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EDITORIAL COMMENT

Body Composition and Advanced Heart Failure Therapy

Weighing the Options and Outcomes*

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I have clearly recorded this: for one can learn good lessons also from what has been tried but clearly has not succeeded when it is clear why it has not succeeded.

—Hippocrates (1)

Obesity has reached epidemic proportions in the United States and most of the Western world, with a prevalence of 38% in U.S. adults from 2013 to 2014 (based on body mass index [BMI] ≥30 kg/m^2) with class III obesity (BMI ≥40 kg/m^2) approaching 8% (2). Considering the effect of obesity on worsening hypertension and coronary heart disease, 2 strong contributors to heart failure (HF), as well as its adverse effects on systolic and predominantly diastolic ventricular dysfunction, HF prevalence is markedly increased in the presence of obesity (3-5). Nevertheless, we and others have repeatedly pointed out the "obesity paradox" in HF outcomes, with many studies and meta-analyses suggesting that overweight and even obese HF patients have better short- and medium-term prognoses than do underweight HF patients but also HF patients with "normal" BMI (18.5 to 24.9 kg/m^2) (3-5). However, patients with severe class III obesity generally have a poor prognosis (4,5).

In recent decades, significant advances have improved outcomes in advanced HF by the judicious application of durable left ventricular assist devices (LVADs) coupled with heart transplantation (HT) in eligible patients. Obese patients undergoing heart surgery have poor wound healing, increased risk of infection, pulmonary complications, and lower extremity venous thrombosis (5). Obese patients with HT have earlier high-grade acute rejection and higher 5-year mortality compared with normal weight or overweight HT recipients (5-7). Whether obesity is a contraindication for HT remains somewhat controversial. However, it seems that pre-HT obesity or preoperative weight >140% of ideal body weight are associated with poor outcomes after HT (5,7). Therefore, the International Society for Heart and Lung Transplantation (ISHLT) HT candidacy guidelines support weight reduction to achieve optimal post-HT outcomes (7). Severe class III obesity is a contraindication for HT, and for most candidates, every effort must be made to achieve BMI ≤30 kg/m^2 or preoperative ideal body weight <140% before HT, with current guidelines suggesting BMI at least ≤35 kg/m^2 before listing for HT (7).

However, obesity has not universally been considered a contraindication for durable LVAD implantation (5). Nevertheless, adverse effects of obesity, such as increased driveline infection rates, have created concern, and generally clinical trials have excluded class III obesity, limiting data in this area. In fact, older pulsatile LVADs that used to reside in the abdominal cavity weighed substantially more than today's smaller and more durable devices and consistently resulted in considerable weight loss (sometimes as much as 30 pounds) due to reduction

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in appetite and a sensation of fullness. The newer continuous-flow (CF) devices, on the other hand, have shown no ancillary weight loss or mostly demonstrate weight gain due to increased appetite and inability to fully engage in effective exercise training (ET) (8). Thus, the presence of significant obesity may dampen enthusiasm for long-term LVAD support as a bridge to HT, knowing that post-HT outcomes are less than ideal.

In this issue of *JACC: Heart Failure,* Clerkin et al. (9) used the United Network for Organ Sharing (UNOS) database and analyzed 3,856 patients who underwent LVAD implantation as a bridge to HT during a 10-year period through June 2014. They demonstrated that the risk of death or delisting was not different between BMI groups. However, the risk of device-related complications resulting in UNOS listing urgency upgrade was increased by nearly 50% in patients with class II (BMI ≥35 kg/m²) or greater obesity, driven by increased infections and thromboembolism. Not surprisingly, obese patients also had worse post-HT outcomes. Unlike some earlier data, weight loss to decrease BMI was uncommonly achieved by those with class I obesity or greater (approximately 10% to 15%).

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Obviously, the group examined in this study is a very specific cohort that was confounded by selection bias because only those rigorously evaluated and then listed as HT candidates were included. Interestingly, there was a 10% nonconformity with ISHLT listing guidelines, where it is recommended that patients with BMI ≥35 kg/m² should not ideally undergo HT (7). The complications of infection and thromboembolism with the LVAD, as well as device malfunction, are well known in the very obese and are serious deterrents to placement of these devices (5). However, this also leads to a "perverse benefit" in that this results in an increased chance for an upgrade in listing to the high urgency category because of device complications. Certainly, these findings imply that the device should not have been placed in the first place and essentially support the caution expressed in the ISHLT guidelines that very obese patients do not do well after HT (7).

Although obesity poses problems for the use of LVAD and HT, this difficulty also may provide a potential opportunity to improve prognosis of the very obese with advanced HF. We need better directed efforts at assessing the phenotype of true fatness (and differentiating fat and muscle), pursuing more aggressive ET in patients with obesity, including those with an LVAD, and targeting much better weight reduction during LVAD therapy. We recently demonstrated the accuracy of BMI for predicting risk in a general population (10), but clearly BMI does not differentiate fat from muscle, and muscle mass and muscular strength certainly are important for predicting both cardiovascular prognosis and prognosis in HF (11). Therefore, more precise estimates of fat versus muscle, as well as muscular strength, and efforts to increase muscle mass and strength with resistance ET certainly would be advantageous for patients with advanced HF, including those with obesity. Programmable LVADs to support effective cardiac unloading during ET could help in achieving weight loss.

Recently, efforts to increase ET as therapy in those with advanced HF have received rejuvenated attention (12). Although LVAD therapy improves functional capacity and quality of life in patients with advanced HF, the benefits are less than expected (13). Total cardiac output in CF-LVAD patients during ET is predominantly determined by pump speed, pressure across the pump, and, in some cases, ejection through the aortic valve (13). Unfortunately, fixed pump speeds utilized in CF-LVADs may provide ineffective circulatory support, resulting in only modest cardiac output increases during ET. Therefore, optimizing peripheral function (e.g., in those with anemia or general deconditioning with low muscle mass) as well as reducing obesity may enhance functional capacity in LVAD patients and therefore improve subsequent HT prognosis (13).

Finally, in obese patients receiving an LVAD in anticipation of subsequent HT, much greater efforts for weight loss are needed, including use of a multidisciplinary team approach that incorporates cardiac and HF physicians, physiologists, nurses, dietitians, and perhaps even bariatric surgeons (5,14). The potential for unique strategies of CF-LVAD coupled with bariatric surgery (particularly the potential for sleeve gastrectomy) should be explored further as a more viable strategy in the very obese with advanced HF (14,15). Potentially, bariatric surgery may serve as an added bridge to HT in otherwise poorly eligible obese patients, allowing for much greater weight loss and better ET that increases muscle mass and function, and perhaps even facilitating ventricular recovery. It is time that the cogent and wisdom-laced comment of Hippocrates be adopted.

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