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EDITORIAL COMMENT

Is There an Obesity Paradox in Transcatheter Aortic Valve Replacement?*

Carl J. Lavie, MD,[a] Abhishek Sharma, MD,[b] Jose Tafur Soto, MD[a]

Obesity has clearly reached near epidemic levels in the United States and much of the Westernized world.[1,2] In fact, recent statistics suggest that 75% of the U.S. population are now either overweight or obese, 42% meet the current body mass index (BMI) criteria (BMI ≥30 kg/m^2) for obesity, and even more concerning, 9% of U.S. adults now meet criteria for severe, class III, or morbid obesity (BMI ≥40 kg/m^2).[1] Although obesity is much less prevalent in Asia than in Europe and North America,[3] this has greatly increased in recent decades in much of Asia, affecting cardiovascular disease (CVD) risk factors and CVD prevalence. Obesity adversely affects CVD by worsening almost all the CVD risk factors, including increasing levels of arterial pressure; increasing plasma glucose levels, thus leading to metabolic syndrome and diabetes mellitus; worsening lipids, especially triglycerides; and increasing systemic inflammation. Not surprisingly, almost all CVD is increased with obesity, including hypertension, coronary heart disease, heart failure, and atrial fibrillation. However, in all of these conditions, we and others have described an "obesity paradox," where overweight and obese patients with these established CVDs have a better short- and, at least, medium-term prognosis and survival than do leaner patients with these same diseases,[2] which has extended to valvular heart disease (VHD), at least transcatheter aortic valve replacement (TAVR),[4] and transcatheter mitral valve procedures.[5] Part of this obesity paradox may be caused by the known adverse effects that underweight, frailty, and cachexia have on prognosis in many diseases, including CVD and VHD.[6]

Additionally, TAVR has emerged as a very effective alternative to surgical aortic valve replacement for many patients with severe aortic stenosis (AS), initially for high- and intermediate-risk AS patients and now evolving into lower-risk AS patients.[4,7] The data on the impact of body composition on outcomes in patients undergoing TAVR are more limited, particularly from Asia.[7] Visceral adipose tissue seems to be a better predictor of complications compared with subcutaneous adipose tissue.[8] Clearly, Asian patients undergoing TAVR have much lower BMIs than do patients in Western Europe and North America, and the true impact of lower BMIs on TAVR outcomes remains uncertain, especially in an Eastern Asian population.

In this issue of *JACC: Asia*, Tezuka et al[7] analyzed a data set of 1,693 TAVRs from Japan and analyzed 30-day and midterm (average follow-up close to 2 years) all-cause, CVD, and non-CVD mortality in the various BMI groups, including underweight (BMI <18.5 kg/m^2), "normal" BMI (18.5-25 kg/m^2), and overweight (BMI ≥25 kg/m^2). Both 30-day and midterm survival were significantly lower in the underweight TAVR patients compared with the other 2 groups. In multivariate analysis, the underweight were associated with non-CVD compared with CVD mortality. Although the authors referred to this as an "obesity paradox," these data from East Asia are more consistent with an expected poor outcome in underweight patients.

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From the [a]John Ochsner Heart and Vascular Institute, Department of Cardiovascular Diseases, Ochsner Clinical School-The University of Queensland School of Medicine, New Orleans, Louisiana, USA; and the [b]Structural Heart Disease Program, Rutgers New Jersey Medical School, Newark, New Jersey, USA.

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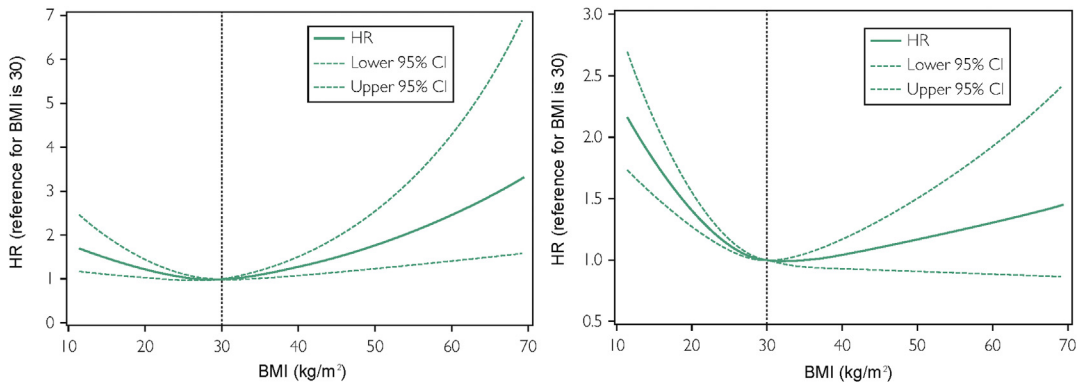
FIGURE 1 Obesity Paradox in TAVR



Association between body mass index (BMI) and 30-day **(left)** and 1-year **(right)** mortality in 31,929 U.S. transcatheter aortic valve replacement (TAVR) patients (using restricted cubic spines with 3 knots). The nadir mortality was at 30 kg/m^2. The data are from Sharma et al.[4]

In this study from Tezuka et al,[7] underweight accounted for 14.3% of their 1,693 patients (n = 242), whereas a study from Germany (5.7% of 16,865 patients; n = 956)[9] and our study from the United States (2.5% of 31,929 patients; n = 806)[4] had much larger numbers of underweight patients, with very high 30-day (7.6% and 11%, respectively) and 1-year mortality (27% and 35%, respectively). The study by Tezuka et al[7] showed better survival in the normal and overweight groups compared with the underweight, but the average BMI was only 27.7 kg/m^2 in their overweight patients; this may meet obesity criteria in Asia, but these are much lower BMIs than in the TAVR obese patients in Europe and North America.[3,8] In fact, our data from the United States showed much more of an obesity paradox, where overweight and class I (BMI ≥30-34.9 kg/m^2) and II (BMI 35-39.9 kg/m^2) obese patients had lower mortality at 1 year (−12%, −20%, and −16%, respectively), compared with those patients with normal BMI, clearly suggesting an obesity paradox in TAVR.[4] In fact, the nadir for mortality in our U.S. TAVR cohort was at a BMI of approximately 30 kg/m^2 (**Figure 1**),[4] which is well above the average BMI of 27.7 kg/m^2 in the overweight Asian TAVR patients. However, more in line with the Asian data from Tezuka et al,[7] the underweight in our U.S. cohort had the highest 30-day and 1-year mortality, increased by 35% and 41%, respectively, compared with the normal-weight patients, supporting the very high-risk of being underweight when undergoing TAVR,[4] similar to the high risk noted with other CVD.[2]

Clearly, underweight patients have a high comorbidity burden, having the highest prevalence of peripheral arterial disease, severe lung disease, and current and recent smoking, as well as having higher Society of Thoracic Surgeons and EuroScore, as seen in Tezuka et al[7] and other studies of TAVR[4,9]; in addition, although not statistically significant, there is a numeric higher incidence of cancer in underweight patients. Certainly, when clinicians are treating underweight patients, they must be aware that these patients tend to be sicker than their usual heavier patients, and, therefore, cautious attention to their underlying conditions is of crucial importance to avoid poor outcomes.

Also, vascular access tends to be more challenging in the underweight patients, who not only have more peripheral arterial disease, but who also have proportionally smaller vessels, making it more challenging to deliver the equipment necessary for successful TAVR, which is the same equipment used in much larger patients.[4,7] This fact is evident in the current paper, demonstrating the higher rates of nontransfemoral TAVR used in the underweight patients, which are generally associated with worse outcomes.[6]

Additionally, frailty and cachexia have been proven to be excellent predictors of outcomes in many non-CVD and CVD disorders,[6] including VHD and TAVR.[10] In our practices, nutritional status and objective strength measurements, like handgrip strength, are part of our usual frailty assessment, because muscular strength plays a very major role in the prognosis of most CVDs,[11] including VHD and

TAVR.[12] Clearly, underweight patients are at a significant disadvantage regarding these last 2 factors. Physical therapy and nutritional improvements before TAVR potentially could improve outcomes.[13] Nevertheless, these interventions can also delay the final treatment of TAVR that is often very much needed in these patients.

Finally, this study is based on a single measurement of BMI, which does not separate muscle and fat, and there may need to be different criteria for underweight in Asia compared with Europe and North America, although this study confirms the fact that BMI <18.5 kg/m^2 is associated with a poor prognosis in TAVR worldwide. Tezuka et al[7] should be applauded for their efforts in this important area of CVD investigation.

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ADDRESS FOR CORRESPONDENCE: Dr Carl J. Lavie, Ochsner Medical Center, 1514 Jefferson Highway, New Orleans, Louisiana 70121, USA. E-mail: clavie@ochsner.org.

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