

ORIGINAL ARTICLE

Morbid obesity in liver transplant recipients adversely affects longterm graft and patient survival in a single-institution analysis

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Abstract

Objective: The effects of obesity in liver transplantation remain controversial. Earlier institutional data demonstrated no significant difference in postoperative complications or 1-year mortality. This study was conducted to test the hypothesis that obesity alone has minimal effect on longterm graft and overall survival.

Methods: A retrospective, single-institution analysis of outcomes in patients submitted to primary adult orthotopic liver transplantation was conducted using data for the period from 1 January 2002 to 31 December 2012. Recipients were divided into six groups by pre-transplant body mass index (BMI), comprising those with BMIs of <18.0 kg/m², 18.0–24.9 kg/m², 25.0–29.9 kg/m², 30.0–35.0 kg/m², 35.1–40.0 kg/m² and >40 kg/m², respectively. Pre- and post-transplant parameters were compared. A *P*-value of <0.05 was considered to indicate statistical significance. Independent predictors of patient and graft survival were determined using multivariate analysis.

Results: A total of 785 patients met the study inclusion criteria. A BMI of >35 kg/m² was associated with non-alcoholic steatohepatitis (NASH) cirrhosis (*P* < 0.0001), higher Model for End-stage Liver Disease (MELD) score, and longer wait times for transplant (*P* = 0.002). There were no differences in operative time, intensive care unit or hospital length of stay, or perioperative complications. Graft and patient survival at intervals up to 3 years were similar between groups. Compared with non-obese recipients, recipients with a BMI of >40 kg/m² showed significantly reduced 5-year graft (49.0% versus 75.8%; *P* < 0.02) and patient (51.3% versus 78.8%; *P* < 0.01) survival.

Conclusions: Obesity increasingly impacts outcomes in liver transplantation. Although the present data are limited by the fact that they were sourced from a single institution, they suggest that morbid obesity adversely affects longterm outcomes despite providing similar short-term results. Further analysis is indicated to identify risk factors for poor outcomes in morbidly obese patients.

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Introduction

The national obesity epidemic continues to progress at an alarming rate, affecting 78 million adult Americans. The prevalence of obesity amongst potential liver transplant recipients is also rising;

more than half are overweight or obese.¹ The full impact of this chronic health condition in the context of liver transplantation is yet to be determined. Non-alcoholic steatohepatitis (NASH), the hepatic manifestation of obesity and metabolic syndrome, is now the fourth leading indication for orthotopic liver transplantation (OLT) in the USA and accounted for 7.4% of OLTs performed in 2010.² Non-alcoholic steatohepatitis is predicted to surpass hepatitis C as the leading indication for OLT in the next 10 years.^{3,4} An

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estimated 25 million Americans will develop NASH by 2025 and as many as five million will suffer from chronic liver failure.^{2,5} These numbers may further stress a system in which demand for deceased donor livers already exceeds supply.

Previous studies evaluating the outcomes of patients transplanted for NASH cirrhosis have shown conflicting results in terms of the effects of pre-transplant NASH on post-transplant morbidity and mortality.^{2,6–8} Some suggest that recipients with NASH have higher perioperative rates of cardiovascular events, including myocardial infarction, acute heart failure, arrhythmia and cerebrovascular accident.⁸ Additionally, pre-transplant NASH may increase the risk for recurrent non-alcoholic fatty liver disease (NAFLD) and allograft cirrhosis post-transplantation.⁹

The severely and morbidly obese [those with a body mass index (BMI) of >35 kg/m²] are significantly more likely to undergo liver transplantation for NASH cirrhosis than subjects of normal weight.^{3,10} The effect of BMI on longterm outcomes in liver transplant recipients, as distinct from the effects of NASH, is not well understood. Historically, obesity was considered a relative contraindication to transplantation, largely because of concerns about technical feasibility and worse outcomes. In non-transplant transabdominal surgery, obesity has been associated with increases in blood loss, resource utilization, and perioperative morbidity and mortality.^{11,12} In liver transplantation, severe obesity (BMI >35 kg/m²) has also been associated with increased rates of perioperative complications, such as wound infection and bleeding.^{10,13,14} Despite initial studies evaluating its effects on short-term outcomes and complication rates, the impacts of BMI on longterm overall and graft survival are indeterminate. This paper reports the present authors' institutional experience with liver transplantation in the obese population.

Materials and methods

A retrospective study of outcomes in all patients submitted to primary OLT at Washington University in St Louis between 1 January 2002 and 31 December 2012 was conducted. Recipients aged <18 years were excluded. Liver transplant recipients were divided into six groups based on their pre-transplant BMI in accordance with the World Health Organization classification of obesity: Group 1 (BMI: <18.0 kg/m²); Group 2 (BMI: 18.0–24.9 kg/m²); Group 3 (BMI: 25.0–29.9 kg/m²); Group 4 (BMI: 30.0–35.0 kg/m²); Group 5 (BMI: 35.1–40.0 kg/m²), and Group 6 (BMI: >40.0 kg/m²). Data for BMI were not adjusted for ascites because the volume of ascites drained at the time of transplant did not differ significantly between groups. The mean $\pm$ standard deviation (SD) duration of follow-up was 4.5 ± 3.0 years. Pre- and post-transplant parameters were compared among the BMI groups (Table 1). Pre-transplant recipient variables included patient age, race, gender, medical comorbidities [hypertension, coronary artery disease (CAD), non-CAD cardiac disease, diabetes mellitus, renal insufficiency], aetiology of liver disease, presence of hepatocellular carcinoma (HCC), haemodialysis at time

of transplant, Model for End-stage Liver Disease (MELD) score (determined by laboratory values), and time on waiting list. Primary outcome measures were graft and overall patient survival at 90 days, 1 year, 3 years, 5 years and 7 years. Secondary outcome measures included operative time, cold and warm ischaemic times, operative transfusion requirement of ≥ 10 units of packed red blood cells (uPRBC), intensive care unit (ICU) length of stay (LoS), hospital LoS, re-exploration for bleeding, infection, disease recurrence (hepatitis C, NASH and HCC), allograft rejection, aetiology of graft failure, retransplantation, and cause of death.

Statistical analysis

Categorical variables were compared using the chi-squared test and continuous variables were compared using Student's *t*-test; a *P*-value of <0.05 was considered to indicate statistical significance. Overall patient and graft survival curves were determined using Kaplan–Meier methods and compared using the log-rank test. Independent predictors of patient and graft survival were determined by multivariate Cox regression analysis.

This study was approved by the Washington University School of Medicine Institutional Review Board.

Results

Study population characteristics

A total of 785 patients met the study inclusion criteria (Table 1). Numbers of recipients in each group were: Group 1 (BMI: <18.0 kg/m²): *n* = 9 (1.2% of study population); Group 2 (BMI: 18.0–24.9 kg/m²): *n* = 210 (26.8%); Group 3 (BMI: 25.0–29.9 kg/m²): *n* = 294 (37.5%); Group 4 (BMI: 30.0–35.0 kg/m²): *n* = 169 (21.5%); Group 5 (BMI: 35.1–40.0 kg/m²): *n* = 77 (9.8%), and Group 6 (BMI: >40.0 kg/m²): *n* = 26 (3.3%). There were no significant differences between groups with regard to age (mean ages: 47.8–55.7 years; *P* = NS) or race. Patients with a BMI of <18 kg/m² or >40 kg/m² were more likely to be female (56.6% and 63.0%, respectively) compared with all other groups (*P* < 0.001). Analysis of comorbid medical conditions demonstrated a significantly increased rate of hypertension in patients with a BMI of >35 kg/m² (*P* = 0.001). There were no differences in prevalences of diabetes mellitus, CAD, other (non-CAD) cardiovascular disease, renal insufficiency or dialysis-dependent renal failure.

Liver disease and waiting time

The aetiology of liver disease varied among the groups. Chronic hepatitis C infection was the most common cause of cirrhosis in patients with a BMI of >18 kg/m², whereas a BMI of <18 kg/m² was most commonly associated with alcohol cirrhosis. Non-alcoholic steatohepatitis represented the second leading cause of liver disease in patients with a BMI of >35 kg/m². Recipients (22.8%) with a BMI of >35 kg/m² were significantly more likely to have NASH as the primary aetiology compared with patients in all other groups (*P* < 0.0001). Only two patients (0.9%) with a BMI of <25 kg/m² had NASH. All groups with BMIs of >18 kg/m² had similar rates of HCC (26.9–38.6%; *P* = NS). Average MELD scores

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