





Analysis of the Incidence of Cardiovascular Events in Post-Renal Transplant Patients Treated at a Specialized Service in Blumenau (SC)

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Abstract: **Introduction:** The main causes of death in kidney transplant recipients are infectious and cardiovascular diseases, both very common in Brazilian reality. In addition to conventional risk factors, specific risk factors may influence the development of cardiovascular disease in these patients. **Objectives:** To determine the incidence of cardiovascular events in post-kidney transplant patients, to analyze the cardiovascular risk factors in the first, third and fifth year post-transplant, and to characterize the profile of transplanted people in this study. **Methods:** Retrospective observational cohort study carried out in patients over 18 years of age who underwent kidney transplantation, from 2010 to 2016, followed up by the *Associação Renal Vida*, in Blumenau, Santa Catarina state, in Brazil. **Results:** The sample totaled 577 patients (392 males and 185 females); mean age group of 46.5 years; and 157 deaths, 43 of which were caused by cardiovascular diseases. It was observed that weight, body mass index and high-density lipoprotein (HDL) increased in the first year post-transplantation and stabilized after 36 months. Cholesterol increased in the first year, remained unchanged in the third and decreased in the fifth year. In addition, there was an increase in 64 patients with diabetes mellitus three years after transplantation, which is a risk factor for stroke, congestive heart failure (CHF), peripheral vascular disease and left ventricular hypertrophy in the third year after transplantation. Obesity was found to be a risk factor for acute myocardial infarction (AMI), since 60% of patients who had AMI had a body mass index > 30 kg/m². In contrast, HDL levels greater than 40 seem to be a protective factor for left ventricular hypertrophy in the third year and for stroke in the fifth year. Age younger than 50 years also seems to be a protective factor for AMI, stroke, CHF and left ventricular hypertrophy in the first 36 months and for CHF after 60 months, as 66.67% of patients with CHF in this period were older than 50 years old. **Conclusion:** It was observed that part of the risk factors for cardiovascular diseases is modifiable. Thus, maintaining healthy habits, especially over 50 years of age, seems to be a strategy that can improve cardiovascular risk and life expectancy after kidney transplantation.

Descriptors: Kidney Transplantation; Cardiovascular Diseases; Risk Factors.

INTRODUCTION

Cardiovascular diseases (CVD) are one of the most common complications and one of the leading known causes of death in patients after kidney transplantation, in addition to infectious diseases.^{1,2} According to the Ministry of Health,³ a person with chronic kidney disease (CKD) is any individual who, regardless of the cause, has, for

at least three consecutive months, a glomerular filtration rate (GFR) lower than 60 mL/min/1.73 m². In cases of patients with a GFR greater than or equal to 60 mL/min/1.73 m², CKD is considered to be associated with at least one marker of parenchymal renal damage or alteration in the imaging exam.

Although kidney transplantation substantially reduces cardiovascular risk in patients with CKD, CVD remains one of the most important causes of morbidity and mortality in transplant recipients.^{2,4} The procedure is indicated when there is end-stage chronic renal failure (CRF) associated with a TGF of less than 10 mL/min/1.73 m² or 15 mL/min/1.73 m² in diabetic patients or patients younger than 18 years of age.³

The relationship between CKD and CVD is complex, dynamic and multifactorial. In addition to both sharing risk factors, such as systemic arterial hypertension (SAH), diabetes mellitus (DM) and advanced age, there is a higher prevalence of traditional risk factors for CVD in patients with CKD.⁵ The variables to predict cardiovascular events in patients with CRF are: recipient and donor age; recipient and donor gender; ethnicity; etiology of CRI; time and type of dialysis (hemodialysis or peritoneal dialysis); type of transplant (kidney or kidney associated with another organ); human leukocyte antigen (HLA) compatibility; and ABO system. In addition, other important variables are cardiovascular risk factors, including: previous CVD, obesity/high body mass index (BMI), SAH, left ventricular hypertrophy (LVH), DM and pre-transplant smoking.⁶

Given the above, determining the incidence of cardiovascular events after a kidney transplant and the associated risk factors is important to inform the medical community about the need for CVD screening and prevention as part of the transplant evaluation. In addition, estimating a patient's cardiovascular risk can identify people at high risk and proactively intervene before the disease develops.¹

METHODS

This is a retrospective observational cohort study carried out in patients undergoing kidney transplant surgery at Hospital Santa Isabel, Blumenau, Santa Catarina, Brazil, and who are followed up by *Associação Renal Vida*, also based in Blumenau. All data collected are from the NephroSys® system, used by *Associação Renal Vida*.

Patients aged over 18 years, undergoing kidney transplantation, from January 2010 to January 2016, were included in the study, and data from the pre-transplant period, the first (12 months), the third (36 months) and the fifth (60 months) post-transplant year.

The variables analyzed were: recipient and donor age; recipient and donor gender (male, female); etiology of CRI; time and type of dialysis (hemodialysis or peritoneal dialysis); and type of transplant (kidney only or kidney associated with another organ). The cardiovascular risk factors analyzed were obtained through data from medical records previously completed by assistant physicians, namely: history of acute myocardial infarction (AMI), angina, arrhythmias, cerebrovascular accident (CVA), congestive heart failure (CHF), peripheral vascular disease (PVD), LVH, BMI, total cholesterol and high-density lipoprotein (HDL) level, SAH, DM and smoking before and after kidney transplantation, data according to medical records. In this study, cardiovascular events were considered: AMI, absent angina in the pre-transplant period, arrhythmias, stroke, CHF and death from cardiovascular events.⁵

The data were exported in an electronic spreadsheet, and the statistical part was analyzed later. Data analysis was outlined using Microsoft Excel 2016, Past 3.20 and Statistical Package for the Social Sciences (SPSS), version 21 (2012), a statistical package with different modules developed by IBM for the use of human and exact sciences professionals.

Data were organized into descriptive tables, containing mainly absolute and relative frequencies, proportion and mean estimates in the form of 95% confidence intervals, with the adopted significance level $P \leq 0.05$. For association between variables and comparison between groups, association tables and statistical tests were used. The Shapiro-Wilk test was used to verify data normality with respect to quantitative variables. That is, for any normality test, when $p > 0.05$, the null hypothesis is accepted, which states that the data distribution being tested is approximately normal or statistically normal. The McNemar test and the binomial test were used to compare the moments with each other, and the non-parametric paired test compared exactly two groups or moments. In cases where the expected frequency was at most five, the binomial test/equivalent test was used. The Friedman test made it possible to compare two dependent groups, whose measurement variable was quantitative, while the χ^2 test of independence made the association between possible risk factors and CVDs.

The study was approved by the Ethics in Human Beings Committee of the Universidade Regional de Blumenau, via Plataforma Brasil, under the Certificate of Presentation of Ethical Appreciation (CAAE) 29698320.2.0000.5370. Patients who participated in the database signed the Free and Informed Consent Term (FICT) about the study in question.

RESULTS

A sample of 577 patients was used in the study. It is noteworthy that, in most of the quantitative variables measured, there was the occurrence of missing or incomplete data, resulting in a lack of normality in most situations. Thus, the median was used for the analysis of the measure of central tendency and quartile deviation for the measure of variability.

According to Table 1, the profile of the 577 patients was verified. In the sample, 392 patients were male (67.9%) and 185 were female (32.1%). As for age, the mean was 46.5 ± 13.7 years, with 47.19 ± 13.93 years for males and 45.06 ± 13.12 years for females. In absolute numbers, 83 participants were aged between 18 and 30 years (14.4%); 162, between 30 and 45 years old (28.1%); 222, between 45 and 60 years (38.5%); and 110, between 60 and 81 years old (19.1%).

A total of 157 deaths (27.2%) were obtained, of which 43 were due to CVD (27.4%), 88 due to non-cardiovascular diseases (56.1%) and 26 due to unknown or undetermined reasons (16.6%). Regarding the period of death, 47 occurred within one year after transplantation (29.9%), 36 between the first and third year (22.9%) and 74 between the third and fifth year after transplantation (47.1%).

As for smoking in the pre-transplant period, 385 patients were non-smokers (66.7%), while 192 were (33.3%). In the post-transplant period, 538 patients were non-smokers (93.2%) and 39 were smokers (6.8%).

Regarding the profile of kidney donors, 342 were male (59.3%) and 235 were female (40.7%), with a mean age of 41.41 ± 13.07 years. The age range variation included six donors aged between 2 and 12 years (1%); 51, between 12 and 22 years old (8.8%); 91, between 22 and 32 years old (15.8%); 96, between 32 and 42 years old (16.6%); 175, between 42 and 52 years old (30.3%); 149, between 52 and 62 years old (25.8%); six, between 62 and 72 years (1%); one, between 72 and 82 years (0.2%); and two who did not have their ages revealed/not informed in the medical records.

It was observed that, in relation to DM, from the pre-transplant period to the first year after renal transplantation, there was an increase of 60 patients who developed DM (11.9%). That is, before the transplant they did not have DM and after a year they started to have the disease. This increase in the number of cases of patients with DM was considered significant according to the McNemar test, as $P < 0.05$. When analyzing the pre-transplant period and three years after kidney transplantation, 64 new cases of DM (14.35%) were obtained – significant data, according to the McNemar test, as $P < 0.05$. From the first to the third year after kidney transplantation, there was an increase of 14 patients with DM (3.14%), but this data was not considered significant, as $P > 0.05$. From the third to the fifth year, there was also an increase in DM cases: there were 11 new cases (3.38%), which was seen as significant according to the McNemar test, as $P < 0.05$.

When analyzing the influence of the presence or absence of SAH in the pre-transplantation periods, 12, 36 and 60 months after kidney transplantation, none of the data was significant, as all results obtained $P > 0.05$.

When analyzing the influence of the presence or absence of smoking in the pre-transplantation periods, 12, 36 and 60 months after kidney transplantation, none of the data was significant either, with $P > 0.05$.

The pre-transplant, first, third and fifth year post-transplant moments were analyzed in terms of quantitative factors (weight, BMI, total cholesterol and HDL), and all tests showed significant differences ($P < 0.05$). It was observed that weight, BMI and HDL increased significantly in their values in the first year post-transplant and remained at the same level in the third and fifth year post-transplant. The total cholesterol level increased significantly in the first year, remained in the third year and presented lower values in the fifth year, according to the median.

Table 2 shows the associations between pre- and post-transplant moments (12, 36 and 60 months) considering the CVD results of post-renal transplant patients. It is noted that most diseases did not present significant differences between the moments (they obtained $P > 0.05$), with the exception of cardiovascular events of AMI, PVD and LVH, which had some marked differences in their results, according to the McNemar test, where $P < 0.05$. In the case of AMI, it was found that, of the nine patients who had an AMI prior to transplantation (1.79%), none of them repeated the event one year after transplantation. As for PVD, 10 patients developed the disease in the first year after transplantation (1.98%), and this result was also significant. In the case of LVH, in the first year after transplantation, 29 patients no longer had it (5.75%) against four who acquired it (0.79%). Comparing the pre-transplantation time with the third year post-transplantation, there were 27 transplant patients who no longer had LVH (6.04%) against seven who acquired it (1.57%).

Table 3 shows the association between risk factors and cardiovascular events in the third year after kidney transplantation (36 months). Of the correlations analyzed, a significant finding with $P < 0.05$ was that 418 patients had no AMI, of which 321 had a BMI $< 30 \text{ kg/m}^2$ (76.79%) and 97 BMI $> 30 \text{ kg/m}^2$ (23.21%). During this period, five patients had an AMI, whereas three of them had a BMI $> 30 \text{ kg/m}^2$ (60%) and two had a BMI $< 30 \text{ kg/m}^2$ (40%). It was thus seen that, for an AMI to occur, having a BMI $> 30 \text{ kg/m}^2$ (obesity) is a probable risk factor.

At 36 months post-transplant, there was a relationship between DM and cardiovascular events, with a significance of $P < 0.05$ in cases of stroke, CHF and LVH. For example, in stroke, of the 443 patients who did not have the cerebrovascular event, 316 did not have DM (71.33%) and 127 did (28.67%). On the other hand, of the four transplant patients who suffered a stroke, three of them had DM (75%) and only one did not have the hyperglycemic disease (25%). Analyzing the CHF, 437 patients did not have this insufficiency, of which 313 were not diabetic (71.62%) and 124 were (28.38%). Of the 10 individuals who developed CHF, six of them had DM (60%) and four were not diabetic (40%). In the case of LVH, it was observed that 436 patients did not develop hypertrophy, including 313 non-diabetics (71.79%) and 123 diabetics (28.21%). On the other hand, of the 11 transplant patients who developed LVH, seven had DM (63.64%) and only four did not (36.36%).

Up to 36 months post-transplant, age ≥ 50 years of renal recipients has great statistical significance in the cardiovascular events of AMI, CVA, CHF and LVH, with data of $P < 0.05$. All patients with AMI were aged ≥ 50 years (five individuals). Among the other 443 individuals without AMI, 62.3% (276 patients) were < 50 years and 37.7% (167) ≥ 50 years. For stroke, in the third year post-transplant, it was also observed that all who had a stroke (total of four patients) were also aged ≥ 50 years. In comparison, of the 444 transplant recipients who did not have a stroke, 276 were aged < 50 years (62.16%) and 168 ≥ 50 years (37.84%). Regarding CHF, 438 patients did not develop this CVD, of which 273 were aged < 50 years (62.33%) and 165 ≥ 50 years (37.67%), however, 10 patients developed CHF, seven of them aged ≥ 50 years (70%) and three aged < 50 years (30%). In LVH, it was found that 437 transplant patients did not have hypertrophy – 273 aged < 50 years (62.47%) and 164 ≥ 50 years (37.53%). A total of 11 transplant patients developed LVH, of which eight were aged ≥ 50 years (72.73%) and three < 50 years (27.27%). Also, in this regard, age ≥ 50 years seems to influence the occurrence of arrhythmia, since, of five patients who developed arrhythmia, four were aged ≥ 50 years (80%) and only one was < 50 years (20%). It is also considered that 443 patients did not develop arrhythmia, among which 275 were aged < 50 years (62.08%) and 168 ≥ 50 years (37.92%). Thus, it is approximated that, of the 172 patients aged ≥ 50 years, five had AMI, four had stroke, seven had CHF, eight developed LVH and four arrhythmia in the third year after transplantation.

Also, in the third year after kidney transplantation, HDL levels > 40 seem to be a likely protective factor for LVH. It was seen that, of 407 patients who did not have LVH, 323 had HDL > 40 (79.36%) and 84 HDL < 40 (20.64%). In comparison, of the 11 transplanted with LVH, six of them had HDL > 40 (54.55%), while five had HDL < 40 , which is a significant finding, with $P < 0.05$.

Table 4 shows the analysis of CVD in the fifth year after kidney transplantation (60 months). By relating stroke to the patients' HDL cholesterol level, the following results were obtained: 304 patients had no stroke in that period, of which 239 had HDL > 40 (78.62%) and 65 HDL < 40 (21.38%). On the other hand, only one patient had a stroke, with this single patient having an HDL < 40 , which is a significant finding, as $P < 0.05$. Therefore, according to the statistical test, HDL levels > 40 seem to be a likely protective factor for stroke.

Table 1. Profile in the form of absolute, relative, mean, median frequency distributions and estimates of proportion and mean of the characteristics of patients undergoing kidney transplantation.

Characteristics	n (%) (n = 577)	CI95%
Gender		
Male	392 (67,9%)	(64,13–71,75)
Female	185 (32,1%)	(28,25–35,87)
Age (years):		
(i) Female (n = 185)		
(Mean \pm SD)	(45,06 \pm 13,12)	(43,17–46,96)
(Median \pm QD)	(45 \pm 11)	
(ii) Male (n = 392)		
(Mean \pm SD)	(47,19 \pm 13,93)	(45,81–48,57)
(Median \pm QD)	(48 \pm 11)	
(iii) Both (n = 577)		
(Mean \pm SD)	(46,51 \pm 13,7)	(45,39–47,63)
(Median \pm QD)	(48 \pm 11)	
Age range (years)		
18 - 30	83 (14,4%)	(11,52–17,25)
30 - 45	162 (28,1%)	(24,41–31,74)
45 - 60	222 (38,5%)	(34,51–42,44)
60 - 81	110 (19,1%)	(15,86–22,27)

Continue...

Table 1. Continuation...

Characteristics	n (%) (n = 577)	CI95%
ABO typing		
A	254 (44%)	(39,97–48,07)
AB	19 (3,3%)	(1,84–4,75)
B	44 (7,6%)	(5,46–9,79)
O	260 (45,1%)	(41–49,12)
Diagnosis		
Undetermined	150 (26%)	(22,42–29,58)
Diabetes	107 (18,5%)	(15,37–21,72)
Arterial hypertension	108 (18,7%)	(15,53–21,9)
Polycystic kidney disease	54 (9,4%)	(6,98–11,74)
Lithiasis	21 (3,6%)	(2,11–5,17)
Glomerulopathy	73 (12,7%)	(9,94–15,36)
Malformation	23 (4%)	(2,39–5,58)
Interstitial nephritis	11 (1,9%)	(0,79–3,02)
Retransplant	19 (3,3%)	(1,84–4,75)
Others	11 (1,9%)	(0,79–3,02)
Type of dialysis		
Preemptive	18 (3,1%)	(1,7–4,54)
Hemodialysis	537 (93,1%)	(91–95,14)
CAPD	22 (3,8%)	(2,25–5,38)
Death		
No	417 (72,3%)	(68,62–75,92)
Yes	157 (27,2%)	(23,58–30,84)
Not informed	3 (0,5%)	(0–1,11)
Death from cardiovascular disease (considering the total number of deaths equal to 157)		
No	88 (56,1%)	(48,29–63,81)
Yes	43 (27,4%)	(20,41–34,36)
Unknown	26 (16,6%)	(10,75–22,38)
Pre-transplant smoking		
No	385 (66,7%)	(62,88–70,57)
Yes	192 (33,3%)	(29,43–37,12)
Post-transplant smoking		
No	538 (93,2%)	(91,19–95,29)
Yes	39 (6,8%)	(4,71–8,81)
Donor information		
Gender		
Male	342 (59,3%)	(55,26–63,28)
Female	235 (40,7%)	(36,72–44,74)
Age (years)		
(i) Female (n = 235)		
(Mean ± SD)	(43,23 ± 12,1)	(41,68–44,78)
(Median ± QD)	(46 ± 8,5)	
(ii) Male (n = 340)*		
(Mean ± SD)	(40,03 ± 13,72)	(38,57–41,49)
(Median ± QD)	(43 ± 12,5)	
(iii) Both (n = 574)*		
(Mean ± SD)	(41,41 ± 13,07)	(40,34–42,48)
(Median ± QD)	(44 ± 10,5)	
Donor age group (years) (10-year intervals)		
2 - 12	6 (1%)	(0,21–1,87)
12 - 22	51 (8,8%)	(6,52–11,15)
22 - 32	91 (15,8%)	(12,8–18,75)
32 - 42	96 (16,6%)	(13,6–19,68)
42 - 52	175 (30,3%)	(26,58–34,08)
52 - 62	149 (25,8%)	(22,25–29,39)
62 - 72	6 (1%)	(0,21–1,87)
72- 82	1 (0,2%)**	(0–0,51)
Not informed	2 (0,3%)*	(0–0,83)

CI95%: confidence intervals for proportion with 95% confidence; SD: standard deviation; QD: quartile deviation; CAPD: continuous ambulatory peritoneal dialysis; *two male donors did not inform their age; **one donor aged 74 years.

Table 2. Comparison between pre- and post-transplant moments (12, 36 and 60 months) considering the results of cardiovascular diseases in post-renal transplant patients. (Cardiovascular diseases: AMI, angina, arrhythmia, CVA, CHF, PVD and LVH)*.

Illnesses / moments	No	Yes	No (%)	Yes (%)	Total pairs	P	Test
AMI							
Pre × 12m							
Yes	9	0	1,79	0		0,0039	Binomial
No	495	0	98,21	0	504		
12 m × 36 m							
Yes	0	0	0	0		0,0625	Binomial
No	442	5	98,88	1,12	447		
36 m × 60 m							
Yes	4	0	1,23	0		0,3750	Binomial
No	321	1	98,47	0,31	326		
Pre × 36 m							
Yes	6	1	1,34	0,22		0,7518	McNemar
No	436	4	97,54	0,89	447		
Pre × 60 m							
Yes	5	0	1,54	0		0,2188	Binomial
No	319	1	98,15	0,31	325		
Angina							
Pre × 12 m							
Yes	0	0	0	0		0,1250	Binomial
No	500	4	99,21	0,79	504		
12 m × 36 m							
Yes	2	0	0,45	0		0,5000	Binomial
No	444	0	99,55	0	446		
36 m × 60 m							
Yes	0	0	0	0		1,0000	Binomial
No	324	1	99,69	0,31	325		
Pre × 36 m							
Yes	0	0	0	0		1,0000	Binomial
No	446	0	100	0	446		
Pre × 60 m							
Yes	0	0	0	0		1,0000	Binomial
No	324	1	99,69	0,31	325		
Arritmia							
Pre × 12 m							
Yes	3	4	0,6	0,79		1,0000	Binomial
No	494	3	98,02	0,6	504		
12 m × 36 m							
Yes	1	4	0,22	0,89		1,0000	Binomial
No	441	1	98,66	0,22	447		
36 m × 60 m							
Yes	1	2	0,31	0,61		0,6250	Binomial
No	320	3	98,16	0,92	326		
Pre × 36 m							
Yes	3	4	0,67	0,89		0,6250	Binomial
No	439	1	98,21	0,22	447		
Pre × 60 m							
Yes	2	2	0,62	0,62		1,0000	Binomial
No	318	3	97,85	0,92	325		
CVA							
Pre × 12 m							
Yes	13	3	2,58	0,6		0,2636	McNemar
No	481	7	95,44	1,39	504		
12 m × 36 m							
Yes	2	1	0,45	0,22		1,0000	Binomial
No	441	3	98,66	0,67	447		
36 m × 60 m							
Yes	2	0	0,61	0		1,0000	Binomial
No	323	1	99,08	0,31	326		

Continue...

Table 2. Continuation...

Illnesses / moments	No	Yes	No (%)	Yes (%)	Total pairs	P	Test
Pre × 36 m							
Yes	9	1	2,01	0,22		0,1489	McNemar
No	434	3	97,09	0,67	447		
Pre × 60 m							
Yes	5	0	1,54	0		0,2188	Binomial
No	319	1	98,15	0,31	325		
CHF	No	Yes	No (%)	Yes (%)	Total pairs	P	Test
Pre × 12 m							
Yes	2	6	0,4	1,19		0,4531	Binomial
No	491	5	97,42	0,99	504		
12 m × 36 m							
Yes	1	9	0,22	2,01		1,0000	Binomial
No	436	1	97,54	0,22	447		
36 m × 60 m							
Yes	0	9	0	2,76		1,0000	Binomial
No	317	0	97,24	0	326		
Pre × 36 m							
Yes	2	6	0,45	1,34		0,6875	Binomial
No	435	4	97,32	0,89	447		
Pre × 60 m							
Yes	1	5	0,31	1,54		0,3750	Binomial
No	315	4	96,92	1,23	325		
PVD	No	Yes	No (%)	Yes (%)	Total pairs	P	Test
Pre × 12 m							
Yes	2	3	0,4	0,6		0,0433	McNemar
No	489	10	97,02	1,98	504		
12 m × 36 m							
Yes	6	6	1,34	1,34		0,5078	Binomial
No	432	3	96,64	0,67	447		
36 m × 60 m							
Yes	1	5	0,31	1,53		0,6250	Binomial
No	317	3	97,24	0,92	326		
Pre × 36 m							
Yes	3	2	0,67	0,45		0,3428	McNemar
No	435	7	97,32	1,57	447		
Pre × 60 m							
Yes	1	1	0,31	0,31		0,0703	Binomial
No	316	7	97,23	2,15	325		
LVH	No	Yes	No (%)	Yes (%)	Total pairs	P	Test
Pre × 12 m							
Yes	29	5	5,75	0,99		0,0000	McNemar
No	466	4	92,46	0,79	504		
12 m × 36 m							
Yes	1	7	0,22	1,57		0,3750	Binomial
No	435	4	97,32	0,89	447		
36 m × 60 m							
Yes	1	5	0,31	1,53		0,0703	Binomial
No	313	7	96,01	2,15	326		
Pre × 36 m							
Yes	27	4	6,04	0,89		0,0011	McNemar
No	409	7	91,5	1,57	447		
Pre × 60 m							
Yes	20	1	6,15	0,31		0,1508	McNemar
No	293	11	90,15	3,38	325		

P: P-value of McNemar's test, nonparametric test of paired association (of nominal variables). Note the cases that show changes between the first and second results that appear in cells A and D. An individual allocated in cell A went from yes to no, and in cell D, from no to yes. McNemar's test takes into account only the changes that have occurred (A and D). If $P < 0.05$, then there are significant differences between moments; *in case of expected frequencies of houses A and D less than or equal to 5, the binomial test is used (equivalent test); AMI: acute myocardial infarction; CVA: cerebrovascular accident; CHF: congestive heart failure; PVD: peripheral vascular disease; LVH: left ventricular hypertrophy.

Table 3. Association of possible risk factors with cardiovascular diseases in post-kidney transplant patients in the third year after kidney transplantation.

Factors	AMI		c2	P
	Absent	Present		
HAS	No	122 (27,54%)	1,89228	0,16894
	Yes	321 (72,46%)		
DM	No	315 (71,27%)	2,34352	0,12580
	Yes	127 (28,73%)		
BMI (>30=1)	No	321 (76,79%)	3,70548	0,05423
	Yes	97 (23,21%)		
Cholesterol (>=190=1)	No	256 (61,69%)	0,70259	0,40191
	Yes	159 (38,31%)		
HDL (<=40=1)	No	325 (78,69%)	0,00504	0,94341
	Yes	88 (21,31%)		
Post-T-Post smoking	No	415 (93,68%)	0,33710	0,56151
	Yes	28 (6,32%)		
Age (receptor ≥50=1)	No	276 (62,3%)	8,11381	0,00439
	Yes	167 (37,7%)		
Factors	Angina		c2	P
	Absent	Present		
HAS	No	122 (27,29%)	-	-
	Yes	325 (72,71%)		
DM	No	316 (70,85%)	-	-
	Yes	130 (29,15%)		
BMI (>30=1)	No	322 (76,3%)	-	-
	Yes	100 (23,7%)		
Cholesterol (>=190=1)	No	260 (62,05%)	-	-
	Yes	159 (37,95%)		
HDL (<=40=1)	No	328 (78,66%)	-	-
	Yes	89 (21,34%)		
Post-T-Post smoking	No	419 (93,74%)	-	-
	Yes	28 (6,26%)		
Age (receptor ≥50=1)	No	276 (61,74%)	-	-
	Yes	171 (38,26%)		
Factors	Arritmia		c2	P
	Absent	Present		
HAS	No	121 (27,31%)	0,13346	0,71487
	Yes	322 (72,69%)		
DM	No	314 (71,04%)	0,29221	0,58881
	Yes	128 (28,96%)		
BMI (>30=1)	No	319 (76,32%)	0,03715	0,84716
	Yes	99 (23,68%)		
Cholesterol (>=190=1)	No	256 (61,69%)	0,70259	0,40191
	Yes	159 (38,31%)		
HDL (<=40=1)	No	326 (78,93%)	1,05688	0,30393
	Yes	87 (21,07%)		
Post-T-Post smoking	No	415 (93,68%)	0,33710	0,56151
	Yes	28 (6,32%)		
Age (receptor ≥50=1)	No	275 (62,08%)	3,70083	0,05439
	Yes	168 (37,92%)		
Factors	CVA		c2	P
	Absent	Present		
HAS	No	122 (27,48%)	1,51042	0,21908
	Yes	322 (72,52%)		
DM	No	316 (71,33%)	4,12598	0,04223
	Yes	127 (28,67%)		
BMI (>30=1)	No	321 (76,61%)	1,55430	0,21250
	Yes	98 (23,39%)		

Continue...

Table 3. Continuation...

Cholesterol (>=190=1)	No	258 (62,02%)	2 (50%)	0,24270	0,62227
	Yes	158 (37,98%)	2 (50%)		
HDL (<=40=1)	No	327 (78,99%)	2 (50%)	1,98615	0,15874
	Yes	87 (21,01%)	2 (50%)		
Post-T-Post smoking	No	416 (93,69%)	4 (100%)	0,26907	0,60396
	Yes	28 (6,31%)	0 (0%)		
Age (receptor ≥50=1)	No	276 (62,16%)	0 (0%)	6,47643	0,01093
	Yes	168 (37,84%)	4 (100%)		
Factors		CHF		c2	P
		Absent	Present		
HAS	No	120 (27,4%)	2 (20%)	0,26997	0,60335
	Yes	318 (72,6%)	8 (80%)		
DM	No	313 (71,62%)	4 (40%)	4,74067	0,02946
	Yes	124 (28,38%)	6 (60%)		
BMI (>30=1)	No	316 (76,33%)	7 (77,78%)	0,01025	0,91936
	Yes	98 (23,67%)	2 (22,22%)		
Cholesterol (>=190=1)	No	255 (62,04%)	5 (55,56%)	0,15722	0,69173
	Yes	156 (37,96%)	4 (44,44%)		
HDL (<=40=1)	No	322 (78,73%)	7 (77,78%)	0,00475	0,94505
	Yes	87 (21,27%)	2 (22,22%)		
Post-T-Post smoking	No	410 (93,61%)	10 (100%)	0,68189	0,40894
	Yes	28 (6,39%)	0 (0%)		
Age (receptor ≥50=1)	No	273 (62,33%)	3 (30%)	4,32009	0,03766
	Yes	165 (37,67%)	7 (70%)		
Factors		PVD		c2	P
		Absent	Present		
HAS	No	118 (26,88%)	4 (44,44%)	1,37313	0,24127
	Yes	321 (73,12%)	5 (55,56%)		
DM	No	308 (70,32%)	9 (100%)	3,76669	0,05228
	Yes	130 (29,68%)	0 (0%)		
BMI (>30=1)	No	318 (76,81%)	5 (55,56%)	2,20468	0,13759
	Yes	96 (23,19%)	4 (44,44%)		
Cholesterol (>=190=1)	No	255 (62,04%)	5 (55,56%)	0,15722	0,69173
	Yes	156 (37,96%)	4 (44,44%)		
HDL (<=40=1)	No	323 (78,97%)	6 (66,67%)	0,79583	0,37234
	Yes	86 (21,03%)	3 (33,33%)		
Post-T-Post smoking	No	411 (93,62%)	9 (100%)	0,61230	0,43392
	Yes	28 (6,38%)	0 (0%)		
Age (receptor ≥50=1)	No	272 (61,96%)	4 (44,44%)	1,14379	0,28485
	Yes	167 (38,04%)	5 (55,56%)		
Factors		LVH		c2	P
		Absent	Present		
HAS	No	119 (27,23%)	3 (27,27%)	0,00001	0,99756
	Yes	318 (72,77%)	8 (72,73%)		
DM	No	313 (71,79%)	4 (36,36%)	6,52849	0,01062
	Yes	123 (28,21%)	7 (63,64%)		
BMI (>30=1)	No	316 (76,7%)	7 (63,64%)	1,01272	0,31425
	Yes	96 (23,3%)	4 (36,36%)		
Cholesterol (>=190=1)	No	252 (61,61%)	8 (72,73%)	0,56102	0,45385
	Yes	157 (38,39%)	3 (27,27%)		
HDL (<=40=1)	No	323 (79,36%)	6 (54,55%)	3,93579	0,04727
	Yes	84 (20,64%)	5 (45,45%)		
Post-T-Post smoking	No	410 (93,82%)	10 (90,91%)	0,15533	0,69349
	Yes	27 (6,18%)	1 (9,09%)		
Age (receptor ≥50=1)	No	273 (62,47%)	3 (27,27%)	5,62040	0,01775
	Yes	164 (37,53%)	8 (72,73%)		

P: P-value of the χ^2 independence test; χ^2 : test statistics; SAH: systemic arterial hypertension; DM: diabetes mellitus; BMI: body mass index; HDL: high density lipoprotein; T-post: post-transplant; AMI: acute myocardial infarction; CVA: stroke; CHF: congestive heart failure; PVD: peripheral vascular disease; LVH: left ventricular hypertrophy.

Table 4. Association of possible risk factors with cardiovascular diseases in post-kidney transplant patients in the fifth year after kidney transplantation.

Factors		AMI		c ²	P
		Absent	Present		
HAS	No	95 (29,23%)	0 (0%)	0,41252	0,52069
	Yes	230 (70,77%)	1 (100%)		
DM	No	226 (69,54%)	1 (100%)	0,43747	0,50835
	Yes	99 (30,46%)	0 (0%)		
BMI (>30=1)	No	240 (77,67%)	1 (100%)	0,28723	0,59200
	Yes	69 (22,33%)	0 (0%)		
Cholesterol (>=190=1)	No	201 (66,12%)	1 (100%)	0,51158	0,47446
	Yes	103 (33,88%)	0 (0%)		
HDL (<=40=1)	No	238 (78,29%)	1 (100%)	0,27706	0,59864
	Yes	66 (21,71%)	0 (0%)		
Post-T-Post smoking	No	307 (94,46%)	1 (100%)	0,05862	0,80869
	Yes	18 (5,54%)	0 (0%)		
Age (receptor ≥50=1)	No	207 (63,69%)	1 (100%)	0,56905	0,45064
	Yes	118 (36,31%)	0 (0%)		
Factors		Angina		c ²	P
		Absent	Present		
HAS	No	95 (29,23%)	0 (0%)	0,41252	0,52069
	Yes	230 (70,77%)	1 (100%)		
DM	No	227 (69,85%)	0 (0%)	2,29998	0,12938
	Yes	98 (30,15%)	1 (100%)		
BMI (>30=1)	No	240 (77,67%)	1 (100%)	0,28723	0,59200
	Yes	69 (22,33%)	0 (0%)		
Cholesterol (>=190=1)	No	202 (66,45%)	0 (0%)	1,96762	0,16070
	Yes	102 (33,55%)	1 (100%)		
HDL (<=40=1)	No	238 (78,29%)	1 (100%)	0,27706	0,59864
	Yes	66 (21,71%)	0 (0%)		
Post T-post smoking	No	307 (94,46%)	1 (100%)	0,05862	0,80869
	Yes	18 (5,54%)	0 (0%)		
Age (receptor ≥50=1)	No	208 (64%)	0 (0%)	1,76814	0,18361
	Yes	117 (36%)	1 (100%)		
Factors		Arritmia		c ²	P
		Absent	Present		
HAS	No	93 (28,97%)	2 (40%)	0,28997	0,59024
	Yes	228 (71,03%)	3 (60%)		
DM	No	223 (69,47%)	4 (80%)	0,25814	0,61140
	Yes	98 (30,53%)	1 (20%)		
BMI (>30=1)	No	237 (77,7%)	4 (80%)	0,01497	0,90260
	Yes	68 (22,3%)	1 (20%)		
Cholesterol (>=190=1)	No	199 (66,33%)	3 (60%)	0,08820	0,76648
	Yes	101 (33,67%)	2 (40%)		
HDL (<=40=1)	No	235 (78,33%)	4 (80%)	0,00806	0,92848
	Yes	65 (21,67%)	1 (20%)		
Post T-post smoking	No	303 (94,39%)	5 (100%)	0,29676	0,58592
	Yes	18 (5,61%)	0 (0%)		
Age (receptor ≥50=1)	No	206 (64,17%)	2 (40%)	1,24584	0,26435
	Yes	115 (35,83%)	3 (60%)		
Factors		CVA		c ²	P
		Absent	Present		
HAS	No	95 (29,23%)	0 (0%)	0,41252	0,52069
	Yes	230 (70,77%)	1 (100%)		
DM	No	226 (69,54%)	1 (100%)	0,43747	0,50835
	Yes	99 (30,46%)	0 (0%)		
BMI (>30=1)	No	240 (77,67%)	1 (100%)	0,28723	0,59200
	Yes	69 (22,33%)	0 (0%)		

Continue...

Table 4. Continuation...

Cholesterol (>=190=1)	No	201 (66,12%)	1 (100%)	0,51158	0,47446
	Yes	103 (33,88%)	0 (0%)		
HDL (<=40=1)	No	239 (78,62%)	0 (0%)	3,63312	0,05664
	Yes	65 (21,38%)	1 (100%)		
Post T-post smoking	No	307 (94,46%)	1 (100%)	0,05862	0,80869
	Yes	18 (5,54%)	0 (0%)		
Age (receptor ≥50=1)	No	208 (64%)	0 (0%)	1,76814	0,18361
	Yes	117 (36%)	1 (100%)		
Factors	CHF			c²	P
		Absent	Present		
HAS	No	93 (29,34%)	2 (22,22%)	0,21457	0,64321
	Yes	224 (70,66%)	7 (77,78%)		
DM	No	223 (70,35%)	4 (44,44%)	2,77679	0,09564
	Yes	94 (29,65%)	5 (55,56%)		
BMI (>30=1)	No	236 (77,89%)	5 (71,43%)	0,16497	0,68462
	Yes	67 (22,11%)	2 (28,57%)		
Cholesterol (>=190=1)	No	198 (66,67%)	4 (50%)	0,96751	0,32530
	Yes	99 (33,33%)	4 (50%)		
HDL (<=40=1)	No	232 (78,11%)	7 (87,5%)	0,40469	0,52468
	Yes	65 (21,89%)	1 (12,5%)		
Post T-post smoking	No	299 (94,32%)	9 (100%)	0,54091	0,46206
	Yes	18 (5,68%)	0 (0%)		
Age (receptor ≥50=1)	No	205 (64,67%)	3 (33,33%)	3,72088	0,05374
	Yes	112 (35,33%)	6 (66,67%)		
Factors	PVD			c²	P
		Absent	Present		
HAS	No	92 (28,93%)	3 (37,5%)	0,27751	0,59834
	Yes	226 (71,07%)	5 (62,5%)		
DM	No	221 (69,5%)	6 (75%)	0,11176	0,73815
	Yes	97 (30,5%)	2 (25%)		
BMI (>30=1)	No	235 (77,56%)	6 (85,71%)	0,26306	0,60803
	Yes	68 (22,44%)	1 (14,29%)		
Cholesterol (>=190=1)	No	198 (66,67%)	4 (50%)	0,96751	0,32530
	Yes	99 (33,33%)	4 (50%)		
HDL (<=40=1)	No	233 (78,45%)	6 (75%)	0,05472	0,81505
	Yes	64 (21,55%)	2 (25%)		
Post T-post smoking	No	300 (94,34%)	8 (100%)	0,47929	0,48874
	Yes	18 (5,66%)	0 (0%)		
Age (receptor ≥50=1)	No	203 (63,84%)	5 (62,5%)	0,00604	0,93808
	Yes	115 (36,16%)	3 (37,5%)		
Factors	LVH			c²	P
		Absent	Present		
HAS	No	93 (29,62%)	2 (16,67%)	0,93888	0,33257
	Yes	221 (70,38%)	10 (83,33%)		
DM	No	218 (69,43%)	9 (75%)	0,16978	0,68031
	Yes	96 (30,57%)	3 (25%)		
BMI (>30=1)	No	233 (77,93%)	8 (72,73%)	0,16574	0,68393
	Yes	66 (22,07%)	3 (27,27%)		
Cholesterol (>=190=1)	No	194 (66,21%)	8 (66,67%)	0,00107	0,97394
	Yes	99 (33,79%)	4 (33,33%)		
HDL (<=40=1)	No	229 (78,16%)	10 (83,33%)	0,18216	0,66952
	Yes	64 (21,84%)	2 (16,67%)		
Post T-post smoking	No	296 (94,27%)	12 (100%)	0,72810	0,39350
	Yes	18 (5,73%)	0 (0%)		
Age (receptor ≥50=1)	No	203 (64,65%)	5 (41,67%)	2,64361	0,10397
	Yes	111 (35,35%)	7 (58,33%)		

P: P-value of the χ^2 independence test; χ^2 : test statistics; SAH: systemic arterial hypertension; DM: diabetes mellitus; BMI: body mass index; HDL: high density lipoprotein; T-post: post-transplant; AMI: acute myocardial infarction; CVA: stroke; CHF: congestive heart failure; PVD: peripheral vascular disease; LVH: left ventricular hypertrophy.

In addition, the fifth post-transplant year showed significance with $P < 0.05$ in the analysis of the incidence of CHF, when related to the age of the recipient, since, of 317 patients who did not have CHF, 205 were aged < 50 years (64.67%) and 112 ≥ 50 years (35.55%). On the other hand, nine patients developed CHF, of which three were aged < 50 years (33.33%) and six were aged ≥ 50 years (66.67%). Thus, age below 50 years seems to be a likely protective factor for CHF.

The other associations performed were not significant ($P > 0.05$).

DISCUSSION

In the present study, data were collected from 577 patients undergoing kidney transplantation, the predominant gender being male, with 67.9% of the sample, and mean age of 46.5 ± 13.7 years. Such data are in agreement with the findings in the literature, in which the main profile of kidney transplant patients was men and the average age was approximately 46 years.⁶⁻⁹

In this study, the survival rate was 72.3% up to the fifth year post-transplantation, which is higher when compared to patients on hemodialysis - it can reach values between 60 and 64% in a period of five years, depending on the country in question.^{10,11} In the countries of the European Dialysis and Transplantation Association, for example, the survival rate of hemodialysis patients after five years is even lower, around 50%,¹² while in the United States this rate is 36%.¹³

According to the results of our research, the predictors for cardiovascular events are: male gender, recipient age ≥ 50 years, presence of DM, BMI > 30 kg/m² and HDL < 40 . These factors were also found in some sources of information literature.^{7,14} However, no relevant results were found between pre-transplant smoking, previous CVD and the presence of SAH⁶ and the cardiovascular events of the study in question.

A non-modifiable risk factor is the age of the transplant recipient. It was observed that, after three years of transplantation, being ≥ 50 years old is a potential risk factor for developing AMI, stroke, CHF and LVH and, after five years, it is relevant for the prevalence of CHF. The importance of the age factor is also observed in other comparative studies with cardiovascular events,^{6-8,14,15} being decisive for the survival of the population in general, as well as of renal transplant patients.

A conflicting data in the literature is the influence of smoking and SAH, since in the present study such variables did not demonstrate significance for the emergence of CVD. The lack of relevance of SAH can be justified by the fact that it is commonly treated with cardiorenal protection drugs, which could mask its real impact on patients' survival if they did not use the medications, information that is in line with findings in the literature.⁷ However, in another reference, this data is not consistent, as the influence of SAH and smoking on the development of CVD has been reported.⁶

The incidence of DM increased from the pre-transplantation period to the post-transplantation period,⁸ being relevant in the third year after transplantation, for cardiovascular events, as it is a potential risk factor for stroke, CHF, PVD and LVH. This situation has also been shown to be present in the literature for CVD.¹⁴

In this study, contrary to the findings in the literature that claim that BMI < 30 kg/m² is an increased risk factor for CVD,⁶ the BMI > 30 kg/m² proved to be a risk factor in the third year for AMI. Also differently from the literature, in which the cholesterol level was not considered a significant data, in this study HDL > 40 was shown to be a probable protective factor for stroke in the third year and for LVH in the fifth year.

For cerebrovascular diseases (CVA), after kidney transplantation, the risk factors found are: presence of DM, age ≥ 50 years and HDL < 40 . This data partially agrees with the finding in the literature, in which it is stated that, for the onset of cerebrovascular accident after kidney transplantation, the risk factors are: age, pre- and post-transplant smoking, DM, SAH, obesity and coronary comorbidity.⁶

CONCLUSION

Regarding the profile of patients undergoing kidney transplantation in the sample, it could be defined that, of the total of 577 transplant patients, most are male (67.9%), with a mean age of 47.19 ± 13.93 years. In females (32.1%) the mean age was 45.06 ± 13.12 years. In both sexes, the mean age was 46.51 ± 13.7 years. Of the total number of patients, 417 did not die (72.3%). Of the 157 deaths in this period, 74 occurred between the third and fifth year after transplantation (47.1%). Of the deaths, 88 patients were not due to cardiovascular events (56.1%); 43 deaths were due to CVD (27.4%) and 26 due to undetermined causes (16.6%).

In addition, it was possible to conclude that the incidence of patients with DM increased after kidney transplantation. The incidence of SAH and smoking did not change in the pre- and post-transplant period, being considered statistically irrelevant.

As for the presence of CVD and the possible risk factors in the third year after transplantation, the presence of DM proved to be a risk factor for stroke, CHF, and LVH, with $P < 0.05$, as well as a BMI > 30 kg/m² is a risk factor for AMI. In relation to age,

individuals over 50 years old are more predisposed to AMI, CVA, CHF and LVH. As for HDL, being greater than 40 seems to be a protection factor only for LVH.

In the fifth year after transplantation, HDL cholesterol levels < 40 appear to be a probable risk factor for stroke, and age \geq 50 years seems to be a probable risk factor for CHF.

With the conclusion of the present study, it becomes evident that changing lifestyle and maintaining healthy habits are simple and low-cost strategies that can significantly improve cardiovascular risk and life expectancy in post-kidney transplant patients. It is known that BMI and HDL cholesterol levels are modifiable risk factors, and BMI < 30 kg/m² and HDL > 40 have been shown to be protective factors for the development of AMI, LVH and stroke in post-kidney transplant patients. In addition, a thorough screening of diseases and risk factors is necessary in post-kidney transplant patients aged 50 years or older, since this is the age group with the highest risk for developing CVD after kidney transplant surgery.

AUTHORS' CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Soejima SN, Silva JC and Tondo ACC; **Conception and project:** Soejima SN, Silva JC and Tondo ACC; **Technical procedures:** Soejima SN, Silva JC and Tondo ACC; **Data analysis and interpretation:** Soejima SN, Silva JC and Tondo ACC; **Statistical analysis:** Soejima SN, Silva JC and Tondo ACC; **Manuscript writing:** Silva JC and Tondo ACC; **Critical review:** Soejima SN, Silva JC and Tondo ACC; **Final approval:** Soejima SN, Silva JC and Tondo ACC.

DATA STATEMENT AVAILABILITY

Research data will be made available upon request.

FUNDING

Not applicable.

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