

Commentary

Integrating Metabolic and Surgical Care to Optimize Kidney Transplantation Outcomes in Patients with Obesity

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Abstract

Recent studies have analysed the impact of obesity on kidney transplant outcomes, revealing worse one-year survival rates for patients with higher BMI levels. Data indicates that the prevalence of obesity among kidney transplant candidates is rising, with significant concerns about reduced transplant access and inferior outcomes. Integrated metabolic care, including surgical and medical treatments like sleeve gastrectomy and GLP-1 agonists, can improve kidney function and transplantation outcomes for patients with obesity and kidney disease. Data has also shown that BMI is insufficient to diagnose obesity and predict related cardio metabolic complications, thus additional diagnostic methods, such as waist circumference, should be considered. Robotic-assisted kidney transplantation has demonstrated excellent outcomes with minimal complications in patients with obesity. Multidisciplinary, integrated metabolic medicine programs in both the pre- and post-transplant phase of care are essential to optimize outcomes and address fragmented treatment pathways currently seen in healthcare institutions. Ongoing education for patients and medical care teams is essential to optimize metabolic care for kidney transplant recipients.

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Abbreviations

BMI: Body Mass Index

eGFR: Estimated Glomerular Filtration Rate

GLP-1: Glucagon-Like Peptide

ML: Machine Learning

RAKT: Robotic-Assisted Kidney Transplantation

SG: Sleeve Gastrectomy

UNOS: United Network for Organ Sharing database

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In a recent publication, authors Thongprayoon et al., provide an analysis of the United Network for Organ Sharing database (UNOS)/ OPTN database [1]. This study analysed kidney transplant recipients with a Body Mass Index (BMI) $\geq 40 \text{ kg/m}^2$ using unsupervised machine learning on data from 2010 to 2019. Five distinct clusters were identified based on recipient, donor, and transplant characteristics. Key findings by cluster are shown in (Table 1.) One-year patient survival rates ranged from 94.4% to 98.7%, with Cluster 2 performing the worst. One-year death-censored graft survival ranged from 93.0% to 98.8%, with Clusters 2 and 5 having the lowest rates. Based on this data, recipients with earlier access to transplant and living donation had better outcomes, and post-transplant support and socioeconomic factors likely influenced graft survival. Differences in outcomes can be further explained by differences in individual recipient characteristics. Importantly, this Machine Learning (ML)-based clustering approach offers a more nuanced and individualized risk assessment that goes beyond conventional BMI thresholds. By capturing the complex interplay among recipient comorbidities, donor characteristics, and transplant specific factors, these models enable clinicians to better predict both short- and long-term outcomes, refine candidate selection, and tailor perioperative and postoperative management strategies. Looking ahead, ML-driven phenotyping holds the potential to support truly personalized care pathways for transplant candidates with obesity shifting the field away from rigid BMI cut-offs and toward a more precise, patient is centered approach to transplantation. Nonetheless, this study and the UNOS data are limited by the lack of detailed information on metabolic risk factors, like diabetes, hypertension, and hyperlipidaemia as well as interventions to optimize pre- or post-transplant outcomes.

The increasing prevalence of kidney disease can be significantly attributed to the currently rising rates of obesity. In 2023, the percentage of waitlisted candidates with elevated BMI levels saw a significant increase. Specifically, 19.3% had a BMI of 35 kg/m^2 or higher, while 27.5% had a BMI between 30 and 35 kg/m^2 [2]. Moreover, an increase in the number of individuals with obesity receiving kidney transplants is expected. This trend reflects the overall rise in obesity

Cluster	Key Cluster Characteristics
1	Predominantly white, non-sensitized, preemptive, or short dialysis duration, likely to have living donor transplants
2	Older, diabetic, over 3 years on dialysis, likely to receive standard KDPI deceased donor kidneys
3	Young, retransplants, sensitized
4	Diabetic, variable dialysis duration, received either non-ECD standard KDPI kidneys or living donor transplants
5	Young, retransplants, sensitized

Table 1: Key Cluster Characteristics Based on Recipient, Donor, and Transplant Variables. BMI, Body Mass Index; ECD, Extended Criterion Donor; KDPI, Kidney Donor Profile Index.

rates across the United States. Data has shown that obesity is linked to both reduced access to kidney transplant and concerns for inferior outcomes [3-5]. Segev et al. showed that the likelihood of kidney transplant decreased with increasing obesity, and the chances of being bypassed when an organ was available increased with higher BMI categories [3]. Similarly, a 2020 study found that BMI has a “J-Shaped” risk profile for overall graft loss, with higher risks for both low BMI and obesity although risk varied significantly with recipient characteristics such as age, diagnosis, gender, and race/ethnicity, suggesting that transplant considerations should be personalized rather than based on absolute BMI thresholds [4]. Presence of obesity in the transplant population presents distinct challenges that extend beyond those encountered in the general population [6]. Increased visceral adiposity adds surgical complexity, often resulting in longer operative times and elevating the risk of perioperative complications such as delayed wound healing and hernia formation [6]. In the postoperative period, excessive adiposity fosters a persistent pro-inflammatory state that contributes to graft inflammation, accelerates chronic allograft injury and undermines long-term graft survival [7]. Additionally, obesity heightens the risk of delayed graft function, driven by increased vulnerability to ischemia reperfusion injury and impaired microvascular perfusion. Furthermore, growing data suggests that BMI is a suboptimal tool to diagnose obesity and predict cardiometabolic complication from this disease [5]. Therefore, other diagnostic methods including waist circumference, dual x-ray composition and consideration of other comorbidities should be utilized in conjunction to BMI to better predict outcomes and complication risk. Not all individuals with elevated BMI carry the same metabolic risk. Some patients exhibit what is termed “metabolically healthy obesity,” characterized by preserved insulin sensitivity and minimal inflammation despite excessive body weight. In contrast, visceral adiposity is more closely linked to insulin resistance, systemic inflammation, and poor transplant outcomes. Evaluating fat distribution and metabolic function may offer more accurate assessment of transplant risk rather than relying on BMI alone [8].

As such, there has been increasing awareness surrounding the need for comprehensive metabolic care for patients with kidney disease and incorporation of this approach into both the pre- and post-transplant phases. Treatment modalities have included both surgical and medical treatment. In a study of 104 patients with obesity, those who underwent Sleeve Gastrectomy (SG) showed significant improvement in body mass index and were more likely to receive kidney transplants compared to nonsurgical controls [9]. Additionally, in a study assessing preemptive obese patients, the mean Estimated Glomerular Filtration Rate (eGFR) significantly increased on patients who underwent a pretransplant SG; those patients also saw a decrease in BMI and

insulin requirements. Accordingly, the use of pretransplant SG may improve kidney function and increase rates of preemptive kidney transplantation for candidates not yet on dialysis while also allowing for optimization of their metabolic profile [10]. Similarly, studies have found significant improvements in survival, urine albumin to creatinine ratio, and eGFR in kidney transplant recipients treated with Glucagon-Like Peptide-1 (GLP-1) agonists [11]. Beyond promoting weight loss, GLP-1 receptor agonists improve glycemic control, enhance insulin sensitivity and reduce systemic inflammation, all of which may help mitigate chronic allograft injury [12]. In addition, GLP-1 agonists have been shown to lower proteinuria and improve endothelial function, offering potential renal protective benefits that extend beyond weight reduction alone [13]. These multifaceted effects make GLP-1 agonist particularly appealing for managing kidney transplant recipients with obesity, who often present with complex and interrelated metabolic disturbances. Unfortunately, treatment pathways for obesity, diabetes, kidney disease, and transplantation are often siloed with limited comprehensive treatment strategies within healthcare institutions (Figure 1). This fragmented care is further complicated by insurers who cover the cost of the kidney transplant but do not necessarily guarantee coverage for obesity treatment. In response to these challenges, several centers have begun developing integrated metabolic transplant programs that bring together expertise from transplant surgery, bariatric surgery, endocrinology, nutrition, and nephrology. These multidisciplinary models are designed to optimize candidate selection, streamline pre- and post-transplant metabolic care and ultimately improve both graft function and patient outcomes in this complex and high-risk population [14].

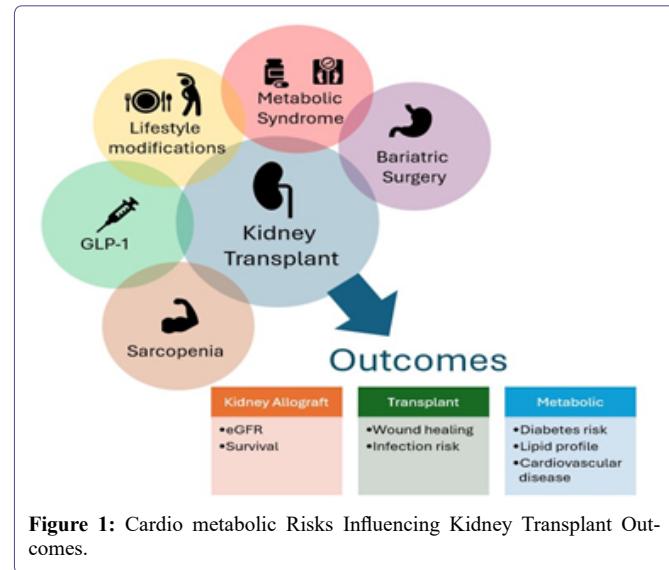


Figure 1: Cardio metabolic Risks Influencing Kidney Transplant Outcomes.

Lastly, experience with Robotic-Assisted Kidney Transplantation (RAKT) has also further developed as an opportunity to improve surgical outcomes in obese kidney transplant recipients by limiting wound and hernia-related complications. In a series of 239 patients with obesity undergoing RAKT, Tzvetanov et al demonstrated 98% and 93% graft survival at 1 and 3 years [15]. Wound complications occurred in 3.8% of patients, and there was a low incidence of surgical site infections. The study concluded that RAKT is safe for obese patients, with excellent outcomes and comparable data to national statistics.

In summary, rising obesity rates in the US correlate with increased obesity among kidney transplant recipients, negatively impacting

both access to transplant and outcomes. Comprehensive metabolic care, including medications such as GLP-1 agonists and surgical interventions like sleeve gastrectomy and robotic-assisted kidney transplantation, have shown promise in improving kidney function, transplant rates, and surgical outcomes for patients with obesity. It is essential to provide ongoing education to both patients and medical care teams about the benefits of comprehensive metabolic care. Additionally, there is a need for more inclusive medical benefits to ensure cost coverage.

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