



Published in final edited form as:

Liver Transpl. 2015 October ; 21(10): 1238–1240. doi:10.1002/lt.24227.

Impact of Body Mass Index on Post-Transplant Outcomes Re-examined

Khurram Bari, MD¹ and Pratima Sharma, MD, MS²

¹Division of Gastroenterology, University of Cincinnati, Cincinnati, Ohio

²Division of Gastroenterology, University of Michigan, Ann Arbor, Michigan

Keywords

Liver Transplantation; Body mass index; Post-transplant outcomes

According to the National Health and Nutritional Examination survey (NHANES) from 2011–12, the prevalence of obesity defined as BMI>30 among 20 year or older individuals is 35%¹. This is reflected among liver transplant (LT) recipients resulting in a doubling of the prevalence of obesity from 16.8% (Class I BMI 30–34=9.4%; Class II BMI 35–39 =5.3% and Class III BMI 40=2.1%) in 1987–96 to 33% (Class I BMI 30–34=21%; Class II BMI 35–39 =9% and Class III BMI 40=3%) in 2002–2011.^{2, 3}

Obesity as a predictor of post-transplant outcomes has been addressed using national data.^{2, 4, 5} In one of the older study that examined the national data from the Scientific Registry of Transplant Recipients from 1987–96, the adjusted risk of post-transplant death at 2 year was 52% higher among obese compared to non-obese LT recipients.² Another study using the data from the SRTR found that although severely obese (BMI 35–39) and morbidly obese recipients (BMI 40) derive survival benefit from LT⁵, their likelihoods of being turned down for an organ were 10% and 16% higher, and rates of liver transplant were 11% and 29% lower among severely obese and morbidly obese LT recipients, respectively.⁶ These results suggest that current practices reflect an inherent reluctance to transplant morbidly obese LT candidates. In the most recent American Association for the Study of Liver Disease guidelines on selection of LT candidates, class III obesity is still considered a relative contraindication for LT despite demonstrable survival benefit from LT in this subgroup of patients.^{3, 5, 7}

Malnutrition, sarcopenia and frailty are common but under recognized complications of decompensated cirrhosis associated with poor waitlist and post-transplant outcomes. Low BMI is one of the manifestations of malnutrition and associated with poor outcomes in general. Sarcopenia, as defined by decreased dorsal muscle group area at thoracic spine level (T11-T12) or psoas muscle area measured by analytic morphomics, is an important predictor of post-transplant mortality.^{8, 9} Additionally, sarcopenia among LT recipients is also

associated with increased rates of infection and significant higher hospital stay in an adjusted analysis of 248 LT recipients¹⁰. Englesbe et al., in a retrospective analysis of 509 LT recipients, reported one year adjusted post-transplant survival of 49.7% for the LT recipients with lowest quartile of psoas area compared to 87.0% for those with the highest quartile of psoas area.⁹

Bambha et al., in this issue of *Liver Transplantation* carefully examined the impact of BMI on short-term post-transplant outcomes using the national data of adult liver transplant recipients who received LT between March 2002 and September 2011 (N=45551).³ The main results of their study reconfirmed that obesity did not affect short-term post-transplant outcomes. However, underweight LT recipients with BMI<18.5 had 43% and 28% increased risk of 1-year post-transplant death and graft failure, respectively, after adjusting for various recipients and donor factors. These findings validated results from the previous studies.^{4, 5} Pelletier et al. in their elegant analyses of the national data from September 2001 to December 2008 found no difference in post-transplant mortality risk across all BMIs.⁵ However, the relative risk of post-transplant mortality was two folds higher within 7 days of LT for those with BMI<20 compared to those with normal BMI.⁵ Dick et al. further examined the effect of BMI spectrum on post-transplant mortality across three eras (1987–1992; 1993-Feb 2002; March 2002–2007).⁵ Their study showed higher risk of post-transplant mortality across three eras among patients with extremes of BMI (<18.5 and 40).⁵

One of the novel findings in Bambha et al.'s study was the interaction between low BMI and low MELD score. Their study showed that the effect of low BMI (<18.5 kg/m²) on post-transplant mortality was accentuated at low MELD scores (MELD <20)³. A similar interaction was seen at the threshold MELD score of 26 (75th percentile). It would be important to know if the interaction between low BMI and MELD score was significant for the lowest quartile of MELD score (<13, 25th percentile). The authors failed to show any significant associations between patient, donor and transplant factors and 3-month and 1-year post-transplant mortality among low BMI-low MELD patients. Low BMI-low MELD patients represented only 1% (N=435) of total cohort. The sample size may be too small to show any association. Although the authors adjusted for most of the pertinent recipients and donor covariates, the effect of serum sodium as well as year of transplant was not tested in the multivariable model. Both of these covariates are important because of their associations with post-LT outcomes. 'Share 15' was implemented during the span of this cohort. Era effect may have some influence on low MELD-low BMI interaction. Donor risk index (DRI) was independently associated with low BMI-low MELD LT recipients.³ Data suggested that high DRI organs were more often transplanted into lower-MELD recipients and vice versa. Compared to waiting for a lower-DRI organ, the lowest-MELD category recipients (MELD 6–8) who received high-DRI organs experienced significantly higher post-transplant mortality.¹¹ There might be an inherent selection bias (accepting high DRI allograft for low BMI) resulting in the significant interaction between low MELD and low BMI. This may be one of the plausible explanations for observed high post-transplant mortality among low BMI-low MELD patients.³

Frailty is another biologic syndrome of decreased reserve and resistance to stressors, resulting from cumulative declines across multiple physiologic systems, and causing vulnerability to adverse outcomes. Clinical assessment of frailty is performed using performance and cognitive criteria which are well established in geriatrics literature. Frailty is associated with increased waitlist as well as post-transplant mortality.^{12, 13} Bambha et al., did not find any association between functional status and the short term post-transplant outcomes in low BMI-low MELD patients.³

The risk factors associated with high BMI including diabetes mellitus, coronary artery disease, metabolic syndrome, obstructive sleep apnea and their effect on post-transplant outcomes are well established;¹⁴ risk factors associated with low BMI affecting post-transplant outcomes require further investigation to better understand if low BMI, sarcopenia, malnutrition and frailty are different entities or if significant overlap exists between them and how the interaction(s) between them affect waitlist and post-transplant outcomes. Our group had shown the feasibility of 10-week prehabilitation program for waitlisted patients focusing on nutrition and supervised exercise session in improving in physical activity and dietary habits.¹⁵

Finally, malnutrition, sarcopenia, and frailty are somewhat modifiable and adversely affect outcomes including quality of life. Future studies focusing on improving malnutrition, sarcopenia and frailty before transplant using targeted prehabilitation intervention(s) may improve short-term and long-term post-transplant outcomes.

Acknowledgement

Dr. Sharma is supported by National Institutes of Health (NIH) grant DK-088946.

Abbreviations

BMI	Body Mass Index
DRI	Donor Risk Index
LT	Liver Transplantation
MELD	Model for End-stage Liver Disease
NHANES	National Health and Nutritional Examination survey
SRTR	Scientific Registry of Transplant Recipients

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