Renal Failure

ISSN: 0886-022X (Print) 1525-6049 (Online) Journal homepage: informahealthcare.com/journals/irnf20

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To cite this article: Thaís Rodrigues Moreira, Tayron Bassani, Gizele de Souza, Roberto Ceratti Manfro & Luiz Felipe Santos Gonçalves (2013) Obesity in kidney transplant recipients: association with decline in glomerular filtration rate, Renal Failure, 35:9, 1199-1203, DOI: 10.3109/0886022X.2013.819735

To link to this article: https://doi.org/10.3109/0886022X.2013.819735

Published online: 01 Aug 2013.

RENAL FAILURE

http://informahealthcare.com/rnf
ISSN: 0886-022X (print), 1525-6049 (electronic)

Ren Fail, 2013; 35(9): 1199–1203
 DOI: 10.3109/0886022X.2013.819735

informa healthcare

CLINICAL STUDY

Obesity in kidney transplant recipients: association with decline in glomerular filtration rate

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Abstract

In this study we aimed to evaluate the influence of obesity in kidney and patient survival and graft function. Retrospective cohort study of kidney transplant recipients performed between 2001 and 2009. The body mass index was calculated at time of transplantation, one and five years after. The main outcomes studied were incidence of delayed graft function, new onset diabetes after transplantation, patient and graft survival, and glomerular filtration rate. The prevalence of obesity and overweight patients were 10.7% and 26.8% respectively, with an increase to 16.9% and 32.5% one year after transplantation. Underweight and obese recipients presented a higher incidence of early graft loss. The incidence of new onset diabetes after transplantation was significantly higher at one and five years in overweight or obese recipients at baseline. Overweight and obese recipients presented significantly lower estimated glomerular filtration rate at five years posttransplantation ($p = 0.002$). In the Kaplan–Meier analyses no statistically significant differences in patients or grafts survivals were observed. Obese patients have a higher rate of early graft failure and a higher new onset diabetes after transplantation incidence. Also, the finding of decreased glomerular filtration rate is worrisome and perhaps longer follow-up will reveal more graft failures and patients deaths in the group of obese recipients.

Keywords

Body mass index, glomerular filtration rate, kidney transplantation, obesity

History

Received 9 March 2013
Accepted 23 June 2013
Published online 31 July 2013

Introduction

Renal transplantation (RT) is currently considered the treatment of choice for patients with end-stage renal disease providing better survival and quality of life.[1] However, long-term outcomes remain unsatisfactory mainly because chronic allograft losses and cardiovascular mortality. In the general population obesity is recognized as an important risk factor for the development of hypertension and diabetes and mortality.[2–5] However, its impact on RT remains controversial. Several studies have shown a significant increase in the incidence of postoperative complications, graft loss and patient mortality.[6–11] Contrariwise some recent studies found no significant difference in graft and patient survival in these patients.[2,12]

There is also concern regarding renal graft function in obese patients. In the general population recent evidences suggest obesity as an independent risk factor for the development and progression of chronic kidney disease.[13,14] The main mechanisms implicated are glomerular hyperfiltration and albuminuria, insulin resistance and renin-angiotensin-aldosterone system activation, increased pro-inflammatory cytokines, oxidative stress and endothelial dysfunction.[15] Griffin et al. proposed that weight gain may be detrimental in individuals with low nephron number both congenital or acquired.[16] Therefore it is conceivable that the same or related mechanisms could be operative in overweight and obese kidney transplant recipients aggravated by the presence of a single functioning kidney and also possible size mismatch between recipient and donor.

In this study, we evaluated BMI of kidney transplant recipients pre and one year after transplantation with the aim to verify the influence of obesity and BMI changes in their outcomes, mainly kidney and patient survival and graft function.

Materials and methods

This is a retrospective cohort study of 471 kidney transplant recipients performed between 1 January 2002 and 31 December 2009. After exclusion of pediatric patients (age < 18 years), recipients of multiple organs and incomplete data from medical records, 447 recipients were available for the study. Demographic and clinical data were collected through medical records review and 31/12/2011 was

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established as the final moment to events registration and follow-up. Body mass index (BMI) was calculated at time of transplantation and patients categorized according to the World Health Organization criteria into four groups: underweight, normal, overweight and obese. Modifications of nutritional status after transplantation were verified by BMI evaluations one year after transplantation following the same grouping method. Clinical records were reviewed for recipient age, gender and race; donor age and gender, type of donor, hypertension, immunosuppressive regimen, number of hospitalizations, cold ischemia time, and panel reactivity activity. The outcomes studied were incidence of delayed graft function (DGF), defined by the need of dialysis within the first post-transplant week, surgical wound complications, graft survival, patient survival, early graft loss (<3 months post-RT), acute rejection incidence, cause of death, glomerular filtration rate (GFR) estimated by the abbreviated equation developed for the Modification of Diet in Renal Disease Study (MDRD), new onset diabetes after transplantation (NODAT) diagnosed as defined by American Diabetes Association criteria, and dyslipidemia after renal transplantation (diagnosis through laboratory tests: low density lipoproteins $\geq$60 mg/dL, triglycerides $\geq$150 mg/dL, total cholesterol $\geq$200 mg/dL and high density lipoproteins men <40 mg/dL and women <50 mg/dL – according to American Association of Clinical Endocrinologists).

All patients receive triple immunosuppressive therapy with prednisone, calcineurin inhibitors (cyclosporine or tacrolimus) and an adjunctive agent (azathioprine or mycophenolic). Patients with increased immunological risk received induction therapy with polyclonal antithymocyte globulin or anti-IL2 receptor monoclonal antibody.

Statistical analyses were performed using SPSS version 18.0. One-way analysis of variance was used to compare means in the four groups and chi-square or Fisher exact test were employed for categorical data. Graft and patient survival rates were evaluated by Kaplan–Meier survival curves.

Estimated glomerular filtration (eGFR) was evaluated over 6 months, 1, 2 and 5 years post-transplantation in the four BMI groups defined at time of transplantation and comparison of these curves were performed with the Generalized Estimating Equations.[17,18] Values of $p < 0.05$ were considered statistically significant.

The study was conducted in accordance with resolution number 196/96 of the National Health Council, and the procedures were approved by the Ethics Committee for Research Involving Human Subjects of Hospital de Clinicas de Porto Alegre, Federal University of Rio Grande do Sul, protocol number 08-641.

Results

Population characteristics are presented in Table 1. Overweight and obese recipients were significantly older than underweight and normal weight patients. A significantly higher proportion of males were present in the overweight and obese groups. Patients were followed for an average period of 54 ± 27 months. Nutritional status pre-RT and one year after transplantation are shown in Table 2. At baseline 31 (6.9%) recipients were underweight, 248 (55.5%) had normal weight, 120 (26.8%) had overweight and 48 (10.7%) were obese. At one year after transplantation 53.8% of the underweight recipients attained normal weight, most of those who were overweight or obese pre-RT remained in these categories.

Table 1. Characteristics of the sample distributed according to baseline BMI.

Characteristics	Underweight ($n = 31$)	Normal ($n = 248$)	Overweight ($n = 120$)	Obese ($n = 48$)	p
Age ($X \pm$ DP)	32.7 ± 10.1	41.5 ± 11.8	47.2 ± 10.2	47.1 ± 9.2	<0.001*
Male gender (*n*/%)	7 (22.5%)	141 (56.8%)	80 (66.7%)	33 (68.7%)	<0.001#
Caucasian (*n*/%)	25 (80.6%)	217 (87.5%)	96 (80%)	40 (83.3%)	0.425#
Deceased donor (*n*/%)	23 (74.2%)	179 (72.2%)	96 (80%)	36 (75%)	0.453#
Re-RT (*n*/%)	2 (6.5%)	28 (11.3%)	9 (7.5%)	2 (4.2%)	0.326#
Hospitalizations ($X \pm$ DP)	3.8 ± 2.9	3.4 ± 2.7	3.9 ± 3.3	3.7 ± 2.8	0.504*
DM (*n*/%)	0 (0%)	16 (6.5%)	15 (12.5%)	6 (12.5%)	0.050#
HCV (*n*/%)	9 (29%)	38 (15.3%)	18 (15%)	8 (16.7%)	0.261#
CyA (*n*/%)	19 (61.3%)	171 (68.9%)	88 (73.3%)	26 (54.2%)	0.144#
Induction (*n*/%)	13 (41.9%)	85 (34.3%)	47 (39.5%)	21 (43.7%)	0.776#
ATG Induction (*n*/%)	3 (9.7%)	18 (7.3%)	8 (6.7%)	2 (4.2%)	0.776#
Class I >50 (*n*/%)	4 (12.9%)	11 (4.4%)	3 (2.5%)	4 (8.3%)	0.071#
Class II>50 (*n*/%)	5 (16.1%)	11 (4.4%)	6 (5%)	2 (4.2%)	0.054#

Re-RT = Retransplantation, DM = Diabetes Mellitus, HCV = Hepatitis C status, CyA = cyclosporine, ATG = Thymoglobulin.
*ANOVA.
#Chi-Square.

Table 2. Nutritional status before and one year after renal transplantation.

Period	Pre-RT, *n*(%)	Post-RT, *n*(%) underweight	Normal weight	Overweight	Obese	Total
Underweight	31 (6.9%)	12 (46.2%)	14 (53.8%)	0	0	26
Normal	248 (55.5%)	4 (1.8%)	150 (69.1%)	56 (25.8%)	7 (3.3%)	217
Overweight	120 (26.8%)	0	14 (13.5%)	64 (61.5%)	26 (25%)	104
Obesity	48 (10.7%)	0	1 (2.6%)	5 (13.2%)	32 (84.2%)	38
Total	447	16 (4.2%)	179 (46.5%)	125 (32.5%)	65 (16.9%)	385

Table 3. Nutritional status at baseline and outcomes at one and five years post transplantation.

Outcomes	Underweight	Normal	Overweight	Obesity	*p**
DGF, *n*(%)	13 (41.9%)	97 (39.1%)	61 (50.8%)	26 (54.2%)	0.081
Early loss, *n*(%)	3 (9.7%)	8 (3.2%)	8 (6.6%)	6 (12.5%)	0.042
Wound complication, *n*(%)	4 (12.9%)	38 (15.3%)	22 (18.3%)	5 (10.4%)	0,603
AR, *n*(%)					
1y	10 (38.5%)	75 (34.5%)	30 (28.8%)	10 (26.3%)	0.544
5y	6 (54.5%)	33 (30.3%)	20 (41.7%)	3 (27.3%)	0.245
Death, *n*(%)					
1y	2 (6.4%)	15 (6.2%)	7 (5.8%)	3 (6.2%)	0.999
5y	4 (25%)	24 (16.9%)	10 (15.6%)	2 (12.5%)	0.790
NODAT, *n*(%)					
1y	4 (15.4%)	27 (12.4%)	26 (25%)	10 (26.3%)	0.018
5y	2 (18.2%)	12 (11%)	14 (29.2%)	4 (36.4%)	0.017
Dyslipidemia, *n*(%)					
1y	17 (65.4%)	163(75.1%)	77 (74%)	32 (84.2%)	0.383
n(%)					
5y	7 (63.6%)	90 (82.6%)	34 (70.8%)	9 (81.8%)	0.240
Graft loss, *n*(%)					
1y	5 (16.1%)	32 (13.2%)	19 (15.8%)	10 (20.8%)	0.568
n(%)					
5y	8 (50%)	43 (30.3%)	27 (42.2%)	6 (37.5%)	0.217

DGF = delayed graft function, AR = acute rejection, NODAT = new onset diabetes after transplantation.
*Chi-Square.

Among those who had normal weight at transplantation 4 (1.8%) became underweight and 63 (29.1%) gained weight becoming overweight or obese.

The impact of pre-RT nutritional status related to outcomes at one and five years post transplantation are shown in Table 3. Underweight and obese recipients presented a higher incidence of early graft loss. The incidence of NODAT was significantly higher at one and five years in overweight or obese recipients at baseline.

Obese patients one year after transplantation have a significantly higher incidence of NODAT (46.1% × 15.6%, $p = 0.006$) and a trend towards a higher incidence of acute rejection (61.5% × 32.5%, $p = 0.065$) in the fifth year of follow-up.

Estimated GFR over the five year period are shown in Figure 1. Analysis of the curves showed that the groups of overweight and obese recipients presented significantly lower eGFR at five years after transplantation ($p = 0.002$). Underweight patients presented an eGFR decrease at two years, but tend to have an increase thereafter. The well nourished group is the only one that remains stable with a small reduction in the eGFR over the five years.

In the Kaplan–Meier analysis no statistically significant differences were found in patients or grafts survivals across the four BMI categories.

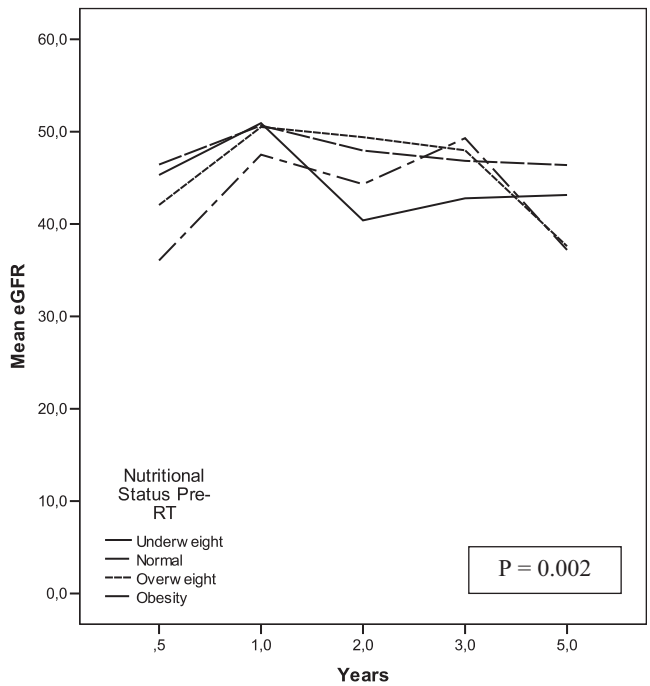

Figure 1. Evolution of estimated GFR means related to nutritional status pre renal transplant.

Discussion

In this retrospective study in a cohort of renal transplant recipients, contrary to our hypothesis, we did not observe an impact of the nutritional status in survival outcomes. We did however found a trend towards a higher incidence of DGF and acute rejection in the overweight and obese groups of patients. More importantly, however, we also found a higher incidence of graft loss within three months after transplantation, NODAT and above all we found that late after transplantation, graft function decreases in patients with higher than ideal weight. Some of our results are in contrast to a previous report by Meier-Kriesche and collaborators using the United States Renal Database – USRDS database[11] in which a lower mortality risk was found in the cohort of patients with BMI between 22 and 32 kg/m^2.

We found a significant increment in the prevalence of overweight and obesity at one year after transplantation as compared to the pre-RT rates. These findings are similar to previous reports from single center[2,17,18] and registry reports.[19,20] Malnourishment is not uncommon before transplantation and is probably due to the effects of uremia, inflammation and perhaps dialysis itself. After transplantation

the end of alimentary restrictions, increased appetite and the use of steroids usually lead to correction of these conditions and lower rates of malnourished patients are found.[19,20] In keeping with some previous reports[12,18–20] but contrary to others,[21–23] in the present study we also found that older age, male gender and pre-RT diabetes are associated with post-RT weight gain.

The early outcomes, up to one year, following RT may also be affected by the nutritional status of the recipients. In the present report we found a significantly higher rate of early graft loss in both malnourished and obese recipients. The increased incidence of early graft loss in these recipients has being described and is probably related to a higher incidence of technical problems with the vascular sutures in the obese and perhaps higher early mortality in the malnourished. In this study we also found a trend towards a higher incidence of DGF in the overweight and obese recipients.[26] This association has being found previously in some[11,24] but not in all studies.[2,12,25] Finally, in the short term outcomes we did not observe a higher incidence of wound complications perhaps due to the retrospective design of our study.

At 5 years after transplantation a higher incidence of NODAT in obese recipients was the only significant outcome. No differences were found in the incidence of cardiovascular events, graft loss or death. In our cohort it is perhaps necessary a longer follow up to uncover differences in these outcomes. Previous studies[27] produced mixed results. Lower graft survival[27] were described in patients with BMI >35 kg/m^2 and in a large registry study,[11] in recipients with BMI either lower than 18 kg/m^2 or higher than 28 kg/m^2. However in others studies no impact of obesity on graft survival has been demonstrated.[2,12] Different studies have shown lower patient survival in obese recipients. Gill and collaborators[27] found a remarkable difference in the survival of patients with BMI higher than 30 kg/m^2 and lower than 27 kg/m^2. Modlin and collaborators[28] in a case-control study described similar results and also reported a two times increased incidence of cardiovascular events. However, Massarweh and collaborators[29] reported that no increased mortality is observed among obese post-RT after adjustment for immediate graft function, donor race and HLA matching. Other smaller studies did not report increased late mortality rates in obese post-RT. However, due to the small samples in these studies the possibility of type II error must be considered.[2,12,19,24]

Perhaps the most relevant finding of the present study is the impact on renal graft function that was found decreased in overweight and obese recipients at five years after transplantation. It is possible that the elevated incidence of hypertension, diabetes and hyperlipidemia contribute to this outcome, particularly in the setting of a single functioning kidney.[11] Besides, the association between chronic kidney disease and obesity as a result of glomerular hyperfiltration and sclerosis has being recognized.[30,31]

The present study has some limitations including the retrospective data analyses, BMI utilization for evaluation of nutritional status that do not permit the lean body and body fat evaluations. Also, the MDRD formula estimation of GFR is perhaps not adequately validated for renal transplant recipients. Another possible weakness is the relatively short follow-up that might not be sufficient to uncover the consequences of obesity in this population, including the impact in patient and graft survivals.

In summary, the present study was able to find that obese patients have a higher rate of early graft failure, have a higher NODAT incidence and perhaps a higher incidence of delayed graft function. Also, our results suggest that overweight and obesity should not be considered contraindications to transplantation. However, the finding of decreased GFR is worrisome and perhaps longer follow-up will reveal more graft failures and patients deaths in the group of obese recipients.

Declaration of interest

The authors report no conflicts of interest. The authors alone are responsible for the content and writing of the paper.

The authors thanks to Fundo de Incentivo a Pesquisa (FIPE) do Hospital de Clínicas de Porto Alegre, RS, Brazil.

References

1. 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: 605–612.
2. Johnson DW, Isbel NM, Brown AM, et al. The effect of obesity on renal transplant outcomes. *Transplantation* 2002;74:675–680.
3. Friedman AN, Miskulin DC, Rosenberg IH, Levey AS. Demographics and trends in overweight and obesity in patients at time of kidney transplantation. *Am J Kidney Dis.* 2003;41:480–487.
4. WHO. Obesity: preventing and managing the global epidemic. Report of a WHO Consultation on Obesity. *Word Health Organ Tech Rep Ser.* 2000;894:1–253.
5. Lopez AD, Mathers CD, Ezzati M, Jamison DT, Murray CJ. Global and regional burden of disease and risk factors, 2001: systematic analysis of population health data. *Lancet* 2006;367: 1747–1757.
6. Amstrong KA, Campbell SB, Hawley CM, Johnson DW, Isbel NM. Impact of obesity on renal transplant outcomes. *Nephrology* 2005; 10:405–413.
7. Bumgardner GL, Henry ML, Elkhammas E, et al. Obesity as a risk factor after combined pancreas/kidney transplantation. *Transplantation* 1995;60:1426–1430.
8. Kent PS. Issues of obesity in kidney transplantation. *J Ren Nutr.* 2007;17:107–113.
9. Potluri K, Hou S. Obesity in kidney transplant recipients and candidates. *Am J Kidney Dis.* 2010;56:143–156.
10. Cacciola RA, Pujar K, Ilham MA, Puliatti C, Asderakis A, Chavez R. Effect of degree of obesity on renal transplant outcome. *Transplant Proc.* 2008;40:3408–3412.
11. Meier-Kriesche HU, Arndorfer JA, Kaplan B. The impact of body mass index on renal transplant outcomes: a significant independent risk factor for graft failure and patient death. *Transplantation* 2002; 73:70–74.
12. Howard RJ, Thai VB, Patton PR, et al. Obesity does not portend a bad outcome for kidney transplant recipients. *Transplantation* 2002; 73:53–55.
13. Hsu CY, McCulloch CE, Iribarren C, Darbinian J, Go AS. Body mass index and risk of end-stage renal disease. *Ann Intern Med.* 2006;144:21–28.
14. Ejerblad E, Fored M, Lindblad P, Fryzek J, McLaughlin J, Nyrén O. Obesity and risk for chronic renal failure. *J Am Soc Nephrol.* 2006; 17:1695–1702.
15. Kopple JD. Obesity and chronic kidney disease. *J Renal Nutr.* 2010; 20:29–30.
16. Griffin KA, Kramer H, Bidani AK. Adverse renal consequences of obesity. *Am J Physiol Renal Physiol.* 2008;294:685–696.
17. El Agroudy AE, Wafa EA, 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: 1381–1385.

18. Cheung CY, Chan YH, Chan HW, Chau KF, Li CS. Optimal body mass index that can predict long-term graft outcome in Asian renal transplant recipients. *Nephrology* 2010;15:259–265.
19. Chang SH, Coates TH, McDonald SP. Effects of body mass index at transplant on outcomes of kidney transplantation. *Transplantation* 2007;84:981–987.
20. Gore JL, Pham PT, Danovitch GM, et al. Obesity and outcome following renal transplantation. *Am J Transplant.* 2006;6:357–363.
21. Bernardi A, Biasia F, Pati T, Piva M, D'Angelo A, Bucciante G. Long-term protein intake control in kidney transplant recipients: effect in kidney graft function and in nutritional status. *Am J Kidney Dis.* 2003;41:146–152.
22. Olarte IG, Hawasli A. Kidney transplant complications and obesity. *Am J Surg.* 2009;197:424–426.
23. Abou-Jaoude MM, Nawfal N, Najm R, Honeidi M, Shaheen J, Almawi WY. Effect of pretransplantation body Mass index on allograft function and patient survival after renal transplantation. *Transplant Proc.* 2010;42:785–788.
24. Drafts HH, Anjum MR, Wynn JJ, Mulloy LL, Bowley JN, Humphries AL. The impact of pre-transplant obesity on renal transplant outcomes. *Clin Transplant.* 1997;11:493–496.
25. Yamamoto S, Hanley E, Hahn AB, et al. The impact of obesity in renal transplantation: an analysis of paired cadaver kidneys. *Clin Transplant.* 2002;16:252–256.
26. Jindal RM, Zawada ET Jr. Obesity and kidney transplantation. *Am J Kidney Dis.* 2004;43:943–952.
27. Gill IS, Hodge EE, Novick AC, et al. Impact of obesity on renal transplantation. *Transplant Proc.* 1993;25:1047–1048.
28. Modlin CS, Flechner SM, Goormastic M, et al. Should obese patients lose weight before receiving a kidney transplant. *Transplantation* 1997;64:599–604.
29. Massarweh NN, Clayton JL, Mangum CA, Florman SS, Slakey DP. High body mass index and short and long-term renal allograft survival in adults. *Transplantation* 2005;80: 1430–1434.
30. Chalmers L, Kaskel FJ, Bamgbola O. The role of obesity and its bioclinical correlates in the progression of chronic kidney disease. *Adv Chronic Kidney Dis.* 2006;13:352–364.
31. Wuerzner G, Prujim M, Maillard M, et al. Marked association between obesity and glomerular hyperfiltration: a cross-sectional study in an African population. *Am J Kidney Dis.* 2010; 56:303–312.