

# Impact of Obesity on Heart and Lung Transplantation: Does Pre-Transplant Obesity Affect Outcomes?

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## ABSTRACT

Increasing prevalence of obesity has led to a rise in the number of prospective obese heart and lung transplant recipients. The optimal management strategy of obese patients with end-stage heart and lung failure remains controversial. This review article discusses and provides a summary of the literature surrounding the impact of obesity on outcomes in heart and lung transplantation. Studies on transplant obesity demonstrate controversy in terms of morbidity and mortality outcomes and obesity pre-transplantation. However, the impact of obesity on outcomes seems to be more consistently demonstrated in lung rather than heart transplantation. The ultimate goal in heart and lung transplantation in the obese patient is to identify those at highest risk of complication that may warrant therapies to mitigate risk by addressing comorbid conditions.

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**R**ATES of obesity have continued to increase over time, reaching epidemic proportions worldwide. In Canada, prevalence of obesity has doubled over the last decade, leading to nearly 15% of the population being classified as obese [1]. Consequently, there is an increased number of obese end-stage heart failure and end-stage lung failure recipients being referred for transplantation. In fact, the average BMI of heart transplant recipients has increased nearly 10% over the last 20-years [2]. Despite a growing number of recipient referrals, there remains a serious shortage of suitable donor organs in both cardiac and pulmonary transplantation, leading to increasing deaths on the waitlist [2–4].

Obesity has been linked to hypertension, diabetes and dyslipidemia, representing the metabolic syndrome. These factors have been shown to result in increased all-cause mortality in these individuals [5]. Obesity and its metabolic sequelae have been implicated as a cause of cardiomyopathy independent of coronary artery disease, hypertension and other heart disease. This has been termed ‘obesity cardiomyopathy’, and its existence has been supported by studies examining the association of adiposity and left ventricular dysfunction [6].

Despite the fact that the prevalence of obesity has been increasing steadily, there remains significant controversy regarding the optimal management strategy for obese

patients with both end-stage heart and lung failure. The purpose of this review is to examine the literature to determine if obesity is a contraindication to thoracic transplantation.

## HEART TRANSPLANTATION

Traditionally, heart transplant programs have had stricter weight guidelines for transplant candidacy than other organ transplant programs. Some of the earliest reports of obesity and heart transplantation are reports from the mid-1980s. Kocher et al [7] published a study in 1999 on the effect of obesity on outcome after cardiac transplantation between 1984–1996. Patients were classified according to pre-transplant BMI. There were 106 underweight patients (BMI <21), 369 recommended-weight patients (BMI 21–27), 80 over-weight patients (BMI 27–30) and 29 obese patients (BMI >30). Survival rate was not

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significantly different between BMI groups. However, the patients with a BMI  $>27$  had a significantly higher incidence of hypertension and wound complications [7].

Bonet et al. published results from the Spanish registry for heart transplantation between 1984–2003 [8]. Obesity was defined as a BMI  $>25$ , and those patients that were categorized as obese in this study had a significant increased association with late mortality. As stated previously, results on obesity and survival after cardiac transplantation were not uniform in early outcome studies on this select patient population.

Another study published in 2009 reviewed the short-term outcomes of cardiac transplant recipients as well as organ allocation based on BMI. Using the United Network of Organ Sharing (UNOS) database Weiss et al [9] were able to evaluate 9,712 patients recommended weight patients (BMI 18.5–24.9), 10,051 overweight patients (BMI 25–29.9), 5,496 obese patients (BMI 30–34.9) and 1,703 morbidly obese patients (BMI  $>35$ ). Among patients reaching transplantation, patients with high BMI levels did not have increases in short-term mortality at 30 days, 90 days, or 1 year after cardiac transplantation. As well, patients with high BMI levels were found to have longer wait times and less frequent selection for transplantation when compared to their lower BMI level counterparts [9]. As well, Russo et al, again using the UNOS database, showed that obesity (BMI 30–34.96) is not associated with significantly higher long-term mortality in cardiac transplant recipients [10].

More recently, Healy et al, utilizing the International Society for Heart and Lung Transplantation (ISHLT) registry, reviewed predictors of 30-day post-transplant mortality in patients bridged with a ventricular assist device. They found that BMI was an independent risk factor for mortality, with increasing mortality as the BMI increases. The median BMI of patients in their review was 28, thus patients with a normal BMI of 20–25 are at a relatively lower risk of mortality post-transplant [11]. Additionally, Kilic et al, using data from the UNOS database, did show that an increasing number of pre-operative metabolic risk factors, including obesity, in cardiac transplant recipients is associated with an exponential increase in post-operative mortality rates [12].

A study published in 2016 by Nagendran et al [13] reviewed the effect of obesity (BMI 30–34.9) and morbid obesity (BMI  $>35$ ) on outcomes following heart transplantation. The data was collected via a provincial registry (APPROACH; Alberta Provincial Project for Outcome Assessment in Coronary Heart Disease) and included 220 total cardiac transplantations. Thirty-nine patients fell into the obese category and 10 in the morbidly obese category. The morbidly obese cohort tended to have longer cardiopulmonary bypass (CPB) times, increased rates of early complications and decreased long-term survival. Interestingly, the obese cohort did not have decreased survival compared with the lower BMI groups. Therefore, it is felt that those patients with a BMI 30–34.9 should not be excluded for heart transplantation based on BMI alone [13].

Taken together, there does appear to be some controversy as to the role of recipient obesity as a relative contraindication to heart transplantation. However, there is significant evidence to suggest that obesity (BMI 30–34.9) may not be associated with worse outcomes and perhaps should not be a contraindication to heart transplantation. Further study into mechanisms of graft dysfunction in the obese patient is warranted in order to further understand if the pre-operative diagnosis of obesity should be a relative contraindication in prospective heart transplantation recipients.

## LUNG TRANSPLANTATION

In the past, there have been limited data available on the influence of obesity on lung transplant outcomes. However, numerous recent studies have been published examining the role of obesity in lung transplant outcomes.

In 2002, Kanasky et al [14], reported results of 85 lung transplant recipients who underwent transplantation from 1994 to 1998. Patients were classified as underweight (BMI  $<18.5$ ;  $n = 19$ ), normal weight (BMI 18.5–24.9;  $n = 37$ ), overweight (BMI 25–29.9;  $n = 19$ ), or obese (BMI  $>30$ ;  $n = 10$ ). Using Kaplan-Meier survival distribution, the researchers concluded that patients with a BMI  $>30$  had nearly a 3-fold reduction in post-transplant survival ( $P <.05$ ). Overweight patients had an equal survival time compared with normal weight patients [14].

Another study examining 90-day mortality following bilateral lung transplantation showed that in patients with a pre-transplant BMI  $>25$ , the risk of dying within 90 days post-transplant was increased [15].

However, Culver and colleagues evaluated both BMI and percent ideal body weight as risk factors for short and long-term survival. One hundred twenty patients were used as normal-weight controls (BMI 18.5–24.9). Lung transplant recipients with a BMI  $>30$  ( $n = 46$ ) had an increased 90-day odds ratio (OR) for death (OR, 3.15; 95% CI, 1.05–9.48). The OR for 74 patients with a BMI of 25–30 was 3.93 (95% CI, 1.49–10.36), and the OR for 43 patients with a BMI  $<18.5$  was 1.72 (95% CI, 0.47–6.27). Even though elevated BMI was a risk for reduced short-term survival, there was no difference in long-term survival according to BMI. In addition, when obesity was defined as  $>130\%$  of ideal weight, there were no differences in survival between obese and non-obese groups [16].

The Lung Transplant Outcomes Group published two important papers investigating the role of obesity in primary graft dysfunction (PGD). In the first, they demonstrated that obesity (BMI  $>30$ ) was an independent risk factor for PGD, increasing the risk of developing PGD two-fold. Additionally, they showed that higher plasma leptin levels were associated with a greater risk of PGD, especially in those patients not undergoing CPB [17]. In their next study, the group included over 1,200 patients, and reaffirmed the link between obesity and PGD with an OR of 2.3 (95% CI, 1.3–3.9;  $P = .004$ ). Furthermore, they determined that PGD

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