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Donor BMI and Post–living Donor Liver Transplantation Outcomes: A Preliminary Report

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Background. Living liver donor obesity has been considered a relative contraindication to living donation given the association with hepatic steatosis and potential for poor donor and recipient outcomes. We investigated the association between donor body mass index (BMI) and donor and recipient posttransplant outcomes. **Methods.** We studied 66 living donors and their recipients who underwent living donor liver transplant at our center between 2013 and 2020. BMI was divided into 3 categories (<25, 25–29.9, and ≥30 kg/m^2). Magnetic resonance imaging–derived proton density fat fraction was used to quantify steatosis. Donor outcomes included length of stay (LOS), emergency department visits within 90 d, hospital readmissions within 90 d, and complication severity. Recipient outcomes included LOS and in-hospital mortality. The Student *t* test was used to compare normally distributed variables, and Kruskal-Wallis tests were used for nonparametric data. **Results.** There was no difference in donor or recipient characteristics based on donor BMI. There was no significant difference in mean magnetic resonance imaging fat percentage among the 3 groups. Additionally, there was no difference in donor LOS ($P = 0.058$), emergency department visits ($P = 0.64$), and hospital readmissions ($P = 0.66$) across BMI category. Donor complications occurred in 30 patients. There was no difference in postdonation complications across BMI category ($P = 0.19$); however, there was a difference in wound complications, with the highest rate being seen in the highest BMI group (0% versus 16% versus 37%; $P = 0.041$). Finally, there was no difference in recipient LOS ($P = 0.83$) and recipient in-hospital mortality ($P = 0.29$) across BMI category. **Conclusions.** Selecting donors with BMI ≥30 kg/m^2 can result in successful living donor liver transplantation; however, they are at risk for perioperative wound complications. Donor counseling and perioperative strategies to mitigate wound-related issues should be used when considering obese living donors.

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Liver transplantation is often the definitive treatment for acute liver failure, end-stage liver disease, and primary hepatic malignancy, and the need for liver transplantations has been increasing worldwide. According to the Scientific Registry of Transplant Recipients Annual Report 2019, there were >13 000 candidates on the liver transplantation waitlist, and the pretransplant mortality rate was 12.3 per 100 waiting list-years in the United States.[1] Higher rates of pretransplant mortality were seen in older patients and those with higher initial Model of End-Stage Liver Disease (MELD) scores. Living donor liver transplantation (LDLT) has emerged as a mechanism to help widen the donor pool and lower recipient mortality on the transplant list, with the first successful LDLT occurring in 1989 in Australia.[2] LDLT has become widespread especially in Asian countries where there is a shortage of deceased organ donations because of social, cultural, and religious reasons, and organ donation rates remain the lowest in the world.[3] In 2005, LDLT comprised >90% of liver transplants in Asia, whereas in 2019, LDLT comprised only 5.3% of liver transplants in the United States.[1,3]

Although the number of LDLT performed in the United States is gradually increasing, the obesity epidemic, especially in the United States, threatens to limit the donor pool. Obesity is the single most significant risk factor for the development of hepatic steatosis, which has been associated with poor recipient outcomes such as ischemic–reperfusion injury, biliary strictures, and primary graft nonfunction.[4–6] Body mass index (BMI) has been used as a surrogate to assess for hepatic steatosis in the evaluation for liver transplantation.[5] Currently, most centers use a threshold of BMI of ≥30 to 35 kg/m² to exclude potential donors.[7] Previous studies have found that recipients who received obese donors (BMI ≥30 kg/m²) had a higher incidence of early allograft dysfunction and acute renal failure but patient and graft survival did not differ significantly.[8,9] Studies looking at donor postoperative outcomes by BMI have similarly found that obese donors have similar postoperative complication rates compared with nonobese donors.[10] Additionally, Hong et al[11] reported no difference in donor complications or hospital stay with laparoscopic hepatectomy in donors BMI ≥30 kg/m² compared with those with BMI <30 kg/m². However, there remain limited studies looking at the impact of donor BMI in LDLT especially when macrovesicular steatosis, defined as >10% steatosis, is excluded. In our study, we investigated the association between donor BMI and donor and recipient posttransplant outcomes in the absence of hepatic steatosis.

MATERIALS AND METHODS

Study Design and Patient Population

The study is a retrospective cohort analysis of all patients, including donors and recipients who underwent adult-to-adult LDLT at the Johns Hopkins Hospital in Baltimore, Maryland, between May 2013 and August 2020. Patients were identified using an electronic patient database, and the study was approved by the Johns Hopkins University School of Medicine Institutional Review Board (IRB00194726). Waiver of informed consent was obtained from the Institutional Review Board, and all research was conducted in accordance with both the Declarations of Helsinki and Istanbul.

The criteria for donors at our institution are as follows: age 18 to 60 y, voluntary directed or nondirected, capacity for informed consent, and BMI <35 kg/m². Donors also undergo extensive blood testing, viral serologies, and imaging studies, as well as medical and psychiatric evaluation. Currently, at our institution, liver biopsies are not routinely performed to determine the presence of steatosis. All donors undergo magnetic resonance imaging (MRI)-derived proton density fat fraction (PDFF) to determine percentage of steatosis. MRI-PDFF is a widely used noninvasive imaging method that quantifies liver fat content.[12] Fat measurements from MRI-PDFF closely correlate with histological evaluation and are reported to be the most accurate imaging method for detection and classification of fatty liver.[13,14] Donors with >10% steatosis independent of BMI are excluded from donation at the time of evaluation but can be reevaluated if the percentage of steatosis decreases. All donors received both mechanical and medical postoperative thromboembolism prophylaxis, which consisted of sequential compression devices and subcutaneous heparin. The prophylaxis is not changed for high-BMI donors. Donor and recipient variables were collected and analyzed retrospectively. Preoperative donor laboratory values were obtained at time of initial evaluation. Donors and recipients were placed in 3 groups according to the Centers for Disease Control and Prevention classification of donor BMI: normal (BMI <25 kg/m²), overweight (25–29.9 kg/m²), and obese (≥30 kg/m²). Donor and recipient outcomes were compared among the groups.

Donor and Recipient Characteristics

The following donor variables were collected for our study: age, sex, BMI, donor relationship with recipient, and MRI-PDFF fat percentage. Preoperative donor laboratory values were also collected. Recipient variables included age, sex, BMI, cause of liver disease, and MELD score at time of liver transplantation. Donor outcomes included length of stay (LOS), emergency visits within 90 d, inpatient admissions within 90 d, and number of complications. The severity of complication was graded using Clavien-Dindo scores and grouped into Clavien-Dindo grade 1 to 2 and ≥3.[15] In this classification scheme, grade 3 is defined as requiring surgical, endoscopic, or radiologic intervention and grade 5 is defined as death of a patient. Recipient outcomes included in-hospital mortality and LOS after surgery.

Statistical Analysis

SPSS 22 statistical package (IBM Corp, Armonk, NY) was used to analyze the data. All data, unless otherwise mentioned, are reported as median (range). The Student *t* test was used to compare normally distributed variables and Kruskal-Wallis for nonparametric data. A P value of <0.05 was considered significant.

RESULTS

Donor and Recipient Preoperative Characteristics

Between May 2013 and August 2020, 66 adult-to-adult LDLTs were performed. Baseline donor characteristics were notable for a median age of 37 y and BMI of 26.2 kg/m² (18.0–33.4; Table 1). The median MRI fat percentage was 2% (0%–8%; Table 1). The most common donor-to-recipient relationship was son (20%), followed by daughter (14%) and friend (14%). Four of the donors were nondirected donors. Baseline recipient characteristics were notable for a median age of 53 y and BMI of 26.4 kg/m² (17.2–38.4; Table 1). The median MELD at time of liver transplantation was 13 (6–26). The most common transplantation indications were for nonalcoholic fatty liver disease cirrhosis, followed by alcoholic cirrhosis and primary sclerosing cholangitis.

Overall, there were 25 donors (39%) in the normal BMI group, 30 (45%) in the overweight group, and 11 (16%) in the obese group (Table 2). There were no significant differences in age, sex, and recipient MELD among the donor groups at time of liver transplantation. There was also no significant difference between donor MRI fat percentage among the 3 groups ($P = 0.75$). Additionally, there was no difference in preoperative alanine aminotransferase, aspartate aminotransferase, alkaline phosphate, albumin, and hemoglobin A1c among the 3 BMI groups (Table 2). There was also no difference in the calculated fibrosis-4 score.

Donor and Recipient Outcomes

There was no difference in donor outcomes among groups when comparing length of postoperative hospital stay, emergency department visits within 90 d, and inpatient admissions within 90 d (Table 3). The overweight BMI category had the greatest number of complications (17 donors, 57% of donors); however, this was not statistically significant ($P = 0.19$). There was also no difference when using Clavien-Dindo to stratify complication severity within 90 d. There was a significant difference in wound complications among the 3 groups (Table 3). The BMI ≥30 kg/m^2 group had the largest percentage of wound complications (27%; n = 3) compared with the BMI 25 to 29.9 kg/m^2 group (17%; n = 5) and BMI <25 kg/m^2 group (0%, n = 0; P = 0.041). All wound complications occurred after discharge at a median time of 11 d. All 3 patients in the BMI ≥30 kg/m^2 group received oral antibiotics, whereas 1 patient in the BMI 25 to 29.9 kg/m^2 group received antibiotics. One patient in the BMI 25 to 29.9 kg/m^2 group underwent scar revision surgery 273 d after discharge, and 1 patient in the BMI ≥30 kg/m^2 group required vacuum-assisted closure. There was no difference in in-hospital mortality or postoperative LOS when looking at recipient outcomes stratified by donor BMI category.

DISCUSSION

Our study demonstrates that select live donors with BMI ≥30 kg/m^2 with no evidence of hepatic steatosis can result in successful LDLTs. Donors categorized as overweight and obese had similar short-term outcomes compared with those with BMI <25 kg/m^2. However, there were more wound complications observed in patients with higher BMIs. Although the sample size was small precluding formal statistical comparison, there appeared to be a higher proportion of patients in the higher BMI group who required antibiotics for their wound complications. Additionally, there was no difference in recipient LOS, in-hospital mortality, and patient survival when stratified by donor BMI.

These findings have been observed by other previous studies as well. Knaak et al[10] in Toronto compared 469 donors with BMI <30 and ≥30 kg/m^2 and found that there were no differences in postoperative complication rates and recipient graft function within the first 30 d. Additionally, they did not find any differences in the rate of wound infections between groups. Interestingly Moss et al[16] did a similar study looking at 68 living donors with BMI <30 kg/m^2 and BMI >30 kg/m^2 and found that those with BMI >30 kg/m^2 had significantly more wound infections (25% versus 4%; P = 0.024), although the overall frequency of complications was equal between the 2 groups. Increased rates of wound infections in this patient population are important to note because this could result in longer hospitalizations and the use of intravenous antibiotics. Studies have shown that BMI >25 kg/m^2 is a risk factor for wound dehiscence, and thus preventative measures against wound infection and preoperative nutrition optimization should be used for donors in this patient population.[17]

Additionally, there was no correlation between MRI-PDFF among the BMI groups seen in our study. The lack of correlation may be a result of selection bias given that our study population consists only of patients with high BMI who met our center's criteria for hepatic steatosis and were deemed appropriate donor candidates. MRI-PDFF can be used to differentiate moderate or severe steatosis from mild or no steatosis with 93% sensitivity and 85% specificity and is commonly used at many transplant centers to quantify liver fat content.[18,19]

Previous studies have shown that there is little to no correlation between BMI and liver fat content.[20,21] Kramer et al[20] was a prospective study of 50 adults (mean BMI, 27.4; SD, 5.4) without known hepatic steatosis who underwent liver imaging with a variety of different imaging modalities, including proton density fat fraction, single- and dual-energy CT, gray-scale ultrasound, and ultrasound shear-wave elastography, with magnetic resonance spectroscopy as the reference. They did not find any significant correlation between BMI and any of the evaluated liver fat imaging modalities (r^2 = 0–0.25). Interestingly, a recent study by Makhija et al[22] looked at 41 adults with nonalcoholic fatty liver disease and obtained MRI-PDFF before and after intervention, which consisted of dietary and lifestyle changes and oral vitamin E for 6 mo. They found poor correlation between MRI-PDFF and BMI before and after intervention (r = 0.1–0.4) but did find good correlation between change in body weight and in mean PDFF after intervention (r = 0.76, P < 0.001). These studies suggest that MRI-PDFF may be a more reliable indicator of hepatic steatosis than BMI alone, given that metabolically healthy individuals who may be obese by BMI can be healthy donors.

A strength of our study is that we categorized our donors according to Centers for Disease Control and Prevention guidelines of BMI into 3 categories instead of 2, which most

TABLE 1.

Baseline characteristics of donor and recipients undergoing living donor liver transplant

Donor characteristics	Donors (N = 66)
Age, median (range), y	37 (20–59)
Sex, n (%)	
Male	34 (52)
Female	32 (48)
BMI, median (range), kg/m^2	26.2 (18.0–33.4)
Donor LOS, median (range), d	7 (4–12)
Total number of ED visits <90 d	4
Total number of admissions <90 d	8
MRI fat, median (range), %	2 (0–8)
Donor relationship, %	
Son	20
Daughter	14
Friend	14
Wife	11
Brother	6
Son-in-law	6
Nondirected	6
Other[a]	24
Recipient characteristics	Recipients (N = 66)
Age, median (range), y	53 (18–73)
Sex, n (%)	
Male	37 (56)
Female	29 (44)
BMI, median (range), kg/m^2	26.4 (17.2–38.4)
Recipient LOS, median (range), d	15 (5–134)
MELD at time of liver transplantation, median (range)	13 (6–26)
Transplant indication, %	
Nonalcoholic steatohepatitis	29
Alcohol	18
Primary sclerosing cholangitis	18
Hepatitis C	14
Hepatocellular carcinoma	9
Hepatitis B	2
Other	10

[a]"Other" includes the following categories: sister, nephew, husband, uncle, mother, daughter-in-law, niece, cousin, cousin-in-law, and sister-in-law.
BMI, body mass index; ED, emergency department; LOS, length of stay; MELD, Model of End-Stage Liver Disease; MRI, magnetic resonance imaging.

TABLE 2.

Comparison of baseline characteristics of donors and recipients by donor BMI

Variable	Donor BMI (<25 kg/m^2)	Donor BMI (25–29.9 kg/m^2)	Donor BMI (≥30 kg/m^2)	*P*
Donors overall, n (%)	25 (39)	30 (45)	11 (16)	
Donor age, y	30	38	40	0.37
Donor sex				0.21
Male, n (%)	10 (40)	19 (64)	5 (45)	
Female, n (%)	15 (60)	11 (36)	6 (55)	
Donor MRI fat, %	1.0	1.5	3.0	0.75
Donor preoperative values, mean (SD)				
AST, U/L	24 (25.3)	21 (8.1)	19 (4.6)	0.66
ALT, U/L	18 (10.4)	25 (11.8)	21 (9.4)	0.08
ALP, U/L	62 (17.6)	70 (21)	69 (17.8)	0.30
Albumin, g/dL	4.7 (0.3)	4.5 (0.8)	4.6 (0.3)	0.28
Hemoglobin A1c, %	5.1 (0.4)	5.2 (0.4)	5.3 (0.3)	0.19
FIB-4	0.80 (0.39)	0.75 (0.39)	0.66 (0.33)	0.59
Recipients overall, n (%)	25 (39%)	30 (45%)	11 (16%)	
Recipient MELD at time of liver transplantation	13	12.5	12	0.76

ALP, alkaline phosphatase; ALT, alanine aminotransferase; AST, aspartate aminotransferase; BMI, body mass index; FIB-4, fibrosis-4; MELD, Model of End-Stage Liver Disease; MRI, magnetic resonance imaging.

TABLE 3.

Comparison of posttransplant outcomes after living donor liver transplant in donors and recipients by donor BMI

Variable	Donor BMI (<25 kg/m^2)	Donor BMI (25–29.9 kg/m^2)	Donor BMI (≥30 kg/m^2)	*P*
Donors overall, n (%)	25 (39)	30 (45)	11 (16)	
Donor LOS, median (range), d	7 (5–12)	7 (4–11)	6 (4–8)	0.058
Donor ED visits <90 d, n (%)	2 (8)	2 (7)	0 (0)	0.64
Donor readmissions <90 d, n (%)	2 (8)	4 (13)	2 (18)	0.66
Complications, n (%)	8 (32)	17 (57)	5 (45)	0.19
Complications by Clavien-Dindo class, n (%)				
1–2	8 (32)	15 (50)	5 (45)	0.40
>3	0 (0)	2 (7)	0 (0)	0.29
Wound complications, n (%)	0 (0)	5 (17)	3 (27)	0.041
Recipients overall, n (%)	25 (39)	30 (45)	11 (16)	
In-hospital mortality, n (%)	0 (0)	2 (7)	0 (0)	0.29
LOS, median (range), d	15 (6–100)	15 (6–134)	14 (5–36)	0.83

BMI, body mass index; ED, emergency department; LOS, length of stay.

previous studies have not done. This allows us to better understand the difference between overweight and obese patients, particularly as the prevalence of patients in these BMI categories continues to rise. Additionally, donor candidates in our study had a wide range of BMI, with 16% of candidates with BMI ≥30 kg/m^2, similar to the proportion of candidates nationwide with BMI ≥30 kg/m^2 (20.5%).[1]

Limitations of this study include its retrospective, single-center design, which inherently leaves open the possibility of confounding factors, despite there being no significant differences observed between BMI groups. Only candidates who are approved by our institution's liver transplant team can proceed with transplantations, and thus inherent selection bias may exist favoring candidates who will tolerate surgery well. We attempted to account for this by only selecting adult-to-adult transplantations within a specified time range. Furthermore, our study is only focused on short-term outcomes. Future investigation is needed to evaluate long-term outcomes in this patient population in both donors and recipients.

In conclusion, select donors with BMI ≥30 kg/m^2 with no evidence of hepatic steatosis by MRI-PDFF can result in successful LDLT; however, they are at risk for perioperative wound complications. Donor counseling and perioperative strategies to mitigate wound-related issues should be used when considering obese living donors. Additionally, there should be consideration to increase the BMI threshold at transplant centers for these donors with no steatosis by MRI-PDFF.

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