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

Su-Hsin Chang, PhD,1 Xiaoyan Liu, MS,2 Nils P. Carlsson, BS,1 Yikyung Park, ScD,1 Graham A. Colditz, PhD,1 Jacqueline M. Garonzik-Wang, MD,3 William C. Chapman, MD,2,4 Jason R. Wellen, MD,3 Maria B. Doyle, MD,3 and Tarek Alhamad, MD4

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.

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 BMI with post-LT mortality.

Accepted 7 April 2017.

1 Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine, St. Louis, MO.
2 Division of Biostatistics, Washington University School of Medicine, St. Louis, MO.
3 Section of Abdominal Transplantation, Department of Surgery, Washington University School of Medicine, St. Louis, MO.
4 Division of Nephrology, Department of Internal Medicine, Washington University School of Medicine, St. Louis, MO.

The Foundation for Barnes-Jewish Hospital and the National Institutes of Health Grant U54 CA155496 supported this research. S-H. Chang is supported by the Agency for Healthcare Research and Quality Grant K01 HS022330.

The authors declare no conflicts of interest.

S-H.C and T.A. had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. S-H.C and T.A. participated in the study concept and design. S-H.C, X.L., T.A. participated in the analysis and interpretation of data. S-H.C participated in the drafting of the article. S-H.C, X.L., N.P.C., Y.P., G.A.C., J.M.G.-W., W.C.C., J.R.W., M.B.D., T.A. participated in the critical revision of the manuscript for important intellectual content. S-H.C, X.L., N.P.C. participated in the statistical expertise. S-H.C and G.A.C. obtained funding. S-H.C and T.A. participated in the administrative, technical, or material support. S-H.C, T.A. participated in the study supervision.

Correspondence: Su-Hsin Chang, PhD, Division of Public Health Sciences, Department of Surgery, Washington University School of Medicine 660S. Euclid Avenue, Campus Box 8100, St. Louis, MO 63110. (changsh@wudosis.wustl.edu).

Supplemental digital content (SDC) is available for this article. Direct URL citations appear in the printed text, and links to the digital files are provided in the HTML text of this article on the journal’s Web site (www.transplantationdirect.com).

Copyright © 2017 The Author(s). Transplantation Direct. Published by Wolters Kluwer Health, Inc. This is an open-access article distributed under the terms of the Creative Commons Attribution-Non Commercial-No Derivatives License 4.0 (CCBY-NC-ND), where it is permissible to download and share the work provided it is properly cited. The work cannot be changed in any way or used commercially without permission from the journal.

ISSN: 2373-8731
DOI: 10.1097/TXD.0000000000000681

Received 5 April 2017.
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; some studies found that obese patients or an elevated BMI were associated with a higher mortality risk, whereas others did not find this association in obese groups. More than 1 in 3 US adults are obese (BMI $\geq 30$). Obesity is associated with elevated risks of morbidity and mortality, including chronic liver disease. As a result, the prevalence of obesity in the new LT waitlist registrant population is high. However, many transplant programs decline LT to obese candidates because they have a higher risk of perioperative and postoperative complications and death 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.

The objective of this study is to reexamine the relationship between BMI and post-LT 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 priorities, 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).

**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, $\chi^2$ 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, 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 (fulminating, noncholestatic cirrhosis, cholestatic cirrhosis, biliary atresia, metabolic disease, malignant neoplasm), 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. $\chi^2$ 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 $<40, \geq 40$), (b) quasi-standard BMI categorizations ($\leq 25$ [reference], $25.1$ to $30, 30.1$ to $35, 35.1$ to $40, 40.1$ to $50, \geq 50$), (c) BMI categorization examining extreme BMI ($<18.5, 18.5$ to $<40$ [reference], $\geq 40^9$ or $<40$ [reference], $\geq 40^9$), (d) continuous BMI,
Sensitivity Analyses

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 significantly 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/m² 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, 1.17-1.38) 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...
| | 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 | 53.86 ± 9.87 | 56.27 ± 9.20 | 55.13 ± 8.82 | 53.60 ± 9.56 | 51.55 ± 10.85 |
| Female, % | 30.94 | 27.31 | 28.02 | 30.32 | 36.09 |
| Race, % | | | | | |
| 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 % | | | | | |
| 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/m² | 28.50 ± 5.64 | 27.82 ± 5.21 | 28.50 ± 5.34 | 28.62 ± 5.66 | 28.75 ± 6.09 |
| Etiology of liver disease, % | | | | | |
| 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, % | | | | | |
| Yes | 21.08 | 50.15 | 27.63 | 10.74 | 7.03 |
| No | 78.92 | 49.85 | 72.37 | 89.26 | 92.97 |
| Hepatitis C, % | | | | | |
| 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, % | | | | | |
| 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 % (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 % (P < 0.001) | 2.50 | 2.49 | 2.77 | 2.24 | 2.39 |
| Underweight (BMI, <18.5) | 36.64 | 36.02 | 35.80 | 36.69 | 37.76 |
| Normal weight (BMI, 18.5-24.9) | 34.43 | 34.48 | 34.30 | 34.19 | 34.69 |
| Overweight (BMI, 25-29.9) | 16.18 | 16.18 | 16.34 | 16.44 | 15.85 |
| Obese class I (BMI, 30-34.9) | 10.21 | 10.78 | 10.73 | 10.41 | 9.28 |
| Obese class II-III (BMI, ≥35) | 0.04 | 0.04 | 0.06 | 0.02 | 0.02 |
| Donor age (mean ± SD), y | 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 | 41.06 | 41.21 |
| Donor race, % | | | | | |
| 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 |
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 survival outcome after LT 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 colleagues7 used BMI of 20 to less than 25 as the reference BMI 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).
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

FIGURE 2. HRs corresponding to different categorizations and forms of BMI.
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, 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. 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. We also need to note that obese patients after LT had a higher chance of death from multisystem organ failure and cardiovascular events. 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       | HRb  | 95% CI       |
|---------|-----------------------|---------|------|--------------|
| Overall (n = 48,226) |                       |         |      |              |
| <28     | 6368/24,769 (25.71)   | <0.001b | 1.12 | 1.08 1.17    |
| 28 to <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     | 1271/49,75 (25.55)    | 0.013b  | 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     | 2101/8,294 (25.33)    | 0.002b  | 1.15 | 1.07 1.23    |
| 28 to <37 | 157/6,806 (23.20)     |         |      | Reference    |
| ≥37     | 303/11,350 (26.81)    | 1.22    | 1.07 | 1.38         |
| MELD3, 19 to <25 (n = 9,440) |            |         |      |              |
| Continuous | 2352/9,440 (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  |

Note: Statistically significant at α = 0.05 for χ² 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, such as this study. Several smaller studies have used computed tomography imaging to measure patients’ pretransplant body composition and its association with posttransplant outcomes. DiMartini et al35 (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 al32 (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 al15 (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, 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.

REFERENCES

1. United Network for Organ Sharing. Transplant trends. United Network for Organ Sharing website, https://www.unos.org/data/transplant/trends/ #transplants_by_organ_type+year+2015. Updated 2015. Accessed April 18, 2016.
2. Moore DE, Feurer ID, Speroff T, et al. Impact of donor, technical, and recipient risk factors on survival and quality of life after liver transplantation. Arch Surg. 2006;140:273–277.
3. Conzen KD, Vachharajani N, Collins KM, et al. Morbid obesity in liver transplant recipients adversely affects longterm graft and patient survival in a single-institution analysis. HPB (Oxford). 2015;17:251–257.
4. Nair S, Verma S, Thuluvath PJ. Obesity and its effect on survival in patients undergoing orthotopic liver transplantation in the United States. Hepatology. 2002;35:105–109.
5. Peletier SJ, Schaubel DE, Wei G, et al. Effect of body mass index on the survival benefit of liver transplantation. Liver Transpl. 2007;13: 1679–1683.
6. Rustgi VK, Marino G, Rustgi S, et al. Impact of body mass index on graft failure and overall survival following liver transplant. Clin Transplant. 2004; 18:634–637.
7. Sawyer RG, Pelletier SJ, Pruett TL. Increased early morbidity and mortality with acceptable long-term function in severely obese patients undergoing liver transplantation. Clin Transplant. 1999;13(1 Pt 2):126–130.
8. Thuluvath PJ. Morbid obesity with one or more other serious comorbidities should be a contraindication for liver transplantation. Liver Transpl. 2007;13:1627–1629.
9. Dick AA, Spitzer AL, Seifert CF, et al. Liver transplantation at the extremes of the body mass index. Liver Transpl. 2009;15:986–977.
10. Flegel KM, Carroll MD, Kit EBK, et al. Prevalence of obesity and trends in the distribution of body mass index among US adults, 1999-2010. JAMA. 2012;307:491–497.
11. Clinical Guidelines on the identification, evaluation, and treatment of overweight and obesity in adults—the evidence report. National Institutes of Health. Obes Res. 1998;6(Suppl 2):515–2005.
12. Must A, Spadano J, Coakley EH, et al. The disease burden associated with overweight and obesity. JAMA. 1999;282:1523–1529.
13. Renehan AG, Tyson M, Egger M, et al. Body-mass index and incidence of cancer: a systematic review and meta-analysis of prospective observational studies. Lancet. 2008;371:569–578.
14. Wool KY, Carson K, Colditz GA. Obesity and cancer. Oncologist. 2010; 15:566–565.
15. Day CP. Non-alcoholic steatohepatitis (NASH): where are we now and where are we going? Gut. 2002;50:585–588.
16. Dam-Larsen S, Franzmann M, Andersen IB, et al. Long term prognosis of fatty liver: risk of chronic liver disease and death. Gut. 2004;53:750–755.
17. Akyo S, Armstrong J, Hurton S, et al. Obesity and liver transplantation. World J Transplant. 2015;5:95–101.
18. Aguilar M, Lu B, Holt EW, et al. Impact of obesity and diabetes on waitlist survival, probability of liver transplantation and post-transplant survival among chronic hepatitis C virus patients. Liver Int. 2016;36:1167–1175.
19. Hakeem AR, Cockbain AJ, Raza SS, et al. Increased morbidity in overweight and obese liver transplant recipients: a single-center experience of 1325 patients from the United Kingdom. Liver Transpl. 2013;19: 551–552.
20. Peletier SJ, Cohen DB, Cohen MP, et al. Postoperative morbidity, mortality, costs, and long-term survival in severely obese patients undergoing orthotopic liver transplantation. Am J Gastroenterol. 2001;96:842–845.
21. Segel DL, Thompson RE, Locke JE, et al. Prolonged waiting times for liver transplantation in obese patients. Ann Surg. 2008;248:863–870.
22. Massie AB, Caffo B, Gentry SE, et al. MELD exceptions and rates of waiting list outcomes. Am J Transplant. 2011;11:2362–2371.
23. Scientific registry of transplant recipients, risk-adjustment models: liver, deceased donor, adult, first-year patient survival. http://www.srtr.org/csr/current/motdtabs.aspx. Accessed June 8, 2016.
24. Ahamed T, Spatz C, Uemura T, et al. The outcomes of simultaneous liver and kidney transplantation using donation after cardiac death organs. Transplantation. 2014;98:1190–1198.
25. Obesity: preventing and managing the global epidemic. Report of a WHO consultation. World Health Organ Tech Rep Ser. 2000;894(i-xii): 1–263.
26. Allison DB, Faith MS, Hivo M, et al. Hypothesis concerning the U-shaped relation between body mass index and mortality. Am J Epidemiol. 1997; 146:339–349.
27. Durazo-arizú R, Mogae D, Li Z, et al. Establishing the nadir of the body mass index-mortality relationship: a case study. J Am Stat Assoc. 1997; 92:1312–1319.
28. Fontaine KR, Redden DT, Wang C, et al. Years of life lost due to obesity. JAMA. 2003;289:187–193.
29. Bambha KM, Dodge JL, Graila J, et al. Low, rather than high, body mass index confers increased risk for post-liver transplant death and graft loss: risk modulated by model for end-stage liver disease. Liver Transpl. 2015; 21:1286–1294.
30. Schmidt DS, Sahluheen AK. Obesity-survival paradox—still a controversy? Semin Dial. 2007;20:486–492.
31. Chapman IM. Obesity paradox during aging. Interdiscip Top Gerontol. 2010;37:20–36.
32. Dolan CM, Kraemer H, Browner W, et al. Associations between body composition, anthropometry, and mortality in women aged 65 years and older. Am J Public Health. 2007;97:913–918.
33. Harris S, Kim KW, Kim KL, et al. Lean mass index: a better predictor of mortality than body mass index in elderly Asians. J Am Geriatr Soc. 2010;58: 312–317.
34. Janssen I, Katzmarzyk PT, Ross R. Body mass index is inversely related to mortality in older people after adjustment for waist circumference. *J Am Geriatr Soc*. 2005;53:2112–2118.

35. Price GM, Uauy R, Breeze E, et al. Weight, shape, and mortality risk in older persons: elevated waist-hip ratio, not high body mass index, is associated with a greater risk of death. *Am J Clin Nutr*. 2006;84:449–460.

36. Reis JP, Macera CA, Araneta MR, et al. Comparison of overall obesity and body fat distribution in predicting risk of mortality. *Obesity (Silver Spring)*. 2009;17:1232–1239.

37. Testa G, Cacciari F, Galizia G, et al. Waist circumference but not body mass index predicts long-term mortality in elderly subjects with chronic heart failure. *J Am Geriatr Soc*. 2010;58:1232–1239.

38. Visscher TL, Seidell JC, Molarius A, et al. A comparison of body mass index, waist-hip ratio and waist circumference as predictors of all-cause mortality among the elderly: the Rotterdam study. *Int J Obes Relat Metab Disord*. 2001;25:1730–1735.

39. Chang S-H, Beason TS, Hunleth JM, et al. A systematic review of body fat distribution and mortality in older people. *Maturitas*. 2012;72:175–191.

40. Schmidt D, Salahudeen A. The obesity-survival paradox in hemodialysis patients: why do overweight hemodialysis patients live longer? *Nutr Clin Pract*. 2007;22:11–15.

41. Habliu A, Lakkis NM, Dokainish H. The obesity paradox: fact or fiction? *Am J Cardiol*. 2006;98:944–948.

42. Halabi S, Small EJ, Vogelzang NJ. Elevated body mass index predicts for longer overall survival duration in men with metastatic hormone-refractory prostate cancer. *J Clin Oncol*. 2005;23:2434–2435; author reply 2435.

43. Carson KR, Bartlett NL, McDonald JR, et al. Increased body mass index is associated with improved survival in United States veterans with diffuse large B-cell lymphoma. *J Clin Oncol*. 2012;30:3217–3222.

44. Matos C, Porayko MK, Francisco-Zullier N, et al. Nutrition and chronic liver disease. *J Clin Gastroenterol*. 2002;35:391–397.

45. Beason TS, Chang S-H, Santillipo KM, et al. Influence of body mass index on survival in veterans with multiple myeloma. *Oncologist*. 2013;18:1074–1079.

46. Marchesini G, Moscucci M, Di Donato S, et al. Obesity-associated liver disease. *J Clin Endocrinol Metab*. 2008;93(11 Suppl 1):S74–S80.

47. Bellantoni S, Scaglioni F, Marino M, et al. Epidemiology of non-alcoholic fatty liver disease. *Dig Dis*. 2010;28:155–161.

48. Ogden CL, Carroll MD, Kit BK, et al. Prevalence of obesity among adults: United States, 2011–2012. *NCHS Data Brief*. 2013;1–8.

49. Ogden CL, Carroll MD, Kit BK, et al. Prevalence of childhood and adult obesity in the United States, 2011–2012. *JAMA*. 2014;311:805–814.

50. Montano-Loza AJ. Skeletal muscle abnormalities and outcomes after liver transplantation. *Liver Transpl*. 2014;20:1293–1295.

51. DiMartini A, Cruz RJ Jr, Dew MA, et al. Muscle mass predicts outcomes following liver transplantation. *Liver Transpl*. 2013;19:1172–1180.

52. Englesbe MJ, Patel SP, He K, et al. Sarcopenia and mortality after liver transplantation. *J Am Coll Surg*. 2010;211:271–278.

53. Jeon JY, Wang HJ, Ock SY, et al. Newly developed sarcopenia as a prognostic factor for survival in patients who underwent liver transplantation. *PLoS One*. 2015;10:e0143966.