

ORIGINAL ARTICLE

# Impact of recipient morbid obesity on outcomes after liver transplantation

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#### Keywords

body mass index, liver, obesity, Scientific Registry of Transplant Recipients, survival, transplantation, University HealthSystem Consortium.

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#### **Conflicts of Interest**

None.

Received: 28 August 2014 Revision requested: 25 September 2014 Accepted: 24 October 2014

doi:10.1111/tri.12483

# **Summary**

The aim of this study was to analyze the impact of morbid obesity in recipients on peritransplant resource utilization and survival outcomes. Using a linkage between the University HealthSystem Consortium and Scientific Registry of Transplant Recipients databases, we identified 12 445 patients who underwent liver transplantation (LT) between 2007 and 2011 and divided them into two cohorts based on recipient body mass index (BMI; <40 vs. ≥40 kg/m²). Recipients with BMI  $\geq$ 40 comprised 3.3% (n=416) of all LTs in the studied population. There were no significant differences in donor characteristics between two groups. Recipients with BMI >40 were significant for being female, diabetic, and with NASH cirrhosis. Patients with a BMI ≥40 had a higher median MELD score, limited physical capacity, and were more likely to be hospitalized at LT. BMI ≥40 recipients had higher post-LT length of stay and were less often discharged to home. With a median follow-up of 2 years, patient and graft survival were equivalent between the two groups. In conclusion, morbidly obese LT recipients appear sicker at time of LT with an increase in resource utilization but have similar short-term outcomes.

#### Introduction

The epidemic of obesity is increasing worldwide and is one of the major health problems in the United States [1]. The National Health and Nutrition Education Survey (NHANES) study estimates that two-thirds of adults in the United States were reported to be overweight or obese [2]. Subsequently, the number of obese patients with end-stage liver disease (ESLD) is increasing, with approximately 1 of 5 being morbidly obese [3,4].

Obesity increases the risk for numerous perioperative complications such as cardiac events, adverse respiratory outcomes [5], infections, wound complications [6], as well as overall mortality [7–9]. However, the impact of recipient obesity on postliver transplant (LT) complications and survival remains controversial. An analysis of the United Network for Organ Sharing (UNOS) database from 1988 to 1996 showed that LT recipients with morbid obesity, defined as body mass index (BMI) ≥40 kg/m², had significantly higher rate of primary graft nonfunction, and immediate, 1-year, and 2-year mortality [3]. Various other single-center studies have shown that there are more postoperative complications and longer lengths of stay for obese LT recipients [10–12]. However, a recent single-center

study from United Kingdom of 1325 patients who underwent LT between 1994 and 2009 showed that there was no difference in death-censored graft survival or patient survival based on recipient BMI [13].

The aim of this study was to analyze the impact of recipient BMI ≥40 on outcomes following LT and specifically evaluate the effects of morbid obesity on peritransplant resource utilization.

#### Patients and methods

## Study population

A retrospective cohort study was performed for all LT recipients transplanted in the United States between January 1, 2007 and December 31, 2011. These data were obtained from two different sources. First, this study used data from the Scientific Registry of Transplant Recipients (SRTR). The SRTR data system includes data on all donor, wait-listed candidates, and transplant recipients in the US, submitted by the members of the Organ Procurement and Transplantation Network (OPTN), and has been described elsewhere. Second, these data were then linked to recipient clinical and hospital encounter-specific data obtained from the University HealthSystem Consortium (UHC) Clinical Data Base/Resource Manager (CDB/RM). UHC is an alliance of 118 academic medical centers and 298 of their affiliated hospitals representing approximately 95% of the nation's major non-for-profit academic medical centers. The CDB/RM is an administrative database, wherein patient demographic, financial, ICD-9 diagnosis, and procedure data are provided by the member medical centers. Hospital charges are reported for each patient encounter and are converted to cost estimates using institution-specific Medicare cost-to-charge ratios and federally reported area wage indexes, to normalize regional variation in labor cost [14-16]. Cost was generated as transplant-to-discharge based on the encounter, and pretransplant costs were removed from the analysis.

A linkage of these two datasets was undertaken as previously described [16–18]. Using recipient age, date of procedure, gender, and transplant center, the two datasets were linked. From January 2007 to December 2011, 28 880 LTs from 135 centers were identified from the SRTR database. Over the same time period, 18 162 LTs from 67 centers were identified from the UHC CDB/RM database. Recipient age less than eighteen years (n=1220) and repeat-LT within the same hospitalization (n=332) were excluded from this dataset. The final matched cohort consisted of 12 445 LT recipients from 65 transplant centers, representing 43.1% of all LTs performed nationally over the study period. The concordance was 100% with the matched variables and comprised all of the available UHC centers that perform LT. This dataset was compared with the entire

SRTR dataset and found to have similar donor, recipient, and center characteristics, suggesting that our linked dataset is reflective of the national experience.

The cohort was then divided into two groups based on recipient BMI (<40 vs. ≥40 kg/m²). A separate analysis was performed at extreme groups of BMI <18 and BMI >45 to ensure the results were not skewed leading to type II error. Donor and recipient demographic characteristics of this population were similar among two groups. With the recipient BMI as a primary predictor variable, the primary outcome was length of stay (LOS), peritransplant mortality, 30-day readmission rate, associated direct cost, and short-term survival. Median follow-up was 2 years.

#### Variables defined

The following donor demographics were collected: age (in years), gender, race (Caucasian, African American, Hispanic, and other), cause of death [trauma, anoxia, cerebrovascular accident (CVA), or other], organ location (local, regional, national), BMI (kg/m2), cold ischemia time (in hours), graft type (split, whole), and donor risk index (DRI) [19]. In comparison, the following recipient characteristics at LT were collected: age (in years), gender, race, and insurance type (private, government, other), hemodialysis treatment, subjective functional status, physical capacity, and medical MELD scores [20,21]. For the statistical analysis, patients were categorized according to quartiles and were similar to categories previously used: 6-14, 15-20, 21-27, and 28-40 [20]. We categorized DRI as: 0 to <1.2, 1.2–1.49, 1.5–1.79, and >1.8, dividing the sample approximately into quartiles by DRI [22].

The cohort was sorted by time (year of procurement) and location (medical center where the recipient underwent LT). The following center characteristics were collected: LOS [total and intensive care unit (ICU)], in-hospital mortality (mortality within index admission for LT), 30-day readmission rates, and associated direct cost (LT-to-discharge). Transplant center volume was determined using previously described methods [14,16,20]. In brief, unique transplant center identifiers, provided in the SRTR dataset, were used to determine the number of LT procedures performed annually at each institution. Centers performing fewer than five LTs per year were excluded. Transplant centers were ranked according to their annual case volumes by year and were subsequently evenly divided into tertiles and categorized into the following groups: high volume (HV, upper one-third of observations), middle volume (MV, middle one-third of observations), and low volume (LV, lower one-third of observations). Center-specific procedure volumes varied from year to year, as such, center rank and subsequent tertile designations were recalculated for each year studied [23].

#### Statistical analysis

Nominal and ordinal categorical variables were tested for statistical significance, defined as P < 0.05, with the Pearson's chi-square tests and the Mantel–Haenszel chi-square tests, respectively. They were described using estimates of central tendency (median), spread (interquartile range, IQR) for continuous data, and percentages (%) for categorical data. The variation in central tendencies of continuous variables between BMI groups was evaluated using the non-parametric Wilcoxon rank-sum test as they do not follow the normal distribution. Univariate analysis of allograft and recipient survival was performed using Kaplan–Meier estimates, and the log-rank test was used to evaluate differences in allograft and recipient survival, respectively, based on recipient BMI. The data were analyzed using the statistical package SAS 9.3 and JMP Pro 10 (SAS Institute, Cary, NC, USA).

This study was approved by the University of Cincinnati's Institutional Review Board and the Health Resources and Services Administration SRTR Project Officer, and the SRTR Technical Advisory Committee approved the linkage of the datasets. The data reported have been supplied by the Minneapolis Medical Research Foundation as the contractor for the SRTR. The interpretation and reporting of these data are the responsibility of the author(s) and in no way should be seen as an official policy of or interpretation by the SRTR or the U.S. Government.

# Results

## Recipient characteristics

Patients' demographics and clinical characteristics are summarized in Table 1. Recipients with BMI ≥40 comprised 3.3% (n = 416) of all LTs performed during the study period. There were more female recipients in the BMI ≥40 group (50.24%, P < 0.0001) versus 32% in the BMI <40 group. Median age of the BMI ≥40 recipients was significantly lower than the median age of the BMI <40 recipients (54 vs. 56 years, P = 0.0002). BMI <40 group comprised of significantly higher proportion of recipients with age >60 years (30.9%, P < 0.0001). Recipients with BMI  $\ge 40$ were more likely to be non-Caucasian. BMI ≥40 group had significantly higher percentage of diabetic patients compared with BMI <40 group (38.2% vs. 23.4% P < 0.0001). Viral cirrhosis was the most common indication for LT among the BMI <40 recipients (38.4%). However, among the BMI ≥40 group, there were significantly more patients with nonalcoholic steatohepatitis (NASH) cirrhosis compared with BMI <40 group (32% vs. 12.1%, *P* < 0.0001).

## Recipient status at transplant

BMI ≥40 recipients had significantly higher median MELD score at LT compared with recipients in BMI <40 group

Table 1. Recipient characteristics of 12 445 liver transplant recipients.

Characteristic	BMI $\ge 40$ ( $n = 416$ )	BMI < 40 $(n = 12 029)$	<i>P</i> -value
Male gender	207 (49.8)	8177 (68)	<0.0001
Race		(,	
White	303 (72.8)	8712 (72.4)	< 0.0001
Black	52 (12.5)	1196 (9.9)	
Hispanic	56 (13.5)	1318 (11)	
Other	5 (1.2)	803 (6.7)	
Age (years)			
18–29	15 (3.6)	445 (3.7)	0.006
30–39	24 (5.8)	574 (4.8)	
40-49	80 (19.2)	1829 (15.2)	
50–59	200 (48.1)	5459 (45.4)	
60–69	94 (22.6)	3402 (28.3)	
≥70	3 (0.7)	320 (2.6)	
BMI (kg/m²)	42.3 (3.9)	27.2 (7.1)	< 0.0001
Cause of liver disease			
Viral	129 (31)	4616 (38.4)	< 0.0001
Alcohol	41 (9.8)	1558 (12.9)	
NASH	133 (32)	1452 (12.1)	
HCC	34 (8.2)	1384 (11.5)	
Other	79 (19)	3018 (25.1)	
Medical history			
Diabetes	159 (38.2)	2812 (23.3)	< 0.0001
Angina	5 (1.7)	303 (3.6)	0.095
Hemodialysis	34 (8.2)	900 (7.5)	0.59
Bacterial peritonitis	18 (4.5)	636 (5.4)	0.39
Portal vein thrombosis	18 (4.5)	359 (3.1)	0.12
TIPS	27 (6.6)	711 (6.1)	0.69

BMI, body mass index; NASH, nonalcoholic steatohepatitis; HCC, hepatocelullar carcinoma; TIPS, transjugular intrahepatic porto-systemic shunt

Categorical variables are presented as numbers and percentages; continuous variables are presented as medians and interquartile range.

(22 vs. 19; P < 0.0001). 29.9% of BMI <40 recipients were transplanted with MELD exception points compared with 22.1% in BMI  $\geq$ 40 group (P = 0.0006). A higher proportion of BMI  $\geq$ 40 recipients were functionally dependent and had limited physical capacity at the time of LT (Table 2). In addition, they were more likely to be in-hospital (ICU 11.5% vs. 7.6%), on life support (7.7% vs. 4.1%), or on ventilator (6.7% vs. 3.7%) at LT in comparison with BMI <40 recipients (P < 0.05).

#### Donor characteristics

There were no differences between the two groups based on donor characteristics including age, gender, race, and DRI (Table 3). Also, there was no difference between the two groups in terms of donation after brain death (standard criteria or extended criteria donors) or donation after cardiac death (DCD) grafts. The median donor BMI of BMI <40 recipients was significantly lower compared with BMI ≥40

Table 2. Recipient status at transplant.

Characteristic	BMI $\ge 40$ ( $n = 416$ )	BMI $< 40$ ( $n = 12 \ 029$ )	<i>P</i> -value
MELD score			
6–13	77 (18.5)	3375 (28.1)	< 0.0001
14–19	98 (23.6)	3075 (25.5)	
20–27	112 (26.9)	2947 (24.5)	
28-40	129 (31)	2632 (21.9)	
Median	22 (14)	19 (13)	< 0.0001
Approved for	92 (22.1)	3599 (29.9)	0.0006
MELD Exception			
Functional status			
Independent	159 (38.2)	5781 (48)	< 0.0001
Dependent	132 (31.7)	3690 (30.7)	
Severely III	88 (21.2)	1994 (16.6)	
Unknown	37 (8.9)	564 (4.7)	
Physical capacity			
Hospitalized or	108 (32.5)	2661 (28.2)	0.05
severely limited			
Limited	62 (18.7)	1526 (16.2)	
No limitations	162 (48.8)	5246 (55.6)	
Prior to LT			
In ICU	48 (11.5)	910 (7.6)	0.008
In hospital ward	60 (14.4)	1630 (13.5)	
Not hospitalized	308 (74.0)	9489 (78.9)	
On life support	32 (7.7)	497 (4.1)	0.0006
On ventilator	28 (6.7)	444 (3.7)	0.002

BMI, body mass index; MELD, model for end-stage liver disease; LT, liver transplantation; ICU, intensive care unit.

The Categorical variables are presented as numbers and percentages; continuous variables are presented as medians and interquartile range.

recipients (26.2 kg/m² vs. 27.2 kg/m², P=0.0012). A higher proportion of recipients with BMI  $\geq$ 40 received grafts from regional donors (21.4% vs. 18.6%; P<0.05) compared with BMI <40 recipients.

## Perioperative transplant characteristics

There was no significant difference between two groups for transplant center volume or perioperative mortality (Table 4). Recipients with BMI  $\geq$ 40 had significantly higher total LOS (11 days vs. 9 days; P < 0.0001). A lower proportion of BMI  $\geq$ 40 recipients were discharged to home (77.0%) after LT compared with BMI <40 recipients (85.9%, P < 0.0001). However, there was no significant difference related to median direct cost between the two groups (P = 0.73). In addition, there was no difference for 30-day readmission rates between the two groups (P = 0.53).

A separate subset analysis of the BMI  $\geq$ 40 recipients in the ICU at time of LT compared to those who were not in the ICU was performed. Patients in the ICU at time of LT certainly are at higher risk for increased length of stay (22 days vs. 11 days; P < 0.0001), in-hospital mortality

Table 3. Donor characteristics for 12 445 liver transplants.

	BMI ≥ 40	BMI < 40	
Characteristic	(n = 416)	$(n = 12 \ 029)$	<i>P</i> -value
Male gender	244 (58.6)	7156 (59.5)	0.73
Age (years)	244 (36.0)	7130 (39.3)	0.73
<40	166 (39.9)	5398 (44.9)	0.35
40–49	85 (20.5)	2436 (20.2)	0.55
50–59	90 (21.6)	2298 (19.1)	
60–69	53 (12.7)	1379 (11.5)	
>70	22 (5.3)	518 (4.3)	
Race	22 (3.3)	310 (4.3)	
White	265 (63.7)	8052 (66.9)	0.10
Black	95 (22.9)	2174 (18.1)	0.10
Hispanic	43 (10.3)	1387 (11.5)	
Other	13 (3.1)	416 (3.5)	
Donor type	15 (5.1)	410 (5.5)	
SCD	270 (65.5)	7818 (68.3)	0.23
ECD	124 (30.1)	3031 (26.5)	0.25
DCD	18 (4.4)	595 (5.2)	
Split graft	6 (1.4)	739 (6.1)	< 0.0001
Living donation	4 (0.9)	585 (4.9)	0.0002
BMI (kg/m²)	27.2 (7.1)	26.18 (7.2)	0.0012
Cause of death	, ,	,	
Trauma	131 (31.5)	3982 (33.1)	0.0006
Anoxia	82 (19.7)	2515 (20.9)	
Cerebrovascular accident	191 (45.9)	4645 (38.6)	
Other	12 (2.9)	887 (7.4)	
Organ location	, ,	, ,	
Local	298 (71.6)	8527 (70.9)	0.04
Regional	89 (21.4)	2237 (18.6)	
National	29 (7)	1265 (10.5)	
DRI			
<1.2	117 (28.1)	3716 (30.9)	0.18
1.2–1.49	113 (27.2)	3144 (26.1)	
1.5–1.79	103 (24.8)	2506 (20.8)	
>1.8	83 (19.9)	2663 (22.2)	
Cold ischemia time (h)	6.89 (3.2)	6.5 (3.3)	0.02

BMI, body mass index; SCD, standard criteria donor, ECD, extended criteria donor; DCD, donation after cardiac death; DRI, donor risk index. Categorical variables are presented as numbers and percentages; continuous variables are presented as medians and interguartile range.

(12.8% vs. 3.8%; P = 0.007), and lower incidence of discharge to home (46% vs. 81%; P < 0.001).

As the results of the study might be due to preponderance of patients with BMI 40–45, which may do just as well as those under 40, we compared outcomes of this group to patients with BMI >45. To address this, a subset analysis between patients with BMI 40–45 (n=314) and >45 (n=102) was performed. No statistically significant differences in outcomes except for discharge-to-home rates (81.4% vs. 63.2%; P=0.0002) were identified. An additional analysis was performed for patients with BMI <18 compared to BMI 18–40 and BMI >40. No statistically significant differences were observed.

Table 4. Overall hospital characteristics.

Characteristic	BMI $\ge 40$ ( $n = 416$ )	BMI $<$ 40 ( $n = 12 \ 029$ )	<i>P</i> -value
Center volume			
LV-C	137 (33)	3997 (33.3)	0.083
MV-C	122 (29.4)	4062 (33.8)	
HV-C	156 (37.6)	3955 (32.9)	
LOS			
Total LOS	11 (10)	9 (8)	< 0.0001
ICU LOS	3 (6)	3 (4)	0.0002
Mortality	20 (4.8)	488 (4.1)	0.45
Routine discharge home	305 (77)	9911 (85.9)	<0.0001
Direct cost (LT-to-discharge)	\$98 541 (\$60 976)	\$100 469 (\$60 721)	0.73
Readmission (30 days)	156 (39.4)	4367 (37.8)	0.53

BMI, body mass index; LV-C, low-volume center; MV-C, medium-volume center; HV-C, high-volume center; LT, liver transplantation; LOS, length of stay; ICU, intensive care unit.

Categorical variables are presented as numbers and percentages; continuous variables are presented as medians and interquartile range.

Additional sensitivity analyses were performed to assess the effect of diabetes and MELD on BMI. Both analyses showed results similar to the overall dataset that the in-hospital outcomes and short-term survival were not different with and without diabetes or by different gradations of MELD score.

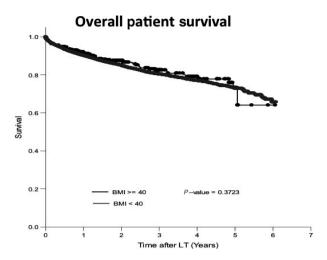
# Survival analysis

With a median follow-up of 2 years, there was no statistically significant difference for overall patient and graft survivals between the two groups (Figs 1 and 2). Also, subset analyses using a data set including patients only with higher MELD scores ( $\geq$ 20) or diabetes did not show any significant difference for survival between the two groups.

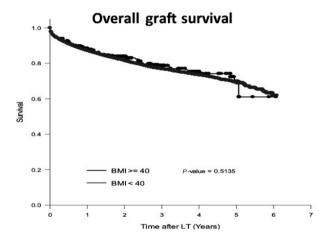
# Discussion

This large retrospective national study has shown that morbidly obese LT recipients appear sicker at time of LT with increase in resource utilization but have similar short-term outcomes. This study is unique because it provides novel insight into the hospital admission for LT to assess if there is any effect of increased BMI on the hospitalization metrics. In a representative view of the national experience with this linked database of 43% of the total LTs performed, we have shown that only 3.3% of all LTs were in recipients with BMI ≥40.

Many single-center studies from the United States and other European countries have been published, which



**Figure 1** Morbidly obese recipients have equivalent patient survival following liver transplantation when compared with all other recipients (log-rank P = 0.37).



**Figure 2** Morbidly obese recipients have equivalent graft survival following liver transplantation when compared with all other recipients (log-rank P = 0.51).

demonstrate variable results for survival outcomes after LT in obese patients. These inconsistent results were mainly because of differences in the definitions of obesity, sample size, surgical techniques, preoperative evaluations, perioperative medical care, statistical analysis reporting, and selection bias. These studies showed a trend toward higher postoperative complications, LOS, and hospital costs for obese LT recipients [10–13,24]. Our results are consistent with recent work reporting that obesity does not worsen mortality after LT [10,22,25–28]. Studies in LT recipients have similarly indicated that obesity is not associated with any of the following outcomes: an increased LOS in the ICU, ventilator support, or 2-year mortality after LT [29,30]. Our results did show that patients with BMI ≥40

had significantly longer LOS after LT and were more often discharged to rehabilitation facility. Sawyer et al. [22] did not find an increase in mortality, but they observed increased infection and multisystem organ failure rates in an acute setting in patients with a BMI >35 kg/m<sup>2</sup>. Hakeem et al. [13] recently published a large single-center study over a long study period showing no difference in deathcensored graft survival or patient survival but increased LOS and ICU stays based on recipient BMI (overweight BMI >25.0-29.9 kg/m<sup>2</sup>; obese BMI >30.0-34.9 kg/m<sup>2</sup>). Compared to the previous literature reported, our study is one of the largest multicenter studies with patients transplanted within the last 6 years with national representation and modern outcomes. Nonetheless, many transplant centers still do not perform LT for obese patients or employ a BMI restriction for listing because of concerns about perioperative complications and overall outcomes [17]. Each center is different with most having a cutoff of a BMI >40 as prohibitive and many consider BMI >35 as a relative contraindication to LT depending on the distribution of adipose tissue and the medical condition of the patient. Few centers although list severely and morbidly obese patients, but among those listed, only a smaller fraction undergoes LT in comparison with a reference group [31].

As the global epidemic of obesity continues to increase, LT programs will be forced to consider the impact of weight and BMI of LT recipients with regard to outcomes. The UNOS database from 1988 to 1996 showed that 16.8% of LT recipients had BMI ≥30 kg/m<sup>2</sup> and of these 5.3% were severely obese (BMI  $\geq$  35 kg/m<sup>2</sup>) and 2.1% were morbidly obese (BMI ≥ 40 kg/m²) [3]. Within a decade, it appears that the prevalence of obesity (BMI ≥ 30 kg/m²) has increased by 93% among LT recipients, and moreover, there was 58% increase in severe obesity and 52% increase in morbid obesity [4]. Our study did show the similar trend regarding the prevalence of obesity for those who underwent LT between 2007 and 2011; 32.8% were obese, and among them, 3.2% were morbidly obese. This is a highly selected group, and we do not know how many candidates were denied transplant or passed over due to their obesity. In order for transplant centers to develop a rational approach to the management of obese patients, the effect of high BMI on patient and graft survival needs to be determined.

The two groups in the present study differ for indications, recipient status, and severity of liver disease at LT, which could have affected the outcomes. Additionally, high BMI patients had a significantly higher median MELD score (22 vs. 19) compared with BMI <40 recipients and a significantly lower proportion of them were transplanted with MELD exception points (22.1% vs. 29.9%). However, these findings did not have the same impact in our study as reported in earlier studies [32–35]. Patients with diabetes or CAD are approximately 40% more likely to die within

5 years from transplantation compared with nondiabetics or those without CAD [36]. The presence of both diseases has a far more negative impact than either disease alone. In our study, BMI ≥40 group had significantly higher proportion (38.2%) of diabetics compared with 23.4% in BMI <40 group. However, a subgroup analysis of these diabetic recipients for survival or secondary outcome measures did not show any difference compared with overall dataset. Therefore, in the present study, these confounding risk factors did not result in any significant difference in morbidity, mortality, or transplantation-related costs between the both groups. A potential high risk group was those patients in the ICU at time of LT with BMI ≥40 as those patients has longer lengths of stay, higher in-hospital mortality, and lower likelihood to be discharged home.

The strengths of this study include the large sample size and the multicenter data. However, there are many limitations to this study that must also be considered. First, although the SRTR has repeatedly showed to be a powerful research tool, the retrospective nature of our analysis raises the possibility of measurement (data recording error) and selection biases. First, the intention and selection of these patients for listing and for eventual transplant is not known. The transplant rate of patients listed with BMI ≥40 is not known, and this would be important to understand the dynamics around which recipients may be appropriate for selection. We have verified that our linkage is representative of 43% of the entire transplant SRTR experience, and groups are similar in terms of donor, recipient, and center characteristics; however, the risk of bias in this population still exists given that over half of the LTs are not represented. Despite many differences in the two groups including BMI ≥40 including longer inpatient stays, sicker at LT, and more likely to be discharged to a care facility, this group did not have an increase in cost utilization. This was likely due to small number of patients in the BMI ≥40 group in which only small changes in this group may have large impacts on the results.

In summary, despite potential bias in this patient population, morbidly obese recipients appear to have similar in-hospital and short-term outcomes after LT without a profound increase in resource utilization. This suggests that the generally assumed BMI cutoff employed by many centers may be unnecessary and restricts access to acceptable candidates.

## **Authorship**

AS: designed the study concept and drafted the manuscript. GCW: performed acquisition of data and analysed the data. KW: performed acquisition of data, analysed the data, and performed statistical analysis. RCQ and ESW: analysed the data and performed critical revision of manuscript. MC, FP

and TSD: performed critical revision of manuscript. NA: analysed the data and interpreted the data. TEK: analysed the data, interpreted the data, and performed critical revision of manuscript. DEA: designed the study concept, analysed the data, and interpreted the data. SAS: drafted the manuscript, analysed the data, and performed study supervision.

#### **Funding**

None.

# Acknowledgements

The University of Cincinnati's Institutional Review Board approved this study, and the Health Resources and Services Administration SRTR Project Officer and the SRTR Technical Advisory Committee approved the linkage of the two datasets. The data reported here have been supplied by the Minneapolis Medical Research Foundation as the contractor for the SRTR. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the SRTR or the U.S. government. The Health Resources and Services Administration (HRSA), United States Department of Health and Human Services, provides oversight to the activities of the OPTN and SRTR contractors. The data reported here have been supplied by the Minneapolis Medical Research Foundation (MMRF) as the contractor for the SRTR. The interpretation and reporting of these data are the responsibility of the authors and in no way should be seen as an official policy of or interpretation by the SRTR or the US government.

#### References

- Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999–2008. J Am Med Assoc 2010; 303: 235.
- Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999–2004. J Am Med Assoc 2006; 295: 1549.
- 3. 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.
- 4. Pelletier SJ, Schaubel DE, Wei G, *et al.* Effect of body mass index on the survival benefit of liver transplantation. *Liver Transpl* 2007; **13**: 1678.
- 5. Akinnusi ME, Pineda LA, El Solh AA. Effect of obesity on intensive care morbidity and mortality: a meta-analysis. *Crit Care Med* 2008; **36**: 151.
- Schaeffer DF, Yoshida EM, Buczkowski AK, et al. Surgical morbidity in severely obese liver transplant recipients – a single Canadian Centre Experience. Ann Hepatol 2009; 8: 38.

- 7. Choban PS, Flancbaum L. The impact of obesity on surgical outcomes: a review. *J Am Coll Surg* 1997; **185**: 593.
- 8. Choban PS, Heckler R, Burge JC, Flancbaum L. Increased incidence of nosocomial infections in obese surgical patients. *Am Surg* 1995; **61**: 1001.
- 9. Thuluvath PJ, Yoo HY, Thompson RE. A model to predict survival at one month, one year, and five years after liver transplantation based on pretransplant clinical characteristics. *Liver Transpl* 2003; **9**: 527.
- 10. Braunfeld MY, Chan S, Pregler J, *et al.* Liver transplantation in the morbidly obese. *J Clin Anesth* 1996; **8**: 585.
- 11. Mazuelos F, Abril J, Zaragoza C, *et al.* Cardiovascular morbidity and obesity in adult liver transplant recipients. *Transplant Proc* 2003; **35**: 1909.
- 12. Hillingso JG, Wettergren A, Hyoudo M, Kirkegaard P. Obesity increases mortality in liver transplantation—the Danish experience. *Transpl Int* 2005; **18**: 1231.
- 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.
- Macomber CW, Shaw JJ, Santry H, et al. Centre volume and resource consumption in liver transplantation. HPB (Oxford) 2012; 14: 554.
- Shaw JJ, Santry HP, Shah SA. Specialization and utilization after hepatectomy in academic medical centers. *J Surg Res* 2013; 185: 433.
- Quillin RC 3rd, Wilson GC, Wima K, et al. Neighborhood level effects of socioeconomic status on liver transplant selection and recipient survival. Clin Gastroenterol Hepatol 2014; pii: S1542-35(14)00803-9. doi: 10.1016/j.cgh.2014.05. 020 [Epub ahead of print]. PubMed PMID: 24907503.
- 17. Wilson GC, Quillin RC 3rd, Wima K, *et al.* Is liver transplantation safe and effective in elderly (>/=70 years) recipients? A case-controlled analysis *HPB* (Oxford) 2014; doi: 10. 1111/hpb.12312. [Epub ahead of print] PubMed PMID: 25099347.
- Salvalaggio PR, Dzebisashvili N, MacLeod KE, et al. The interaction among donor characteristics, severity of liver disease, and the cost of liver transplantation. Liver Transpl 2011; 17: 233.
- 19. Feng S, Goodrich NP, Bragg-Gresham JL, *et al.* Characteristics associated with liver graft failure: the concept of a donor risk index. *Am J Transplant* 2006; **6**: 783.
- Ozhathil DK, Li YF, Smith JK, et al. Impact of center volume on outcomes of increased-risk liver transplants. Liver Transpl 2011; 17: 1191.
- Kamath PS, Wiesner RH, Malinchoc M, et al. A model to predict survival in patients with end-stage liver disease. Hepatology 2001; 33: 464.
- 22. 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.

- 23. Singla A, Simons J, Li Y, *et al.* Admission volume determines outcome for patients with acute pancreatitis. *Gastro-enterology* 2009; **137**: 1995.
- 24. Nair S, Cohen DB, Cohen MP, Tan H, Maley W, Thuluvath PJ. Postoperative morbidity, mortality, costs, and long-term survival in severely obese patients undergoing orthotopic liver transplantation. *Am J Gastroenterol* 2001; **96**: 842.
- Keeffe EB, Gettys C, Esquivel CO. Liver transplantation in patients with severe obesity. *Transplantation* 1994; 57: 309.
- LaMattina JC, Foley DP, Fernandez LA, et al. Complications associated with liver transplantation in the obese recipient. Clin Transplant 2012; 26: 910.
- 27. Perez-Protto SE, Quintini C, Reynolds LF, *et al.* Comparable graft and patient survival in lean and obese liver transplant recipients. *Liver Transpl* 2013; **19**: 907.
- 28. Orci LA, Majno PE, Berney T, Morel P, Mentha G, Toso C. The impact of wait list body mass index changes on the outcome after liver transplantation. *Transpl Int* 2013; **26**: 170.
- 29. Werneck M, Afonso RC, Coelho GR, et al. Obese and nonobese recipients had similar need for ventilatory

- support after liver transplantation. *Transplant Proc* 2011; **43**: 165.
- 30. Boin IF, Almeida LV, Udo EY, *et al.* Survival analysis of obese patients undergoing liver transplantation. *Transplant Proc* 2007; **39**: 3225.
- 31. Segev DL, Thompson RE, Locke JE, *et al.* Prolonged waiting times for liver transplantation in obese patients. *Ann Surg* 2008; **248**: 863.
- 32. John PR, Thuluvath PJ. Outcome of liver transplantation in patients with diabetes mellitus: a case-control study. *Hepatology* 2001; **34**: 889.
- Nair S, Eustace J, Thuluvath PJ. Effect of race on outcome of orthotopic liver transplantation: a cohort study. *Lancet* 2002; 359: 287.
- 34. Nair S, Verma S, Thuluvath PJ. Pretransplant renal function predicts survival in patients undergoing orthotopic liver transplantation. *Hepatology* 2002; **35**: 1179.
- Yoo HY, Thuluvath PJ. Short-term postliver transplant survival after the introduction of MELD scores for organ allocation in the United States. *Liver Int* 2005; 25: 536.
- 36. Yoo HY, Thuluvath PJ. The effect of insulin-dependent diabetes mellitus on outcome of liver transplantation. *Transplantation* 2002; **74**: 1007.