities such as improving access to transplantation referrals, reducing bias in transplant center reviews, and optimizing the clinical care of waitlisted candidates must be addressed, our results indicate that posttransplant factors may also impact survival. Further study is needed to understand what improvements are necessary to improve outcomes for obese black liver transplant recipients. Possibilities for intervention include postoperative inpatient and outpatient care, patient social support systems, access to affordable immunosuppression, patient-specific education, and access to a transplant center for management of complications [7]. Qualitative studies that focus on patient reported information and explore the biases facing obese black liver transplant recipients would be invaluable.

This work is not without several limitations. First, we analyzed liver transplant outcomes from 1995 to 2019 as a cohort, but acknowledge that there have been significant clinical and medical advances in liver transplantation during this time. Overall, trends need to be interpreted with the potential confounder of medical innovation. Second, the OPTN database utilized for this study has limitations caused by missing or incomplete data. For example, the data fail to correct for fluid overload, which can artificially increase BMI [29]. However, we choose to proceed with our large, national OPTN cohort because of the major benefit of analyzing 115,250 liver transplants, as single-center studies investigating the impact of race and obesity in liver transplant outcomes have been historically conflicting. Of note, the nuanced risk of such a large sample size is finding statistical difference from weak signals caused by sample size alone. Despite the limitations of the OPTN database, we were able to highlight the association between obesity and race with posttransplant survival but were unable to identify the etiology of the disparity in outcome for obese black liver transplant recipients. It is not feasible to statistically model all comorbidities associated with obesity in highly complex liver transplant recipients, and thus, our multivariable Cox model is inherently incomplete. However, we created our model based on the intention to study obesity-related comorbidities and race on long-term liver transplant outcomes.

In conclusion, while overall liver transplant outcomes for obese patients are similar to nonobese patients, some demographic and clinical characteristics (race, age, insurance status, and diabetes) have a significant impact on outcomes. Our results indicate that coupled with obesity, recipients who are either black, older than 50 years, have nonprivate insurance, or have diabetes have worse patient and graft survival. Improved national data gathering and qualitative studies exploring patient experiences are critical to understand why these discrepancies persist and guide interventions. Finally, as advancements in liver transplant are made, it is imperative that these therapies are tested in and accessible to patients of all BMIs, ages, races, and comorbidities. Given current discrepancies in outcomes, it is important to carefully test these novel therapies and their impact on all liver transplant candidates with a goal of improving the care for every liver transplant candidate and recipient.

Authorship

Q.Y., O.H., and L.A.D. wrote the manuscript. Q.Y. ran the statistical analysis. Q.Y., O.H., H.Y., J.F.M., and L.A.D. participated in the critical revision of the manuscript for intellectual content. All authors contributed to the preparation of the manuscript.

Funding

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Conflict of interest

The authors declare no conflicts of interest.

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Data availability statement

The authors declare that the data supporting the findings in this paper are available and if needed, can be provided upon request.

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of the article.

Figure S1. Death-censored graft survival (DCGS) after liver transplant; multivariable Cox Proportional-Hazards model assessing race, diabetes (none vs. type I vs. type II), presence of Nonalcoholic Steatohepatitis (NASH), presence of alcoholic cirrhosis, age less than 50 years versus greater than 50 years, and BMI. Significant differences: * $p < 0.05$, ** $p < 0.01$, *** $p < 0.0001$

Figure S2. Percent of liver transplant recipients with private insurance at year of admission for liver transplant, stratified by race (black vs. nonblack), from 1995 to 2019.

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