ORIGINAL ARTICLE

The Effect of Obesity and Body Mass Index on Post-transplant Renal Graft Function

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ABSTRACT

Objective: *The aim of this five-year study was to investigate the influence of body mass index (BMI) and obesity on post-transplant renal graft function.*
Methods: *This research monitored 500 patients of both genders who had received kidney transplants. Post-transplant measurements of the recipients' biochemical parameters, anthropometric parameters and renal function were performed. Two methods were also applied for assessing renal function: (a) the Cockcroft–Gault formula and (b) the serum creatinine clearance.*
Results: *Five years after transplantation, the patients showed an increase in obesity, accompanied by a lower glomerular filtration rate (GFR). Although the Cockcroft–Gault values were mild, the GFR percentage tended to decrease from the first to the fifth year, with higher serum creatinine levels.*
Conclusion: *The results reflected an increase in body weight and BMI in the five years after transplantation. This led to a lower GFR and subsequent graft damage during this time period.*

Keywords: Anthropometry, glomerular function, hyperfiltration, obesity, renal transplantation

INTRODUCTION

Obesity is a serious risk factor for kidney deterioration and failure. This is true for healthy people as well as those with chronic kidney disease (CKD) (1). The exact mechanisms whereby obesity may worsen or cause CKD remain unclear; however, it is believed that kidney damage is produced by haemodynamic and hormonal effects (2). After a renal graft, it is fairly common for patients to gain weight (3). This is largely due to their improved appetite, the disappearance of dietary restrictions stemming from haemodialysis and CKD, as well as the use of immunosuppressive medications and steroids (4). A wide range of studies have found that kidney graft recipients gain an average of 5–10 kg, which is directly linked to a lower patient survival rate as well as graft loss (5–7). A post-transplant weight gain contributes to an adverse cardiovascular risk profile and can play a role in the pathogenesis of renal graft dysfunction. In fact, it has been associated with post-transplant hypertension, diabetes, dyslipidaemia and ischaemic heart disease (8). Many studies have focussed on the short-term effects of the renal graft deterioration due to obesity and factors related to the post-transplant weight gain. However, there are no long-term data regarding the impact of this weight gain on renal graft function (9–12). Therefore, the aim of this research was to analyse the influence of the body mass index (BMI) and obesity on renal graft function in the five-year period after the transplant. For this purpose, the glomerular filtration rate (GFR) was calculated by two different methods: (a) the Cockcroft–Gault formula (CCr) and (b) the serum creatinine clearance (SCrCl).

SUBJECTS AND METHODS

The population sample consisted of 500 patients (278 men and 222 women), 16–80 years of age. All of the subjects had received renal grafts, and periodically visited the kidney transplant unit at the Virgen de las Nieves University Hospital in Granada, Spain. Patients were chosen because their visits to the hospital for post transplant follow-up and monitoring took place within the time period of our research (June 2010-15). Figure 1 shows their underlying disease.

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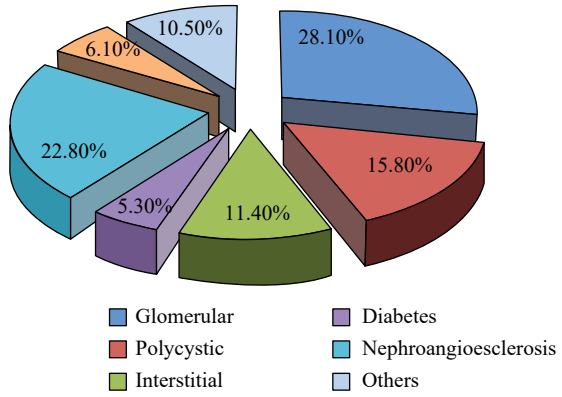

Figure 1: Causes of chronic kidney disease.

The participants' weight and height were measured with a Perperson 113481 scale stadiometer. Their BMI was then calculated as their body weight in kilograms divided by the square of their height in centimetres (weight/height^2). The resulting BMI was evaluated based on the World Health Organization (WHO) classification: (a) underweight (BMI < 18.5 kg/m^2); (b) normal weight (BMI = 18.5–24.99 kg/m^2); (c) overweight (BMI = 25–29.99 kg/m^2); (d) obese (BMI ≥ 30 kg/m^2). Renal function was assessed with the Cockcroft–Gault (CCr) formula and the serum creatinine clearance (SCrCl).

Accordingly the Cockcroft–Gault formula determined the GFR as follows:

In the case of males, normal values are 70 ± 14 mL/min/m^2, whereas for females, they are 60 ± 10 mL/min/m^2. Based on the decreasing GFR, values were classified as follows: (a) Mild decrease (60–41 mL/min); (b) Moderate decrease (40–21 mL/min); (c) Severe decrease (< 21 mL/min).

Serum creatinine clearance determines serum creatinine (SCr) levels in the blood by means of the kinetic Jaffé reaction, in which the creatinine reacts with alkaline picrate to produce a red-coloured complex. Serum creatinine levels were calculated by measuring an increase in absorbance at 512 nm. The rate of the dye formation (colour intensity) is directly proportional to the creatinine concentration in the specimen. A normal result is 0.7–1.3 mg/dL for males and 0.6–1.1 mg/dL for females, respectively. Generally speaking, normal values range from 0.8 to 1.4 mg/dL.

Before being discharged from the hospital, all of the participants were advised to consume 1.4–1.5 g/kg/day of diet protein (30–35 kcal/kg/day) during the first three months after the renal graft. Moreover, they were told that lipids should not exceed 30% of the total dietary intake and simple sugars should be avoided. After this three-month period, patients could reduce their protein consumption to 1 g/kg/day.

The GFR indicates stages of CKD as specified in the guidelines of the National Kidney Foundation (Table 1).

Table 1: Classification of the stages of chronic kidney disease in the guidelines of the National Kidney Foundation

Stage	Description	GFR (mL/min/1.73 m^2)
1	Kidney damage with a normal or higher GFR	≥ 90
2	Kidney damage with a slightly lower GFR	60–89
3	Mild-to-moderate decrease in GFR	30–59
4	Significant decrease in GFR	15–29
5	Kidney failure or dialysis	< 15

GFR = glomerular filtration rate.

Statistical analysis

The statistical analysis was performed with the software package IBM SPSS Statistics 20. Analysis of variance (ANOVA) was used to analyse the differences between the BMI and renal function. All data were expressed as frequencies, percentages and mean values + standard deviation. Values of $p < 0.05$ were regarded as statistically significant.

RESULTS

As can be observed in Table 2, the percentage of overweight patients remained more or less constant in the five-year period after the kidney transplant. However, there was an increase in the patients with obesity, whereas each year the number of normal-weight and underweight patients became steadily lower. In regard to renal function, Table 3 shows that even though Cockcroft–Gault values reflect a mild decrease, this percentage became progressively lower during the five-year time period. The same occurred with the SCr levels in the blood, where from the first to the fifth year, the values tended to increase until they exceeded our laboratory reference values (normal values of 0.8–1.4 mg/dL).

Table 2: Percentage of patients classified according to the WHO classification

BMI (kg/m^2)	Post-transplant years				
	1st*	2nd*	3rd*	4th*	5th*
Underweight: < 18.5	6.1%	5.9%	6.3%	5.3%	5.6%
Normal weight: 18.5–24.99	33.1%	32.5%	31.5%	32.6%	29.1%
Overweight: 25–29.99	34.2%	33.1%	33%	32.6%	33.6%
Obesity: ≥ 30	26.6%	28.5%	29.3%	29.6%	31.8%

*$p < 0.05$.

Table 3: Evolution of the renal function in five years by two methods: the Cockcroft–Gault formula (CCr; mL/min) and serum creatinine (SCr; mg/dL)

Filtration/year	Mean	SD
CCr 1st year	62.09	22.90
CCr 2nd year	61.61	24.36
CCr 3rd year	60.76	24.96
CCr 4th year	60.49	26.00
CCr 5th year	60.15	26.11
SCr 1st year	1.68	0.99
SCr 2nd year	1.77	1.33
SCr 3th year	1.80	1.35
SCr 4th year	1.79	1.20
SCr 5th year	1.78	1.15

*$p < 0.05$.
CCr = Cockcroft–Gault formula; SCr = serum creatinine; SD = standard deviation.

Even though creatinine levels remained elevated, when they are correlated with the BMI, they show a statistically significant increase with a higher BMI, especially in the first three years. However, the tendency was for creatinine levels to rise each year and remain high, especially in patients who are overweight and obese (Table 4).

Table 4: Five-year serum creatinine levels and the BMI (the WHO classification)

GFR	BMI (kg/m²)	N	Mean	SD
SCr 1st year*	Underweight: < 18.5	25	1.31	0.45
	Normal weight: 18.5–24.99	130	1.56	0.66
	Overweight: 25–29.99	175	1.59	0.53
	Obesity: ≥ 30	170	1.68	0.51
SCr 2nd year*	Underweight: < 18.5	25	1.30	0.39
	Normal weight: 18.5–24.99	135	1.55	0.65
	Overweight: 25–29.99	172	1.64	0.90
	Obesity: ≥ 30	168	1.72	0.55
SCr 3rd year*	Underweight: < 18.5	25	1.37	0.43
	Normal weight: 18.5–24.99	135	1.55	0.63
	Overweight: 25–29.99	172	1.65	0.73
	Obesity: ≥ 30	168	1.70	0.57
SCr 4th year	Underweight: < 18.5	25	1.49	0.73
	Normal weight: 18.5–24.99	137	1.56	0.71
	Overweight: 25–29.99	170	1.69	0.83
	Obesity: ≥ 30	168	1.73	0.63
SCr 5th year	Underweight: < 18.5	25	1.70	1.38
	Normal weight: 18.5–24.99	137	1.65	0.94
	Overweight: 25–29.99	170	1.80	1.26
	Obesity: ≥ 30	168	1.79	0.73

*$p < 0.05$.
BMI = body mass index; GFR = glomerular filtration rate; SCr = serum creatinine; SD = standard deviation.

Regarding the glomerular function (Table 5), instead of a decrease, the results obtained with the Cockcroft–Gault formula show a statistically significant increase when correlated with the BMI. During the five-year period after the transplant, the values generally reflect a mild-to-moderate loss decrease (60–41 mL/min).

Table 5: Evolution of the Cockcroft–Gault filtration (CCr) for years and the BMI (the WHO classification)

GFR	BMI (kg/m2)	N	Media	SD
CCr 1st year*	Underweight: < 18.5	25	55.21	16.46
	Normal weight: 18.5–24.99	130	58.37	21.35
	Overweight: 25–29.99	175	63	22.18
	Obesity: ≥ 30	170	67.82	22.79
CCr 2nd year*	Underweight: < 18.5	25	53.58	14.42
	Normal weight: 18.5–24.99	135	58.94	23.17
	Overweight: 25–29.99	172	63.33	21.93
	Obesity: ≥ 30	168	66.55	23.44
CCr 3rd year*	Underweight: < 18.5	25	51.56	13.20
	Normal weight: 18.5–24.99	135	57.87	22.57
	Overweight: 25–29.99	172	62.28	22.21
	Obesity: ≥ 30	168	68.04	26.09
CCr 4th year*	Underweight: < 18.5	25	48.99	14.44
	Normal weight: 18.5–24.99	137	58.12	23.30
	Overweight: 25–29.99	170	61.63	23.73
	Obesity: ≥ 30	168	68.63	28.25
CCr 5th year*	Underweight: < 18.5	25	48.66	18.78
	Normal weight: 18.5–24.99	137	56.56	25.11
	Overweight: 25–29.99	170	61.77	25.27
	Obesity: ≥ 30	168	66.65	28.79

*$p < 0.05$.
BMI = body mass index; GFR = glomerular filtration rate; CCr = Cockcroft–Gault filtration; SD = standard deviation.

DISCUSSION

The results of our study found that there was a high prevalence of obese and overweight patients, which steadily increased over the years. Many research studies have obtained a significant amount of experimental and clinical data that highlight the fact that obesity is an important risk factor for kidney disease (13, 14). Nevertheless, there is a scarcity of epidemiological data that directly point to obesity as a trigger or direct cause of kidney disease. Certain studies have focussed on the association between obesity and proteinuria in the general population (15, 16). However, very few epidemiological studies have quantified the possible relation between obesity and kidney failure (17, 18).

The prevalence of obesity throughout the world is soaring. As a result, there are a growing number of patients with cardiovascular disease, metabolic syndrome and CKD (19). As specified in the Kidney

Disease: Improving Global Outcomes (KDIGO) guidelines, there is an association between obesity, renal graft dysfunction, graft loss and mortality in the kidney transplant recipients. There is also a higher risk of perioperative complications, illnesses and concomitants (20, 21).

In this research, we assessed renal function in a sample of kidney graft recipients during the five-year post-transplant period with a particular focus on their BMI. Many studies have shown how weight gain after transplantation can have long-term adverse effects on the patients' renal function. However, in these studies, weight gain was mainly due to the metabolic syndrome, including hypertension, diabetes and hyperlipidaemia (22). Our study demonstrated that the weight gain in the critical five years after the transplant has an extremely negative impact on kidney function, which can be explained by the increased metabolic load stemming from the weight gain (23).

Factors that explain long-term weight gain in transplant recipients include their improved appetite, disappearance of dietary restrictions and limitations on physical activity due to immunosuppression (24). In regard to delayed graft function, both obesity and overweight prevent the kidney from maintaining a satisfactory filtration rate. This agrees with other studies that underline obesity as a risk factor that endangers normal kidney function (25).

Our research showed that a BMI > 25 kg/m^2 after the kidney transplant correlated with a higher percentage of graft dysfunction. Moreover, as the patients' BMI increased, there was a lower GFR, as measured by the CCr and the SCrCl methods. Since the SCrCl is a kidney damage marker, as the BMI increased, there was a greater kidney distress. This coincides with other studies that found that a higher BMI (26–28) was accompanied by higher creatinine levels, which signify a decrease in glomerular filtration (29, 30).

CONCLUSION

The results showed that five years after kidney transplantation, recipients experienced a weight gain and had a higher BMI. This factor contributed to graft dysfunction as reflected in a lower GFR and graft complications due to the kidney damage and a progressive loss of kidney function.

AUTHORS' NOTE

MS Adelina conceived paper, oversaw data collection, conducted data analysis, wrote manuscript and approved final version. NN Ana María participated in the study design, data analysis and interpretation, critically revised manuscript and approved final version. I García participated in the study design, data analysis, interpretation of data, revision of manuscript and approved final version. RF Castillo participated in the study design, interpretation of data, revision of manuscript and approved final version.

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