

Weight-Gain–Related Factors in Renal Transplantation

Fatemeh Nazemian, Masih Naghibi

Objectives: Previous studies of renal transplant recipients have suggested that weight gain after transplantation is relatively common. The purpose of this study was to define the occurrence, magnitude, and predictors of weight gain in this group.

Material and Methods: We conducted a prospective study of 100 renal transplant recipients from 2002 to 2004 at Imam-Reza Hospital in Mashhad, Iran, to identify patterns of weight change attributed to sex, age at transplantation, socioeconomic class, and duration of dialysis. A descriptive study also was made on serum cholesterol and triglyceride levels in renal transplant recipients 12 months after transplantation. Patients' weights were evaluated at 3, 6, 9, and 12 months after transplantation.

Results: Univariate analyses at 1 year posttransplantation showed that women had greater weight gains than did men ($P = 0.003$); older recipients had greater weight gains than did younger recipients ($P = 0.009$); weight gain was correlated with an increase in serum triglyceride and cholesterol levels ($P = 0.000$ and $P = 0.004$); and socioeconomic class was not correlated with weight changes ($P = 0.955$).

Conclusions: Female sex, older age, and increasing incidences of hypercholesterolemia and hypertriglyceridemia were significantly associated with weight gain 1 year after organ transplantation.

Key words: Renal transplantation, Weight changes, female sex, Socioeconomic class

Nephrology Ward, Department of Internal Medicine, Imam-Reza Hospital, Mashhad University of Medical Sciences, Mashhad, Iran

Address reprint requests to: Fatemeh Nazemian, Nephrology Ward, Department of Internal Medicine, Imam-Reza Hospital, Mashhad University of Medical Sciences (MUMS), Mashhad 9137913312, Iran

Phone: 00 98 915 315 2214 Fax: 00 98 511 851 2166 E-mail: fatemeh_nazemian@yahoo.ca

Experimental and Clinical Transplantation (2005) 1: 329-332

Today, the most-common solid-organ transplantation procedure is renal transplantation (RT) [1]. The growing success of organ transplantation is due in large measure to dramatic improvements in immunosuppressive therapies that have resulted in 1-year graft and patient survival rates of more than 90% [2]. Patient survival has improved in large part because of a reduction in immunosuppression-related infectious mortality. In place of infectious causes of death, several reports have noted a growing incidence of cardiovascular complications, and cardiovascular disease is now believed to be the leading cause of death in RT recipients [3]. Although the etiology of cardiovascular disease in the transplant population is multifactorial, obesity and its complications play a key role. In general population studies, even modest weight gains are associated with an increased incidence of diabetes mellitus, hypertension, and coronary artery disease [4]. In fact, after renal transplantation, an increase in body weight is usually observed [5]. After renal transplantation, the feeling of well-being, the disappearance of dietary restrictions, and also the increased appetite (the latter probably due to steroid medication [6]), may result in an increased nutrient intake. A chronic increase in energy intake without an increase in energy expenditure will lead to weight gain. We conducted a prospective study of 100 renal transplant recipients operated on between 2002 to 2004 at Imam-Reza Hospital in Mashhad, Iran, to identify patterns of weight change attributed to sex, age at transplantation, socioeconomic class, and pretransplantation dialysis duration, incidence of hypercholesterolemia, and incidence of hypertriglyceridemia.

Material and Methods

Between 2002 and 2004, data from 100 renal transplant recipients (41 women, 59 men; mean age at

transplantation, 42.9 and 44.2 years, respectively; range, 18 to 61 years) were collected prospectively as part of a clinical database at our institution. All patients met the inclusion criteria, which consisted of being at least 18 years old at the time of transplantation and having a creatinine level of 1.8 mg/dL or less. Pretransplantation data including sex, age, height, weight, and duration of dialysis therapy were obtained for all patients. Posttransplantation follow-up data at 3, 6, and 12 months included weight, serum glucose level, lipid profile, and creatinine concentration. Body mass index (BMI) was calculated from body weight (kg) divided by height² (m²). Weight gain was determined by subtracting patients' preoperative (baseline) weights from their weights on follow-up.

Immunosuppressive regimens

Patients were treated with a standard triple-drug immunosuppression protocol consisting of cyclosporine, mycophenolate mofetil, and prednisone. Cyclosporine was started at an initial dosage of 10 mg/kg/day and was adjusted according to a protocol based on trough concentrations targeted to 200 to 250 ng/mL during the first 2 months, 150 to 200 ng/mL from 2 to 6 months, and 100 to 150 ng/mL thereafter. The protocol for corticosteroid dosing remained constant throughout the study: 1000-mg doses of methylprednisolone were given in the first 3 days of RT; then, an oral prednisone taper was initiated on the third postoperative day, starting with 1 mg/kg per day orally, based on dry weight and adjusted for body weight if that weight were greater than 130% of ideal body weight. Prednisone was tapered during the first 6 months after transplant to 0.2 mg/kg per day and maintained at this level. Mycophenolate mofetil was given at a dosage of 2 g/day. Acute allograft rejection was initially treated with 3 daily intravenous boluses of 1 gram of methylprednisolone and recycling of oral prednisone, which was rapidly tapered to a dosage of 0.5 mg/kg/day at 10 days from the onset of treatment. Refractory episodes were treated with antilymphocyte serum at a dosage of 15 mg/kg/day for 14 days.

Statistical analyses

Initially, univariate analyses of each factor at baseline and follow-up visits were used separately to screen for potential influences on weight changes. Testing approaches used in univariate analysis were the *t* test for two-level risk factors, correlation analysis

for continuous risk factors, and chi-square analysis for categorical risk factors. Univariate test results were considered statistically significant at level for *P* less than 0.05. All statistical analyses were performed using SPSS software (Statistical Package for the Social Sciences, version 7.5, SSPS Inc, Chicago, Ill, USA).

Results

We followed 100 patients for 1 year after renal transplantation. Age at transplantation ranged from 18 to 61 years. At baseline, all of our patients had a BMI greater than 20. Five patients were overweight (BMI > 25), and 2 patients were obese (BMI > 30). By 1 year after transplantation, the average weight gain was 7.46 kg (range, -8 to 30 kg). By 3 months after transplantation, the average weight gains for men and women were 2.3 kg and 3.4 kg. The patients continued to gain weight and by 6 months after transplantation, the average weight gains for men and women were 3.92 kg and 7.31 kg. At the end of the first year, the median weight gains for men and women were 5.93 kg and 9.65 kg, respectively (Table 1). Univariate analyses at 6 and 12 months after RT showed that women had greater weight gain than did men (*P* < 0.003). At baseline, the percentages of patients considered overweight (BMI > 25) and obese (BMI > 30) were 5.7% and 2.9%, respectively. At 12 months, BMI increased in all patients, and the percentages of patients considered overweight and obese were 20% and 7.1%, respectively. Analysis of the effect of age on weight gain showed that older patients gained more weight than did younger patients (*P* = 0.009) (Table 2).

Patients also were studied with regard to acute rejection. Twelve months after RT, 28 patients experienced acute rejection. On average, the rejection

Table 1. Average Weight Gain for Men and Women During Different Periods after Transplantation

Period after transplantation	Sex	Number of patients	Average weight gain (kg)	Standard deviation
3 months	M	59	2.3051	2.7684
	F	41	3.4634	2.9757
6 months	M	59	3.9322	3.6713
	F	41	7.3171	4.6499
9 months	M	59	5.2542	5.2999
	F	41	8.7317	5.8865
12 months	M	59	5.9322	5.5673
	F	41	9.6585	6.7809

episodes occurred 11.6 ± 8.2 days posttransplantation. There was no significant difference in weight gain in the first year for patients with or without a history of acute rejection.

To facilitate the analysis, we divided the RT patients into 2 groups to assess the relationship between income and posttransplant weight gain. Group 1 consisted of RT patients with a low-to-moderate income; group 2 consisted of patients with a moderate-to-high income. A weak positive relationship was found between income and weight gain (Table 3). No relationship was observed between length of time on dialysis and weight gain. In a descriptive study of serum cholesterol levels at 12 months posttransplantation, 79% of patients showed hypercholesterolemia, and 48.9% showed hypertriglyceridemia in a descriptive study of serum triglyceride levels. A correlation analysis confirmed the predominant effect of weight gain on hypercholesterolemia and hypertriglyceridemia ($P < 0.004$ and $P = 0.000$) (Table 4).

Discussion

We studied changes in body weight after RT. Rela-

tionships between posttransplant weight changes and age, sex, pretransplant BMI, pretransplant dialysis duration, renal function, and acute rejection also were investigated.

On average, patients lost body weight in the first month after RT. This could be due to the catabolic effects of surgery, loss of excess fluid, delayed graft function, or decreased dietary intake in the early posttransplant period. After the first month after RT, patients started to gain weight, with significant weight increments between each measurement interval ($P < 0.05$). The mean weight gain was 2.75 kg at 3 months after RT, 5.31 kg at 6 months after RT, and 7.46 kg at 12 months after RT. Posttransplant weight gain was, however, relatively low when compared with the weight gain reported in other studies [7, 8]. One explanatory factor might be the relatively low steroid dosage used in our study. Merion and coworkers [8] found an average weight gain of 8.9 kg in nonobese patients and 14.2 kg in obese patients during the first year after RT; both the obese and nonobese patients underwent immunosuppressive therapy with high dosages of corticosteroids (> 10 mg/day), cyclosporine, and azathioprine. Some weight gain might be favorable in patients who are malnourished at the time of transplantation. In a prospective pilot study [9], however, van den Ham and colleagues observed that weight gain in the early posttransplant period (at least until 6 months after RT) was predominantly due to an increase of the body fat mass and not to an increase of the lean body mass.

We found a significant relationship between age, sex, and posttransplant weight gain. Our results showed that women had greater weight gains than did men ($P = 0.003$), and older recipients had greater weight gains than did younger recipients ($P = 0.009$). This is in contrast with the study by Johnson and coworkers [10] that found comparable weight gains in men and women during the first year after RT. Johnson and colleagues also found a greater weight gain in younger patients (18-29 years of age) than in middle-aged (30-49 years of age) and older patients (> 50 years of age). Moore and Gaber [11] found no difference in weight gain between men and women in the first 6 months after RT.

In this study, analysis at 1 year showed that socioeconomic class was not correlated with weight change ($P = 0.955$). This is different from other studies that have reported that low-income patients have greater mean weight gains [4].

Table 2. Correlation Between Age and Weight Change

	AGE and DIF3	AGE and DIF6	AGE and DIF9	AGE and DIF12
Pearson correlation*	0.099	0.264	0.263	0.261
P value	0.330	0.008	0.009	0.009

DIF3: Weight change at 3 months after transplantation
 DIF6: Weight change at 6 months after transplantation
 DIF9: Weight change at 9 months after transplantation
 DIF12: Weight change at 12 months after transplantation
 * A Pearson correlation about 0.26 means we have a positive correlation between age and weight gain.

Table 3. Weight Change in Different Socioeconomic Classes after Renal Transplantation

DIF 12	Socioeconomic classes	
	Low to moderate income	Moderate to high income
Less than 5kg	58.8%	41.2%
Between 5 to 10kg	62.5%	37.5%
More than 10kg	51.4%	48.6%

$P = 0.675$

Table 4. Correlation between Cholesterol, Triglyceride, and Weight Change at 12 Months after Transplantation

	DIF12 and cholesterol	DIF12 and triglyceride
Pearson correlation*	0.309	0.375
P value	0.004	0.000

DIF12: Weight change at 12 months after transplantation
 * A Pearson correlation about 0.26 means we have a positive correlation between age and weight gain.

A difference in weight course between patients with or without rejection episodes might be expected. Factors accompanied by rejection episodes such as (prolonged) hospitalization, increased stress, prolonged effects of uremia, catabolism, feeling of malaise, or decreased appetite, might affect weight course after RT. In the present study, however, we did not find any relationship between posttransplant weight changes and acute rejection, which is consistent with the results of Johnson and colleagues. [10]. In contrast, Moore and Gaber [11] noticed that the occurrence of rejection episodes in patients who lost body weight in the first 6 months after RT was significantly greater than it was in patients who gained weight during this period.

Excessive weight gain, a major problem for many RT patients, is associated with increased risks of metabolic and cardiovascular complications—major causes of morbidity and mortality in renal transplant patients [12, 13, 14]. Obesity has been observed as an important predisposing factor for hyperlipidemia [15, 16]. On univariate analysis, our results confirm that an increasing incidence of hypercholesterolemia and hypertriglyceridemia is significantly associated with weight gain after 1 year.

In conclusion, after losing weight in the first month after RT, renal transplant patients began to gain weight from that point forward. Posttransplant weight gain was related to age and sex. Weight gain in the first year after RT was, however, not related to acute rejection episodes or socioeconomic class. Additionally, increasing incidence of hypercholesterolemia and hypertriglyceridemia were significantly correlated with weight gain after transplantation.

References

1. Tauchmanova L, Carrano R, Sabbatini M, De Rosa M, Orio F, Palomba S, et al. Hypothalamic-pituitary-gonadal axis function after successful kidney transplantation in men and women. *Hum Reprod* 2004; 19(4): 867-873. Epub 2004 Mar 11
2. Hariharan S, Johnson CP, Bresnahan BA, Taranto SE, McIntosh MJ, Stablein D. Improved graft survival after renal transplantation in the United States, 1988 to 1996. *N Engl J Med* 2000; 342(9): 605-612
3. Loertscher R. Management issues in renal transplantation. *Transplant Proc* 1998; 30: 1723-1725
4. Willett WC, Dietz WH, Colditz GA. Guidelines for healthy weight. *N Engl J Med* 1999; 341(6): 427-434
5. van den Ham EC, Kooman JP, Christiaans MH, Nieman FH, van Hooff JP. Weight changes after renal transplantation: a comparison between patients on 5-mg maintenance steroid therapy and those on steroid-free immunosuppressive therapy. *Transpl Int* 2003; 16(5): 300-306. Epub 2003 Feb 20
6. Yanovski JA, Cutler GB Jr. Glucocorticoid action and the clinical features of Cushing's syndrome. *Endocrinol Metab Clin North Am* 1994; 23(3): 487-509
7. Patel MG. The effect of dietary intervention on weight gains after renal transplantation. *J Ren Nutr* 1998; 8(3): 137-141
8. Merion RM, Twork AM, Rosenberg L, Ham JM, Burtch GD, Turcotte JG, et al. Obesity and renal transplantation. *Surg Gynecol Obstet* 1991; 172(5): 367-376
9. van den Ham EC, Kooman JP, Christiaans MH, Leunissen KM, van Hooff JP. Posttransplantation weight gain is predominantly due to an increase in body fat mass. *Transplantation* 2000; 70(1): 241-242
10. Johnson CP, Gallagher-Lepak S, Zhu YR, Porth C, Kelber S, Roza AM, Adams MB. Factors influencing weight gain after renal transplantation. *Transplantation* 1993; 56(4): 822-827
11. Moore LW, Osama GA. Patterns of early weight change after renal transplantation. *J Ren Nutr* 1996; 6(1): 21-25
12. Kasiske BL. Epidemiology of cardiovascular disease after renal transplantation. *Transplantation* 2001; 72(suppl 6): S5-S8
13. Larsson B, Svardsudd K, Welin L, Wilhelmsen L, Bjorntorp P, Tibblin G. Abdominal adipose tissue distribution, obesity, and risk of cardiovascular disease and death: 13 year follow up of participants in the study of men born in 1913. *Br Med J (Clin Res Ed)* 1984; 288(6428): 1401-1404
14. Raine AE, Margreiter R, Brunner FP, Ehrlich JH, Geerlings W, Landais P, et al. Report on management of renal failure in Europe, XXII, 1991. *Nephrol Dial Transplant* 1992; 7(suppl 2): 7-35
15. Lopes IM, Martin M, Errasti P, Martinez JA. Benefits of a dietary intervention on weight loss, body composition, and lipid profile after renal transplantation. *Nutrition* 1999; 15(1): 7-10
16. el-Agroudy AE, Wafa EW, Gheith OE, Shehab el-Dein AB, Ghoneim MA. Weight gain after renal transplantation is a risk factor for patient and graft outcome. *Transplantation* 2004; 77(9): 1381-1385