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# Are Females More Prone Than Males to Become Obese After Kidney Transplantation?

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**Background:** Being overweight for kidney transplant recipients can cause serious side effects. Weight gain affects two-thirds of kidney transplant recipients and has been attributed to a more liberal diet after transplantation, recovery of appetite due to lack of uremic toxicity, corticosteroid use, and inadequate lifestyle changes. The aim of this study was to assess gender-dependent profile of body mass index (BMI) changes after kidney transplantation (KTx).

**Material/Methods:** Sixty-two kidney transplant recipients (38 males and 24 females), aged  $46.0 \pm 12.8$  years at KTx, were observed according to weight gain after KTx. BMI was calculated before transplantation (pre-KTx) and at 6, 12, and 24 months post-KTx.

**Results:** During the 24-month observation period, we found an increase in the incidence of kidney transplant recipients being overweight or obese (pre-KTx 43.5% increase and 24-month post-KTx 61.3% increase,  $P=0.036$ ). We analyzed a number of factors that could potentially influence a 24-month BMI gain including age at KTx, gender, pre-KTx BMI, time on dialysis, pre-KTx glucose metabolism disorder, and post-KTx diabetes mellitus. For female recipients, there was a significant step-wise post-KTx increase in BMI during the 24-month observation period. The overall pre-KTx to 24-month net increase for female BMI was 2 times greater than that observed for male recipients ( $1.90 \pm 2.20$  kg/m<sup>2</sup> versus  $0.89 \pm 1.85$  kg/m<sup>2</sup>,  $P < 0.001$ ).

**Conclusions:** Weight gain after KTx was observed in both sexes, but the net BMI increase was more than 2 times greater in females than in males at 24-months post-KTx. This indicated the need for diet education and strict weight control in kidney transplant recipients, especially in female patients.

**MeSH Keywords:** **Kidney Transplantation • Obesity • Overweight • Weight Gain**

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## Background

Kidney transplantation (KTx) is the most preferential treatment for end stage renal disease patients, with prolonged life expectancy, lower morbidity, and better quality of life. An increase in body weight after KTx in kidney recipients is challenging [1,2]. In general, the epidemic of obesity is reflected in the KTx population, where the proportion of recipients with a body mass index (BMI) greater than of 30 kg/m<sup>2</sup> is doubling every 15 years [3–5]. Prevalence of weight gain and obesity in kidney transplant recipients was observed in the first year after transplantation [6–10]. Ryan et al. reported the 10% to 35% average patient post-KTx weight gain [11]. Among the probable factors significantly contributing to increased body weight after KTx was the use of immunosuppressive drugs. Another probable cause was the non-uremic state of kidney transplant recipients, which may lead to increased energy intake [11]. Many reports have shown that transplant recipients do not implement lifestyle modification with adequate levels of physical activity. Lifestyle changes are difficult to make and require strong motivation [11–16].

Excessive weight gain resulting in being overweight or obese may be a detrimental complication in kidney transplant recipients; other detrimental complications include metabolic syndrome and new-onset diabetes after transplantation (NODAT), as well as cardiovascular diseases. These complications are the most important causes of morbidity and mortality after KTx [17–20]. Being overweight before transplantation correlates with insulin resistance after transplantation and is a risk factor for NODAT, so treatment for obesity may be a reasonable target for post-transplantation intervention [21]. Several published studies have shown that the cumulative incidence of obesity in transplant recipients is up to 10-fold higher than that reported in the non-transplanted population [21,22].

The aim of the present study was to assess the profile of BMI pre-KTx and at 6-months, 12-months, and 24-months post-KTx. Furthermore, we investigated the influence of age, gender, and dialysis modality on BMI changes.

## Material and Methods

Our study included 62 Kidney transplant recipients (38 males and 24 females) from the Outpatient Clinic of Wrocław University Hospital, Poland. Study patients were observed for weight changes after KTx (Table 1). We analyzed a number of factors that could potentially influence a 24-month BMI gain, including age at KTx, gender, pre-KTx BMI, time on dialysis, pre-KTx glucose metabolism disorder, and post-KTx diabetes mellitus.

The patient characteristics of the study groups is presented in Table 1. The mean age of study participants was 46.0±12.8 years at transplantation, and follow-up was greater than 2 years. Of these patients, 81% (n=50) underwent hemodialysis and 19% (n=12) underwent peritoneal dialysis pre-KTx. BMI was calculated as the dry weight in kilograms divided by the height in meters squared (kg/m<sup>2</sup>), and BMI was categorized according to World Health Organization guidelines as follows: underweight (<18.5 kg/m<sup>2</sup>), normal weight (18.5 to 24.9 kg/m<sup>2</sup>), overweight (25 to 29.9 kg/m<sup>2</sup>), and obese (>30 kg/m<sup>2</sup>). All the participants gave their informed consent. The research was approved by the Bioethics Committee of Wrocław Medical University, Poland. The statistical analysis was performed with Statistica v13 (Statsoft, Poland). The variables were tested for normality and are presented as mean ± standard deviation (SD) and range. The groups were compared with *t*-test for independent or independent normally distributed variables and Mann-Whitney or Wilcoxon tests in the other cases. The differences in frequencies were tested with Fisher exact test. The *P* value <0.05 was considered statistically significant. The study was supported by the Wrocław statutory funds (ST.C160.17.021).

## Results

The study group included 62 kidney transplant recipients (24 females and 38 males) who did not differ in terms of pre-KTx BMI (*P*=0.368). In our clinic, patients post-KTx were treated with 2 main immunosuppressive protocols as described previously [23]. The protocols included: 1) combination of cyclosporin A (CsA) with mycophenolate mofetil/mycophenolate sodium (MMF/MPA) and corticosteroids (CS), or more frequently 2) combination of tacrolimus (TAC) with MMF/MPA and CS. In the CsA group the steroid administration was as follows: perioperative intravenous (IV) bolus of methylprednisolone 500 mg, followed by 250 mg IV (12 hours and 24 hours post-KTx), and 125 mg IV at day 2. From day 3, prednisone was given orally with the initial dose of prednisone 0.5 mg/kg body weight per day (but no more than 40 mg/day), and then the dose was tapered to reach 10 mg/day after 3 months and 5 mg after 6 months. In the TAC group, significantly smaller steroid doses were given: perioperative bolus of methylprednisolone 500 mg IV bolus, followed by 250 mg IV at day 1, and 125 mg IV at day 2. Since day 3, prednisone was given orally in the fixed dose of 20 mg. After 1 month, the prednisone dose was reduced to reach a daily dose of 15 mg, and then tapered to 10 mg after 2 months and 5 mg after 3 months. The mean yearly cumulative prednisone dose in cyclosporine-receiving patients was about 5600 mg compared with about 3000 mg in TAC-treated recipients. In high immunological risk patients' induction therapy with thymoglobulin (high risk) and anti-CD25 antibody (moderate risk) were introduced with a combination of TAC, MMF/MPA, and CS. There was no steroid withdrawal protocol

**Table 1.** Study group characteristics.

	Females (n=24)	Males (n=38)	p
Age at KTx (years)	45.0±12.5	46.6±13.2	0.600
Original diagnosis			
Polycystic kidney disease	4	6	
Glomerulonephritis	14	25	
Hypertensive nephropathy	5	6	
Other or unknown	1	1	
HD/PD	18/6	32/6	0.283
Time on dialysis [months](median and range)	33 (21.5–60.5)	29 (20–59)	0.418
Weight pre-KTx [kg] (mean ±SD) [kg]	64.3±13.7	76.5±12.1	
BMI pre-KTx (mean ±SD) [kg/m <sup>2</sup> ]	24.17±4.68	25.10±3.39	0.368
Deceased donor/Living donor	24/0	35/3	
Immunosuppressive protocol: CsA/Tac	2/22	7/31	
Post-transplant DM (NODAT) (%)	2/22 (9)	6/32 (18.75)	0.329
Acute Rejection (AR)	5/19	1/37	<b>0.029</b>
Cytomegalovirus disease (CMV)	5/19	13/25	0.201
Pre-KTx GMD(-): BMI gain [kg/m <sup>2</sup> ] (mean ±SD)	2.40±2.17	1.08±2.02	0.061
Pre-KTx GMD(+): BMI gain [kg/m <sup>2</sup> ] (mean ±SD)	0.67±1.87	0.65±1.65	0.977

**Table 2.** Post-transplant BMI profile.

	Pre-KTx*	p-Value pre-KTx vs. 6 <sup>th</sup> month	6 <sup>th</sup> month	p-Value 6 <sup>th</sup> vs. 12 <sup>th</sup> month	12 <sup>th</sup> month	p-Value 12 <sup>th</sup> vs. 24 <sup>th</sup> month	24 <sup>th</sup> month	p-Value pre-KTx vs. 24 <sup>th</sup> month
Females	24.17±4.68	<b>0.032</b>	25.01±4.94	<b>0.017</b>	25.51±5.26	<b>0.008</b>	26.07±5.05	<b>&lt;0.001</b>
Males	25.10±3.39	0.324	25.37±3.45	0.062	25.60±3.32	<b>0.006</b>	25.99±3.61	<b>0.005</b>
p-value Females vs. Males	0.368		0.741		0.933		0.943	

\* KTx – kidney transplant.

after kidney transplant recipients [23]. During the 24-month observation period we observed an increase in the incidence of overweight BMI and obesity BMI in our study group (pre-KTx was 43.5%, and 24-month post-KTx was 61.3%,  $P=0.036$ ).

For female recipients, there was a significant step-wise post-KTx increase in BMI during the 24-month observation period ( $P<0.001$ ). The BMI increased also in male recipients, however, to a lesser extent ( $P=0.005$ ). The overall 24-month net BMI increase in female recipients was 2 times that observed for male recipients ( $1.90\pm 2.20$  kg/m<sup>2</sup> versus  $0.89\pm 1.85$  kg/m<sup>2</sup>,  $P<0.001$ ). However, the gender related difference in 24-month BMI gain did not reach statistical significance ( $P=0.057$ ). Of the 62 kidney transplant recipients (24 females and 38 males), 9 recipients developed NODAT (6 males and 3 females).

None of the other studied factors were proven in multivariate analysis to directly influence the post-KTx BMI gain, however, our results suggested that both female gender and no history of pre-KTx glucose metabolism disorder could be related to an increased BMI gain post-KTx. Detailed data are shown in Table 2.

## Discussion

Kidney transplantation (KTx), unquestionably, is the most effective method of renal replacement therapy that improves graft survival [24–26], quality of life [27], and reduces medical costs [27,28]. Unfortunately, many studies have indicated that kidney transplant recipients continue to have increased mortality compared with the general population [11]. The present

study demonstrated that the post-KTx weight gain increased in both males and females. Importantly, weight gain at 24-month follow-up was shown to be more than 2 times greater in females than in males. This tendency, especially in females, represents a major problem complicating post-KTx patient care, which deserves active prevention. Many published studies have shown that obesity after KTx decreases quality of life and significantly decreases graft survival [30].

Increased weight gain in female patients after KTx may be caused by more free time after KTx. Gętek et al. showed that male KTx patients were more likely than female KTx patients after KTx to assess the possibility of employment, accept their own appearance, and lead a normal lifestyle [31]. This suggests that after KTx female patients may be more likely to give up on work aspirations, and spend more time at home. Bad nutrition, poor diet, or lack of compliance with nutritional recommendations due to free time may contribute to the increased weight gain after KTx.

There are no current clinical guidelines that would be helpful to prevent, detect, or manage weight gain and obesity post-KTx [11]. There is a need to develop therapeutic strategies that would be helpful to minimize or prevent weight gain resulting in overweight BMI or obesity BMI in kidney transplant

recipients. Further research is needed to assess nutrition interventions, lifestyle modifications, educational elements, and physical activity promotions [32].

The apparent greater weight gain and BMI increases in female patients compared to male patients was not statistically significant, which may be related to the small number of study patients. The problem of weight gain related to gender requires further investigation in larger group of kidney transplant recipients.

## Conclusions

Post-transplantation weight increased after KTx in both males and females; in the 24-month follow-up period, the net BMI increase was more than 2 times greater in females ( $P < 0.001$ ). However, the gender related difference in 24-month BMI gain did not reach statistical significance ( $P = 0.057$ ). None of the factors in our multivariate analysis was proven to directly influence post-transplantation BMI gain. However, our results suggest that both female gender and no history of pre-transplantation glucose metabolism disorder could be related to an increased BMI gain after KTx. This results indicated the need for diet education, lifestyle modification, and strict weight control in kidney transplant recipients, especially in female patients.

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