LIVER TRANSPLANTATION 21:1238–1240, 2015

EDITORIAL

Impact of Body Mass Index on Posttransplant Outcomes Reexamined

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Received July 28, 2015; accepted August 5, 2015.

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According to the National Health and Nutritional Examination survey from 2009 to 2010, the prevalence of obesity, defined as body mass index (BMI) > 30 kg/m^2 among ≥20 years old, is 35%.[1] This is reflected among liver transplantation (LT) recipients resulting in a doubling of the prevalence of obesity from 16.8% (class I, BMI 30-34 kg/m^2 = 9.4%; class II, BMI 35-39 kg/m^2 = 5.3%; and class III, BMI ≥ 40 kg/m^2 = 2.1%) in 1987 to 1996 to 33% (class I, BMI 30-34 kg/m^2 = 21%; class II, BMI 35-39 kg/m^2 = 9%; and class III, BMI ≥ 40 kg/m^2 = 3%) in 2002 to 2011.[2,3]

Obesity as a predictor of posttransplant outcomes has been addressed using national data.[2,4,5] In one of the older studies that examined the national data from the Scientific Registry of Transplant Recipients (SRTR) from 1987 to 1996, the adjusted risk of posttransplant death at 2 years was 52% higher among obese compared to nonobese LT recipients.[2] Another study using the data from the SRTR found that although severely obese (BMI, 35-39 kg/m^2) and morbidly obese recipients (BMI ≥ 40 kg/m^2) derive survival benefit from LT,[5] their likelihoods of being turned down for an organ were 10% and 16% higher, and rates of LT 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. 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 the thoracic spine level (T11-T12) or psoas muscle area measured by analytic morphomics, is an important predictor of posttransplant mortality.[8,9] Additionally, sarcopenia among LT recipients is also associated with increased rates of infection and significantly higher hospital length of stay in an adjusted analysis of 248 LT recipients.[10] Englesbe et al.,[9] in a retrospective analysis of 509 LT recipients, reported 1-year adjusted posttransplant survival of 49.7% for the LT recipients with the lowest quartile of psoas muscle area compared to 87.0% for those with the highest quartile of psoas muscle area.

In this issue of *Liver Transplantation*, Bambha et al.[3] carefully examined the impact of BMI on short-term posttransplant outcomes using the national data of adult LT recipients who received LT between March 2002 and September 2011 (n = 45,551).[3] The main results of their study reconfirmed that obesity did not affect short-term posttransplant outcomes. However, underweight LT recipients with BMI < 18.5 kg/m^2 had 43% and 28% increased risk of 1-year posttransplant death and graft failure, respectively, after adjusting for various recipient and donor factors. These findings

Abbreviations: BMI, body mass index; DRI, donor risk index; LT, liver transplantation; MELD, Model for End-Stage Liver Disease; SRTR, Scientific Registry of Transplant Recipients.

Pratima Sharma is supported by National Institutes of Health grant DK-088946.

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DOI 10.1002/lt.24227
View this article online at wileyonlinelibrary.com.
LIVER TRANSPLANTATION.DOI 10.1002/lt. *Published on behalf of the American Association for the Study of Liver Diseases*

validated results from previous studies.[4,5] Pelletier et al.[5] in their elegant analyses of national data from September 2001 to December 2008 found no difference in posttransplant mortality risk across all BMIs. However, the relative risk of posttransplant mortality was 2-fold higher within 7 days of LT for those with BMI $< 20\,kg/m^2$ compared to those with normal BMI.[5] Dick et al. further examined the effect of BMI spectrum on posttransplant mortality across 3 eras (1987 to 1992; February 1993 to 2002; March 2002 to 2007).[4] Their study showed higher risk of posttransplant mortality across 3 eras among patients with extremes of BMI (<18.5 and $\geq 40\,kg/m^2$).[4]

One of the novel findings in the study by Bambha et al.[3] was the interaction between low BMI and low Model for End-Stage Liver Disease (MELD) score. Their study showed that the effect of low BMI ($<18.5\,kg/m^2$) on posttransplant mortality was accentuated at low MELD scores (MELD < 20). 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 posttransplant mortality among low BMI–low MELD patients. Low BMI–low MELD patients represented only 1% ($n = 435$) of the 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 were not tested in the multivariate 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 posttransplant mortality.[11] There might be an inherent selection bias (accepting a high-DRI organ for low-BMI recipient) resulting in the significant interaction between low MELD and low BMI. This may be one of the plausible explanations for observed high posttransplant mortality among low BMI–low MELD patients in Bambha et al. study.

Frailty is another biological 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 wait-list mortality as well as posttransplant mortality.[12,13] Bambha et al.[3] did not find any association between functional status and the short-term posttransplant outcomes in low BMI–low MELD patients.

The risk factors associated with high BMI, including diabetes mellitus, coronary artery disease, metabolic syndrome, obstructive sleep apnea, and their effect on posttransplant outcomes are well established;[14] risk factors associated with low BMI affecting posttransplant 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 wait-list and posttransplant outcomes. Our group has shown the feasibility of a 10-week prehabilitation program for wait-listed patients focusing on nutrition and supervised exercise sessions in making improvements 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 posttransplant outcomes.

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