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OPEN

Reexamining the Association of Body Mass Index With Overall Survival Outcomes After Liver Transplantation

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Background. Several studies have shown that obese patients undergoing liver transplantation (LT) have an increased risk of mortality regardless of Model of End Stage Liver Disease (MELD) scores. The purpose of this study is to identify the range of body mass index (BMI) at LT associated with the lowest risks of posttransplant mortality by MELD category. **Methods.** A retrospective cohort of patients aged 18 years or older from the Organ Procurement and Transplantation Network database undergoing LT between February 27, 2002, and December 31, 2013, was identified and followed up through March 14, 2014. Patients' MELD score at the time of transplantation was categorized into 10 or lower (MELD1), 11 to 18 (MELD2), 19 to 24 (MELD3), and 25 or higher (MELD4). Multivariable adjusted Cox proportional hazard analyses were conducted. **Results.** Among 48 226 patients in the analytic cohort (14.8% were in MELD1, 33.7% were in MELD2, 19.6% were in MELD3, and 32.0% were in MELD4), 25% died with mean follow-up of 1371 days. For MELD1, patient BMI ranging from 30 to 33 was associated with a better survival outcome than BMI less than 30 or 33 or greater; for MELD2, BMI ranging from 28 to 37 had a better survival outcome than BMI less than 28 or 37 or greater; for MELD3, the survival outcome improved with an increasing BMI; for MELD4, the survival outcome was not associated with patient BMI. **Conclusions.** This study provides evidence that obesity in LT patients is not necessarily associated with higher posttransplantation mortality and highlights the importance of the interaction between BMI and MELD category to determine their survival likelihood.

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Liver transplantation (LT) is the definitive treatment for patients with end-stage liver disease. In 2015, 7127 liver transplants were performed in the United States, making it the second most common solid organ transplant performed in the United States.[1]

Studies have shown that risk factors of post-LT mortality include donor age, cold ischemia time, United Network for Organ Sharing urgency status (1, 2A, 2B, or 3),[2] and recipient body mass index (BMI).[3-8] For the latter, there has been continued controversy regarding the association of recipient

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BMI and posttransplant outcomes, with multiple studies reporting conflicting results. Some studies found that LT recipients with extremely low BMI were associated with a higher mortality risk[9]; some studies found that obese patients or an elevated BMI were associated with a higher mortality risk,[3,4,6,9] whereas others did not find this association in obese groups.[5-7]

More than 1 in 3 US adults are obese (BMI ≥30).[10] Obesity is associated with elevated risks of morbidity and mortality,[11-14] including chronic liver disease.[15,16] As a result, the prevalence of obesity in the new LT waitlist registrant population is high.[17,18] However, many transplant programs decline LT to obese candidates[17] because they have a higher risk of perioperative and postoperative complications[19,20] and death[3,4,6,9] than nonobese candidates. Moreover, obese waitlisted candidates have a longer waiting time for LT and the likelihood of receiving a Model for End-Stage Liver Disease (MELD) exception is 30% to 38% lower than normal-weight candidates.[21]

The objective of this study is to reexamine the relationship between BMI and post-LT overall survival after the institution of the MELD system and determine the BMI range associated with the highest post-LT survival chance by MELD category. The evidence provided by this study can either confirm or revert the current understanding of the association between BMI and posttransplantation survival and inform current clinical practice. Additionally, because BMI is a modifiable factor, the results of this study have the potential to inform the waitlisted candidates and their healthcare providers about the optimal BMI associated with the best survival outcomes.

MATERIALS AND METHODS

Data

A retrospective cohort of patients who underwent LT before December 31, 2013, was obtained from the Organ Procurement and Transplantation Network (OPTN) database.

We obtained both recipient and donor demographic data on sex, race, height, weight, BMI, and age at LT. We also collected patient clinical data on etiology of liver disease, comorbidities, whether the patient received dialysis a week before LT, medical conditions, the international normalized ratio, the MELD score, ascites, level of serum albumin, serum creatinine, and total bilirubin at LT. Additionally, LT data on cold ischemia time, level of human leukocyte antigen mismatch, whether the recipient was on ventilator, whether the recipient was on life support, and overall survival outcomes. Lastly, we obtained time of graft failure, if the patient experienced one.

Exempt study approval was obtained from the Washington University School of Medicine Institutional Review Board.

BMI and the MELD Score

Recipient BMI was recorded at the time of LT. Data on BMI were used when available; otherwise, it was computed as weight (measured at LT) in kilograms divided by the square of height in meters. MELD scores, calculated from laboratory values as opposed to scores granted by exception or used to determine allocation priority,[22] were obtained from the database as submitted by transplant centers. Recipient MELD score was then categorized into the following groups: 0 to less than 11 (MELD1), 11 to less than 19 (MELD2), 19 to less than 25 (MELD3), and 25 or greater (MELD4).[22]

Analytic Cohort

The analytic cohort was formed by excluding the following patients: (i) patients with previous LT; (ii) patients who underwent simultaneous kidney transplantation with the LT; (iii) patients receiving a liver from a deceased donor from a cardiac death; (iv) patients with missing data on either BMI or 1 of the height and weight; (v) patients undergoing LT before February 27, 2002, the institution of the MELD system; (vi) patients without a MELD score.

Outcome Measures

The primary outcome was patient survival after LT. Patients without date of death information were assumed to be alive at the time of the last death recorded within the cohort, March 14, 2014.

Statistical Analyses

To compare the MELD categories, χ^2 tests were performed to examine differences in proportions for categorical variables, and analysis of variance was conducted to test the differences in means for continuous variables. When categorical variables were used, an unknown category was created for individuals with missing data.

Cox proportional hazards models were used in the multivariable analyses. Adapted from the risk-adjustment models published by the Scientific Registry of Transplant Recipients,[23] we included the following covariates: recipient and donor sex, race, BMI at LT (recipient: continuous or categorical), age at LT; recipient etiology of liver disease (fulminant, noncholestatic cirrhosis, cholestatic cirrhosis, biliary atresia, metabolic disease, malignant neoplasm[24]), status of hepatocellular carcinoma (HCC), hepatitis C, diabetes, hypertension, dialysis before LT, ascites (absent, slight, moderate), medical conditions when treatment was performed (home, inpatient, ICU), international normalized ratio, level of serum albumin, serum creatinine, and total bilirubin at LT, cold ischemia time, human leukocyte antigen mismatch, whether the recipient was on a ventilator, on life support, time-varying graft failure status. χ^2 Tests were used to examine the statistical significance of the coefficient associated with each covariate.

All tests are 2-sided. Statistical significance was evaluated at the 0.05 level. All statistical analyses were performed using SAS version 9.4 (SAS Institute Inc., Cary, NC).

Determination of BMI Associated With the Lowest Mortality Rate After LT

Using the analytic cohort, we ran multivariable adjusted Cox analyses and tested different functional forms of recipient BMI, including (a) the standard BMI categorization (<18.5, 18.5 to <25 [reference], 25 to <30, 30 to <35, 35 to <40, ≥40[25]), (b) quasi-standard BMI categorizations (≤25 [reference], 25.1-30, 30.1-35, 35.1-40, 40.1-50, ≥50.1[4]; <19, 19 to <23 [reference], 23 to <25, 25- <30, 30 to <35, 35 to <40, ≥40[6]; or <20, 20 to <25 [reference], 25 to <30, 30 to <35, 35 to <40, ≥40[5]), (c) BMI categorization examining extreme BMI (<18.5, 18.5 to <40 [reference], ≥40[9] or <40 [reference], ≥40[3]), (d) continuous BMI,

(e) quadratic BMI, and (f) inverse BMI.[26-28] We then selected the functional form of BMI that provides the best model fit statistics: both the statistical significance of the coefficient (s) associated with BMI and the Akaike information criterion.

For each MELD category, to determine the relationship between BMI and mortality after LT, we repeated the same process. In addition, for each MELD category, we performed Cox analyses using all possible ranges of BMI between 18 and 50 one by one as the reference group to help determine the relationship and to identify the BMI range for the best survival outcomes of LT patients based on the statistical significance.

Sensitivity Analyses

To ensure the robustness of our conclusion, we performed the following sensitivity analyses. First, we excluded all patients diagnosed with HCC or with any known malignancy reported at listing and at LT from the analytic cohort due to the concern about weight loss and higher mortality rate not related to LT in these patients. Second, we excluded patients with any active MELD exception points as of LT. Lastly, we used patient BMI at the time of listing, rather than BMI at LT in the analyses to explore how the variation in weight impacts our conclusion.

RESULTS

We identified 115 473 patients who underwent LT before December 31, 2013, in the OPTN database (Figure 1). We excluded 1638 patients with previous LT. We further excluded 4807 patients who underwent simultaneous kidney transplantation with the LT; 21 143 patients who received liver from a deceased donor with a cardiac death; 860 patients without data on BMI; and 28 342 patients with a LT date before February 27, 2002. Fifty-six patients without a MELD score and 8615 patients younger than 18 years were also excluded. Lastly, 1786 patients with missing data on any continuous covariate or outcome variables were excluded. The analytic cohort included 48 226 patients, among whom, 11 976 (24.8%) died with a mean follow-up time of 1371 days (Table 1).

Among the analytic cohort, 7140 (14.8%) patients were in MELD1, 16 230 (33.7%) patients in MELD2, 9440 (19.6%) patients in MELD3, and 15 416 (32.0%) patients in MELD4 (Table 1). Patients in different MELD categories were statistically different in all variables, except for donor sex and percentage of mortality. Mean BMI increased with MELD category (27.8 for MELD1, 28.5 for MELD2, 28.6 for MELD3, 28.8 for MELD4, $P < 0.001$).

Using our data and different BMI functional forms a to f, some of which replicated the categorization from published studies.[3-6,9] Figure 2 shows the multivariable adjusted hazard ratios (HRs) for categorical and continuous BMI to compare the HRs from our study with the HRs reported in previous studies. Figures 2A to C demonstrated inconsistent conclusions depending on the reference BMI category. In general, patients with extremely low BMI were associated with a higher mortality risk with an HR ranging from 1.12 to 1.24; in contrast, extremely high BMI (BMI ≥40) was insignificantly protective in Figures 2A to B or insignificantly increased mortality risk in Figure 2C, depending on the reference group. Using continuous BMI, Figure 2D shows a linear downward trend (HR, 0.99; 95% confidence interval [CI], 0.989-0.996 per 1 unit increase in BMI); Figure 2E demonstrates a quadratic relation, indicating a BMI at approximately 34 kg/m^2 was associated with the lowest mortality risk; Figure 2F presents a decreasing mortality risk as BMI increases. Among A to F, the quadratic BMI had the best model fit statistics.

Stratifying by MELD category, we plotted the HRs for mortality against BMI in Figure 3. The quadratic BMI for MELD1-2 and BMI for MELD3-4 were chosen based on their Akaike information criterion and statistical significance (see relevant statistics in Figure 3). For MELD1-2, a BMI around 32 was associated with the lowest mortality risk. For MELD3, mortality risk decreased by 1% with a unit increase in BMI (HR, 0.99; 95% CI, 0.984-0.998). For MELD4, BMI was not associated with overall mortality (HR, 0.996; 95% CI, 0.990-1.001).

Exploring the BMI range associated with the lowest mortality risk/best survival chance after LT, we found that for MELD1 patients, BMI less than 30 (HR, 1.27; 95% CI, 1.10-1.47) or BMI of 33 or greater (HR, 1.25; 95% CI, 1.05-1.49) was associated with a higher mortality risk after LT than BMI of 30 to 33 (Table 2 and full results presented in **Table S2, SDC,** http://links.lww.com/TXD/A40). For MELD2, BMI less than 28 (HR, 1.15, 95% CI, 1.07-1.23) or BMI of 37 or greater (HR, 1.22; 95% CI, 1.07-1.38) was associated with a higher mortality risk after LT than BMI of 28 to 37. For MELD3, higher BMI was associated with a lower mortality risk (HR, 0.99; 95% CI, 0.980-0.998 per 1 unit increase in BMI). For all MELD categories (**Table S2, SDC,** http://links.lww.com/TXD/A40), older age in both recipients (HRs, 1.01-1.02 per 1 year increase in age) and donors (HRs, 1.01 per 1 year increase in age) and

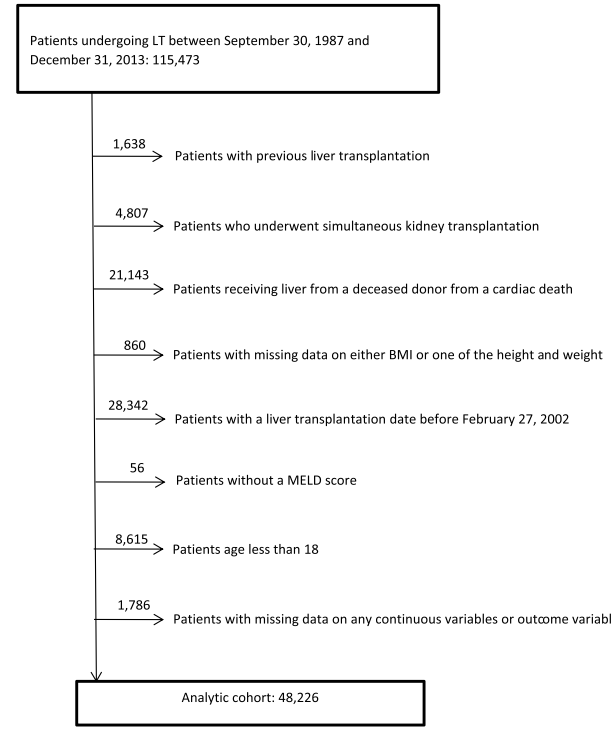


FIGURE 1. Data attrition diagram.

TABLE 1.

Select demographics and characteristics of 48 226 liver transplant patients and their donors

	Overall	MELD1, 0 to < 11	MELD2, 11 to < 19	MELD3, 19 to < 25	MELD4, ≥25
N	48 226	7140	16 230	9440	15 416
%	100.00	14.81	33.65	19.57	31.97
Recipient characteristics					
Age (mean ± SD), y[a]	53.86 ± 9.87	56.27 ± 9.20	55.13 ± 8.82	53.60 ± 9.56	51.55 ± 10.85
Female, %[a]	30.94	27.31	28.02	30.32	36.09
Race, %[a]					
White	72.17	67.45	76.09	76.17	67.79
Black	9.02	9.01	6.70	9.35	11.26
Hispanic	12.95	10.88	12.17	11.12	15.83
Other	5.86	12.66	5.03	3.36	5.12
Recipient BMI[a]					
Underweight (BMI, <18.5)	1.62	1.75	1.32	1.59	1.89
Normal weight (BMI, 18.5-24.9)	27.13	30.31	25.64	26.39	27.68
Overweight (BMI, 25-29.9)	35.82	37.62	37.88	35.49	33.02
Obese class I (BMI, 30-34.9)	22.24	20.59	23.01	22.89	21.78
Obese class II (BMI, 35-39.9)	9.70	7.80	9.46	9.95	10.69
Obese class III (BMI, ≥40)	3.49	1.93	2.68	3.70	4.94
Recipient BMI (mean ± SD), kg/m^2[a]	28.50 ± 5.64	27.82 ± 5.21	28.50 ± 5.34	28.62 ± 5.66	28.75 ± 6.09
Etiology of liver disease, %[a]					
Biliary atresia	2.75	1.96	1.95	3.24	3.67
Cholestatic cirrhosis	5.11	3.24	4.84	6.48	5.43
Fulminant	5.06	1.44	2.29	3.43	10.64
Malignant neoplasm	3.51	5.76	3.06	3.20	3.15
Metabolic disease	22.03	52.98	28.48	11.41	7.41
Noncholestatic cirrhosis	61.52	34.62	59.37	72.24	69.70
HCC, %[a]					
Yes	21.08	50.15	27.63	10.74	7.03
No	78.92	49.85	72.37	89.26	92.97
Hepatitis C, %[a]					
Negative	96.36	95.62	94.89	96.32	98.26
Positive	3.64	4.38	5.11	3.68	1.74
Ascites at LT, %[a]					
Absent	21.99	54.45	23.41	13.14	10.88
Slight	49.52	39.79	58.77	54.54	41.20
Moderate	27.81	5.15	17.23	31.51	47.17
Unknown	0.69	0.60	0.6	0.81	0.75
Graft failure[b] ($P = 0.001$), %					
Yes	0.64	0.48	0.61	0.47	0.84
No	99.36	99.52	99.39	99.53	99.16
Follow-up duration (mean ± SD), d	1371 ± 1154	1309 ± 1116	1508 ± 1291	1448 ± 1157	1208 ± 1107
Donor characteristics					
Donor BMI (%)[b] ($P < 0.001$)					
Underweight (BMI, <18.5)	2.50	2.49	2.77	2.24	2.39
Normal weight (BMI, 18.5-24.9)	36.64	36.02	35.80	36.69	37.76
Overweight (BMI, 25-29.9)	34.43	34.48	34.30	34.19	34.69
Obese class I (BMI, 30-34.9)	16.18	16.18	16.34	16.44	15.85
Obese class II-III (BMI, ≥35)	10.21	10.78	10.73	10.41	9.28
Unknown	0.04	0.04	0.06	0.02	0.02
Donor age (mean ± SD), y[a]	44.01 ± 16.10	44.70 ± 16.23	45.10 ± 16.33	44.46 ± 16.32	42.29 ± 15.51
Female (P =0.462), %	41.42	42.18	41.50	41.05	41.21
Donor race, %[a]					
White	66.94	66.86	67.99	68.31	65.04
Black	16.75	16.74	17.42	17.53	15.57
Hispanic	12.61	12.13	10.91	11.01	15.62
Other	3.67	4.26	3.67	3.11	3.76
Unknown	0.02	0.01	0.02	0.04	0.02

Continued next page

TABLE 1. (Continued)

	Overall	MELD1, 0 to < 11	MELD2, 11 to < 19	MELD3, 19 to < 25	MELD4, ≥25
Outcomes					
Mortality					
Overall death ($P = 0.741$), %	24.83	24.87	24.54	24.92	25.07
No. deaths[a]	11 976	1776	3983	2352	3865
Survival duration (mean ± SD), d	861 ± 920	918 ± 866	1009 ± 971	906 ± 950	655 ± 832

[a] Statistically significant at $\alpha = 0.05$ for χ^2 test or ANOVA test ($P < .0001$).

[b] Statistically significant at $\alpha = 0.05$ for χ^2 test or ANOVA test ($P < .05$).

See **Table S1, SDC,** http://links.lww.com/TXD/A40 for all variables included in the analyses.

ANOVA, analysis of variance.

graft failure (HRs, 72.01-183.86) were risk factors of mortality; in recipients, compared with white race, black race was associated with a higher risk (HR, 1.28; 95% CI, 1.09-1.50 for MELD1; HR, 1.42; 95% CI, 1.27-1.59; for MELD2; HR, 1.24; 95% CI, 1.09-1.42 for MELD3; and HR, 1.30; 95% CI, 1.18-1.44 for MELD4).

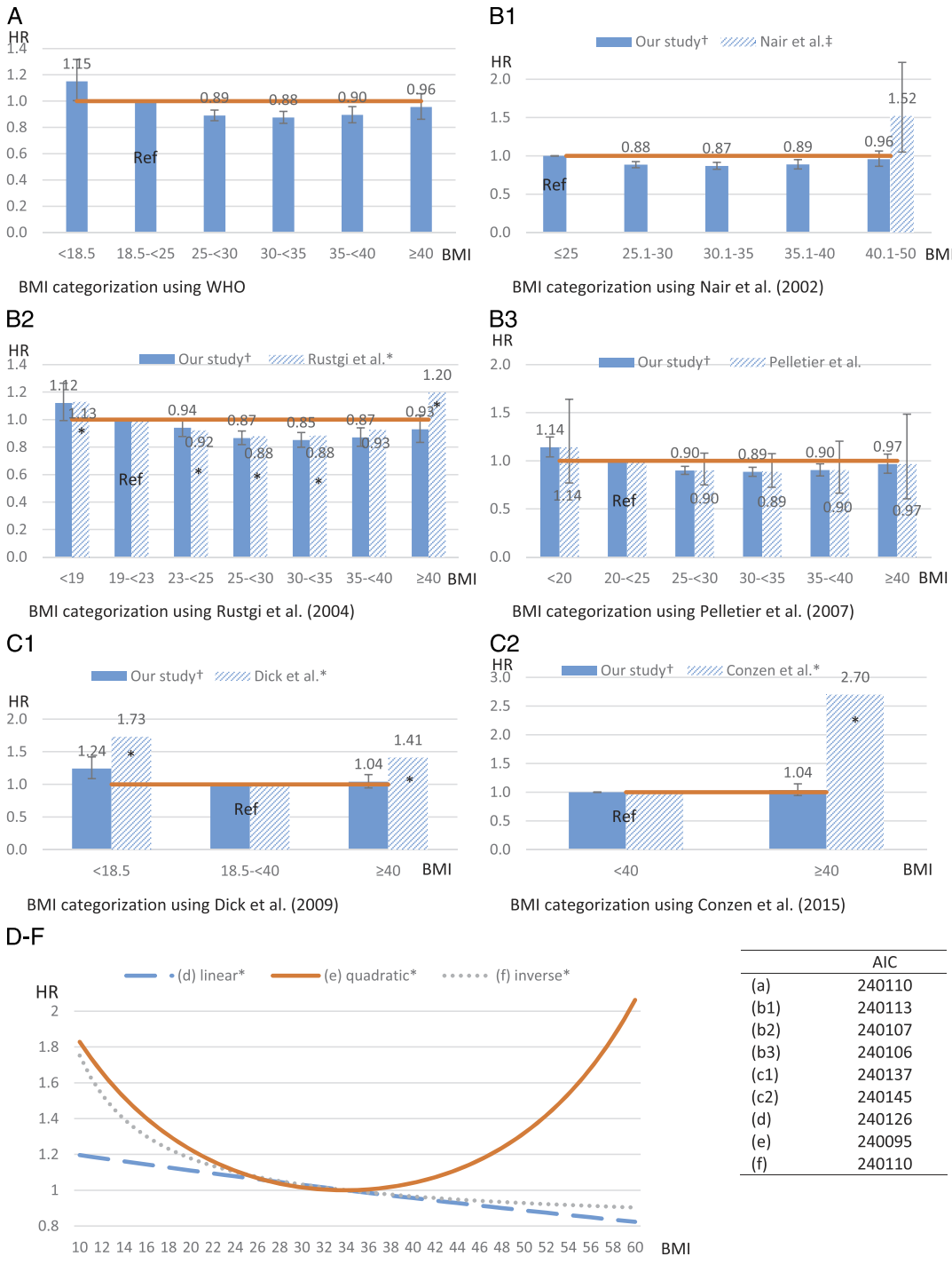
In the sensitivity analyses (**Table S3-S5, SDC,** http://links.lww.com/TXD/A40), both excluding patients with any malignancy (including HCC) and excluding patients with active exception as of LT reduced a large sample size in MELD1-2. The analyses without cancer patients (**Table S3, SDC,** http://links.lww.com/TXD/A40) provide similar results to the main analysis for MELD1, 2, and 4, whereas the inverse association between BMI and mortality in MELD3 was not statistically significant. When excluding patients with exception (**Table S4, SDC,** http://links.lww.com/TXD/A40), only the relationship between BMI and mortality in MELD2 maintains the statistical significance with the BMI associated with the lowest mortality risk after LT being approximately 33.2. Nonetheless, the relationship for each MELD category (ie, the sign of the coefficient estimates,) remains the same as the main analysis without reaching statistical significance. Using BMI at listing (**Table S5, SDC,** http://links.lww.com/TXD/A40), rather than BMI at LT, we found that generally the relationship between BMI and mortality preserve for MELD1-3, whereas BMI associated with the lowest mortality shift to the right for MELD1 (35.6) and MELD2 (34.4). For MELD4, a quadratic relation was observed with a BMI of 39.3 associated with the lowest mortality risk after LT. However, the difference between BMI at listing (median, 27.8; range, 10.8-72.9) and BMI at LT (median, 28.2; range, 10.0-71.6) is small with a median of 81 (range, 0-6286) days on the list (**Table S6, SDC,** http://links.lww.com/TXD/A40).

DISCUSSION

We investigated the association between BMI at LT and overall survival/mortality after LT in patients who underwent LT between February 27, 2002, and December 31, 2013. We found that without stratifying by MELD category, LT patients with a BMI of approximately 34 or within a range of 28 to 37 had the best survival outcome after transplantation. When stratified by MELD category, for MELD1 patients, the BMI range associated with the best survival outcome after LT was 30 to 33; for MELD2 patients, this BMI range was 28 to 37; for MELD3 patients, higher BMI was associated with a better survival outcome; for MELD4 patients, BMI was not associated with overall survival outcome.

Past research has provided inconsistent results regarding the association of BMI and survival outcome after LT largely due to the choice of the reference BMI category, a finding of this study. Nair et al[4] analyzed the relationship of BMI and the 2-year overall survival outcome in 23 675 patients who underwent LT between 1988 and 1996 in the OPTN database and found that morbid obesity (BMI, 40.1-50) was an independent predictor, compared with nonobese (BMI, ≤25) (odds ratio, 1.52; 95% CI, 1.05-2.22). Using the same database, Rustgi et al[6] studied 32 512 patients undergoing LT between 1992 and 2000 and found that patients with a BMI of 40 or greater had 19.7% higher mortality risk and patients with a BMI less than 19 had 12.9% higher risk than patients with a BMI of 19 to 22. However, patients with a BMI of 25 to 34 had a significantly (9.9-11.7%) lower mortality risk than patients with a BMI of 19 to 22. Similarly, Pelletier and colleagues[5] used BMI of 20 to less than 25 as the reference group in 4488 LT recipients from 2001 to 2004 and found a protective trend in BMI of 25 to less than 30 (HR, 0.92; 95% CI, 0.77-1.10) and BMI of 30 to less than 35 (HR, 0.84; 95% CI, 0.68-1.03), but not in BMI of 35 or greater.

Using the same database but only restricting to patients who underwent LT after the implementation of the MELD system, in replicating their BMI categorizations, our study did find a protective effect for patients with an elevated BMI with statistical significance depending on the defined reference BMI. Henceforth, the conclusion is likely to be driven by the predetermined reference group. After testing these different categorizations, our study revealed that the relationship between BMI and survival after LT was not linear. The relationship between BMI at LT and overall mortality risk should be quadratic with the nadir at a BMI of approximately 34. In other words, a reference BMI category defined approximately 34, for example, 28 to 37, would yield the lowest mortality risk. However, after stratifying by the MELD category, this quadratic relationship only maintained in patients with a lower MELD score (<19). For patients with a MELD score of 19 to less than 25, the mortality risk decreased with BMI, whereas no association between BMI and overall mortality was found for patients with a MELD score of 25 or greater. The interactions between BMI and MELD on post-LT mortality in patients with a lower MELD score were also confirmed by Bambha and colleagues.[29] Analyzing patients undergoing LT between 2002 and 2011 in OPTN database, Bambha et al[29] found that for patients



	AIC
(a)	240110
(b1)	240113
(b2)	240107
(b3)	240106
(c1)	240137
(c2)	240145
(d)	240126
(e)	240095
(f)	240110

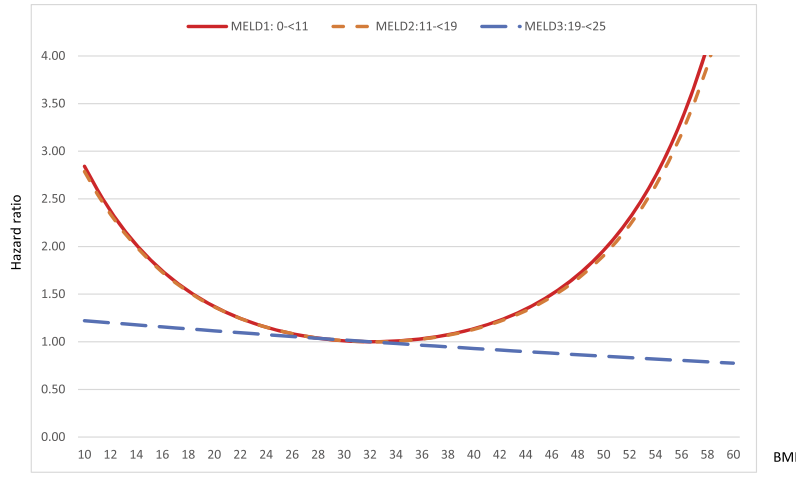
continuous BMI: hazard ratios were obtained by standardizing hazard rates at various levels of BMI to hazard rates at BMI of 34 (HR=1 at BMI of 34)

† All hazard ratios were obtained from multivariable analyses; ‡2-year survival; *statistically significant at α=0.05

FIGURE 2. HRs corresponding to different categorizations and forms of BMI.

with a low MELD score (≤26), underweight (BMI <18.5) patients have an increased risk of 1-year mortality than their normal weight (BMI, 18.5-24.9) counterparts, which partially explain our findings.

Our finding on overweight (BMI 25 to < 30) and even class I and II obesity (BMI 30 to < 40) at LT being associated with a lower overall mortality risk for LT recipients with a lower MELD score is not uncommon for older people or people with severe health conditions, termed as obesity paradox.[30,31] For the association of BMI and mortality risk in older populations, obesity paradox was found in many studies.[32-39] For population with severe health conditions, obesity paradox was found in people undergoing hemodialysis,[30,40] people experiencing heart failure,[41] and cancer survivors.[42-45]



Hazard ratios were obtained by standardizing hazard rates at various levels of BMI to hazard rates at BMI of 32 (HR=1 at BMI of 32)

Parameter estimates associated with BMI (and the square of BMI, BMI2) from multivariable adjusted survival models

		Quadratic BMI				Linear		
MELD category	n	BMI	BMI2	AIC	BMI*	BMI	HR	AIC
MELD1: 0-<11	7,140	-0.13653**	0.00212**	28687.77	32.2	--	--	--
MELD2: 11-<19	16,230	-0.13312**	0.00206**	71064.58	32.3	--	--	--
MELD3: 19-<25	9,440	-0.04171	0.000542	39681.12	--	-0.00908**	0.991 (0.984-0.998)	39680.53
MELD4: ≥25	15,416	-0.03431	0.000484	68839.72	--	-0.00445	0.996 (0.990-1.001)	68840.54

* BMI associated with the lowest hazard rate for overall mortality
** Statistically significant at 0.05 significance level

FIGURE 3. Relationship between mortality risks and BMI by MELD category HRs were obtained by standardizing hazard rates at various levels of BMI to hazard rates at BMI of 32 (HR, 1 at BMI of 32).

The underlying rationales of obesity paradox can be the following. First, weight loss is associated with disease progression at diagnosis or before treatments; therefore, the association of the baseline BMI and mortality is confounded by disease progression or other unmeasured comorbidities. Second, people with a higher BMI had better treatment tolerance, improving survival. While our study cannot completely rule out the potential confounding due to unmeasured or unknown factors, our study has minimized it by controlling for all possible factors in the data, including comorbidities and MELD scores. Therefore, our findings on the association of BMI and mortality risk should be mostly explained by the second rationale.

We need to note that our conclusion does not intend to encourage obesity. Obesity is a risk factor of liver disease of metabolic origin,[46] including nonalcoholic fatty liver disease, cirrhosis, and HCC, all of which could progress to liver failure requiring a LT. Because obesity is prevalent in the United States and other countries, the prevalence of nonalcoholic fatty liver disease is estimated to be 20% to 30% in western countries and 80% to 90% in obese adults.[47] Furthermore, 35.4% LT patients aged 18 years or older were obese in our analytic cohort, which is comparable to the national estimate (35.1%) of the prevalence of obesity in adults aged 20 years or older.[48,49] We also need to note that obese patients after LT had a higher chance of death from multisystem organ failure[7] and cardiovascular events.[4] Nonetheless, our finding suggests that once obese people develop liver disease, progress to a more advanced liver disease, and become wait-listed for LT, maintaining a high BMI may be beneficial to their overall survival after LT, depending on their MELD scores. This finding has the potential to change current practices and policies of many transplant programs, which refuse to transplant a patient with obesity. Our findings suggest that for these patients, their MELD scores should be taken into consideration before denying their LT.

We also need to note that BMI is a measure incorporating patients' height and weight, but it does not capture body fat distribution or body shape. Nonetheless, it is one of the least

TABLE 2.

Deaths after LT and selected results of multivariable adjusted HRs for death stratified by the MELD category

BMI	Deaths after LT/n	(%)	*P*	HR[b]	95% CI	
Overall (n = 48 226)						
<28	6368/24 769	(25.71)	<0.001[a]	1.12	1.08	1.17
28- < 37	4641/19 577	(23.71)			Reference	
≥37	967/3880	(24.92)		1.10	1.03	1.18
MELD1, 0 to < 11 (n = 7140)						
<30	1271/4975	(25.55)	0.013[a]	1.27	1.10	1.47
30 to < 33	213/1007	(21.15)			Reference	
≥33	292/1158	(25.22)		1.25	1.05	1.49
MELD2, 11 to < 19 (n = 16 230)						
<28	2101/8294	(25.33)	0.002[a]	1.15	1.07	1.23
28 to < 37	1579/6806	(23.20)			Reference	
≥37	303/1130	(26.81)		1.22	1.07	1.38
MELD3, 19 to < 25 (n = 9440)						
Continuous	2352/9440	(24.92)	—	0.991	0.984	0.998
MELD4, ≥25 (n = 15 416)						
Continuous	3865/15 416	(25.07)	—	0.996	0.990	1.001

[a] Statistically significant at α = 0.05 for χ^2 test.
[b] All HRs were multivariable adjusted. Please see **Table S2, SDC,** http://links.lww.com/TXD/A40 for full results.

expensive measures used in population health studies,[39] such as this study. Several smaller studies have used computed tomography imaging to measure patients' pretransplant body composition and its association with posttransplant outcomes.[50] DiMartini et al[51] (n = 338) found that muscle mass based on the pretransplant computed tomography data is a significant predictor of post-LT survival in men and that 62% of the patients with a BMI of 25 or greater were cachectic, compared with 80% of the patients with a BMI of 18.5 to 24.9. Englesbe et al[52] (n = 163) found that pretransplant central sarcopenia determined by computerized tomography scans of the psoas muscle strongly correlates with post-LT mortality, whereas Jeon et al[53] (n = 145) demonstrated that pretransplant sarcopenia in LT patients is marginally significantly associated with longer survival.

Our study is the first to closely examine the relationship between BMI and overall survival after LT and identify BMI ranges at transplant associated with the best survival outcome in patients undergoing LT in the era of postinstitution of the MELD system, using a large database. However, our study has several limitations that should be noted. First, like all other studies using the OPTN database, this study is retrospective and uses only those variables available in this database. However, this database offers a large sample size that allows us to identify statistically significant associations. Second, the use of BMI at LT (or at listing) might not reflect a patient's true body weight as some of the patients could have extensive peripheral edema or ascites,[5] although we have controlled for patients' ascites at LT. This could be a reason for no association in the relationship of BMI and overall mortality in the highest MELD category. Third, selection bias could confound our analyses as well as studies using this database due to current practices of many transplant programs, which refuse LT in patients with a BMI of 40 or greater. Lastly, we have not found a better way to categorize MELD scores, which provides more clinical insights about this association. Future studies can explore this.

CONCLUSIONS

Our study provides evidence that obesity in LT patients is not necessarily associated with higher posttransplantation mortality. Current policies about whether a patient is eligible for LT should be reevaluated and should consider patient's BMI along with their MELD category to determine their survival likelihood.

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