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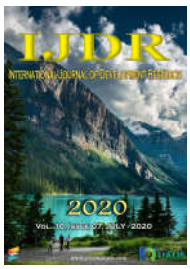

RESEARCH ARTICLE OPEN ACCESS

EVALUATION OF CARDIOVASCULAR RISK IN RENAL TRANSPLANT RECIPIENTS: CLINICAL IMPORTANCE ACCORDING TO THE FRAMINGHAM SCORE

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ABSTRACT

Introduction: Chronic kidney disease belongs to chronic non-communicable diseases. It is understood as a clinical syndrome characterized by a significant reduction in excretory, endocrine and metabolic renal functions. Cardiovascular disease is responsible for a large part of the mortality and comorbidity present in patients with kidney transplantation. **Objectives:** To identify the profile of renal transplant recipients and estimate the risk of future cardiovascular events. **Methods:** Observational, descriptive and analytical study with a quantitative approach, developed at the Renal do Oeste clinic in Santa Catarina, a reference for renal treatment. **Results:** It was possible to identify in patients with kidney transplantation some factors that influence the development of cardiovascular disease, factors such as: biochemical parameters and anthropometric measurements. Since, the parameters of lipid profile, triglycerides, systolic blood pressure, C-reactive protein and Framingham Risk Score showed a significant difference between groups. **Conclusion:** The application of the Framingham risk score generates important and necessary information in order to reduce the risk of developing cardiovascular disease, directly resulting in an increase in the quality of life and survival of patients after kidney transplantation.

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INTRODUCTION

Chronic Kidney Disease (CKD) is understood as a clinical syndrome determined by the significant, slow, gradual and progressive reduction of excretory, endocrine and metabolic renal functions (Barbosa, Salomon, 2013).

In this sense, research has shown that to prevent or delay the symptoms and complications of CKD, the patient may initially undergo changes in habits, with subsequent association with drug therapy (Barbosa *et al*., 1999).

Continuing, in the failure of the initial interventions, individuals should be submitted to Renal Replacement Therapy (RRT), one of them being the Kidney Transplant (RT), the treatment of choice for patients with Chronic Renal Failure (CRF) who do not have contraindications to perform it. lo (Pereira, 2000). RT has numerous benefits for the patient, namely: better quality of life and better survival regardless of dialysis machines, however, the use of immunosuppressants can significantly interfere with their life condition, which may cause some side effects such as nephrotoxicity and metabolic changes. In addition, with the interruption of this immune response due to the use of immunosuppressive drugs, the risks of complications and infections by viruses, bacteria and fungi as well as Cardiovascular Diseases (CVD) increase, characterizing some of the main factors of comorbidity and death after the procedure. transplantation (Tizo, Macedo, 2015). CVD has been widely described in the literature as one of the most common complications after RT (Foley *et al*., 1998; Pilmore *et al*., 2010). It is also responsible for 17% of all deaths in post-transplant patients and, in association with cerebrovascular diseases, represents 22% of all deaths. The most common cardiac causes of death are: cardiac arrest (45%), followed by myocardial infarction (31%) and cardiac arrhythmia (13%) (Meier-Kriesche *et al*., 2004; Liefeldt, Budde, 2010).

In addition to the specific factors that transplantation presents to develop CVD, traditional factors cannot be excluded. Thus, one of the main studies used to check cardiovascular risk is the Framingham Risk Score (ERF). The ERF establishes risk factors as traditional and non-traditional (Greffin *et al*., 2017). Thus, it is observed that the presence of a high risk of CVD in the population with kidney transplantation increases the number of deaths and challenges health professionals to seek improvements and therapeutic grounds in the expectation of offering a greater and better quality of life as well as longer survival for these individuals. Thus, the objective was to verify cardiovascular risk factors in patients receiving renal transplantation (less than 1 year of RT, from 1 to 5 years of RT and more than 5 years of RT), evaluating the probability of future risk of development of CVD.

MATERIALS AND METHODS

Study Design and Population: Observational, exploratory study with a quantitative approach, carried out in a nephrology clinic of reference for the West of the State of Santa Catarina, attending patients in different stages of CKD, including the patient with RT. The study included patients after kidney transplantation, of both sexes, aged 18 years or over and less than 75 years old and who were undergoing medical follow-up in 2018 at the referred clinic. After the patient's' consent with the signature of the Free and Informed Consent Form (ICF), they were divided into three groups: less than 1 year of RT, from 1 to 5 years of RT and more than 5 years of RT.

Data collect: Data collection took place through individual interviews with patients, in which the use of tobacco was researched, as well as the presence of associated comorbidities (diabetes and hypertension). In addition, waist circumference (WC), hip circumference (QC), abdominal circumference (WC) and neck circumference (CP) were acquired. Data collection also extended to electronic medical records, where information was collected regarding the health / disease process, more specifically, Total cholesterol (TC), Low density lipoprotein cholesterol (LDL-C), High density lipoprotein cholesterol (HDL-C), Glucose (Glc), Triglycerides (TG) and C-Reactive Protein (PCR), performed no more than three months prior to data collection. For hemodynamic parameters such as heart rate (HR) and blood pressure (BP), as well as the body mass index (BMI), they were acquired according to the notes made by the reception on arrival (reception and screening) of the users.

Statistical analysis: The information obtained was transferred to spreadsheets in the Libre Office program. Frequency tables were used for categorical variables and descriptive statistics (mean ± standard deviation) as well as for continuous variables and analysis of variance. The normality of the data was verified by the Kolmogorov-Smirnov test. After obtaining normality (parametric), the data were subjected to analysis of variance (one-way ANOVA) and when significant differences were observed, the means were compared with the Tukey test at the 5% level of significance. All analyzes were performed using the GraphPad Prism 6.0 statistical program. The results are presented by the mean ± standard deviation.

Cardiovascular Risk Analysis: For the analysis of cardiovascular risk, the ERF was used, where each variable has values that have specific scores, positive or negative. The total ERF score takes into account the following variables: sex, age, smoking, diabetes mellitus, high density lipoprotein, total cholesterol, systolic blood pressure and diastolic blood pressure. The final value obtained corresponding to a percentage of probability of occurrence of cardiovascular disease in the next ten years. Therefore, individuals are classified into the following risk categories: low risk (less than 10%), intermediate risk (between 10% and 20%) and high risk (above 20%). For its calculation, the Cardiovascular Risk calculator (Framingham Risk Score) version 1.1.2 was used. The results are expressed as a percentage (%) of risk for developing heart disease in the subsequent ten years (Ministério da Saúde, 2014).

Ethical aspects: This study was presented to the Research Ethics Committee with Human Beings (CEP) through the Platform Brazil of the Federal University of Fronteira Sul (UFFS) under number CAAE 68787617.2.0000.5564 and had an approval opinion under number 2,752,288. An informed consent form was obtained from all participants and from the clinic referred to.

RESULTS

65 patients participated in the research, in which they were divided into three groups according to the years after RT. Group 1: <1 year (n = 22), group 2: 1 - 5 years (n = 21), and group 3:> 5 years (n = 22). Among the variables analyzed, we observed a predominance of males in the three groups, with the lowest mean age being 42 years and the highest being 51. We also observed the predominance of patients with systemic arterial hypertension in the group from one to five years (66.7%) and older than five years (68.2%). Regarding the presence or absence of Diabetes, we found that 45.4% of the group with more than five years after transplantation were diabetic, followed by the group with one to five years and less than one year respectively (38.1% and 31.8 %) (Table 1). When we observe the results related to smoking, the group from one to five years after transplantation presented an average of 38.1% for smoking patients, followed respectively

by the other groups (31.8% and 27.2%). Regarding the presence or not of obesity, 31.8% of the patients in the group with more than five years after transplantation were obese, followed by 19.1% in the group of one and five years and 9.1% in the group with less one year after transplant (Table 1). With regard to the analysis of anthropometric parameters (Table 2), we can see that there was no difference between groups in the variables of waist circumference, neck and abdomen, as well as in BMI.

Table 1. Characterization of the sample and prevalence of some risk factors for cardiovascular diseases in patients receiving renal transplantation

	Years After Kidney Transplantation		
Variable	<1 year	1-5 years	>5 years
Patients n (%)	22 (33,8%)	21 (32,4%)	22 (33,8%)
Age group (%)	50,9 ± 9,8	41,7 ± 8,7	50,5 ±12
Female n (%)	7 (32%)	5 (24%)	8 (36%)
Male n (%)	15 (68%)	16 (76%)	14 (64%)
Hypertension			
YES n (%)	8 (36,3%)	14 (66,7%)	15 (68,2%)
NO n (%)	14 (63,6%)	7 (33,3%)	7 (31,8%)
Diabetes			
YES n (%)	7 (31,8%)	8 (38,1%)	10 (45,4%)
NO n (%)	15 (60,1%)	13 (61,9%)	12 (54,5%)
Smoking			
YES n (%)	6 (27,2%)	8 (38,1%)	7 (31,8%)
NO n (%)	16 (72,7%)	13 (61,9%)	15 (68,1%)
Obesity (BMI> 30 kg / m²)			
YES n (%)	2 (9,1%)	4 (19,1%)	7 (31,8%)
NO n (%)	20 (90,9%)	17 (80,9%)	15 (68,1%)

Source: Prepared by the author, 2020. Values expressed as mean ± standard deviation. BMI: body mass index.

Table 2 - Quantitative description of anthropometric parameters

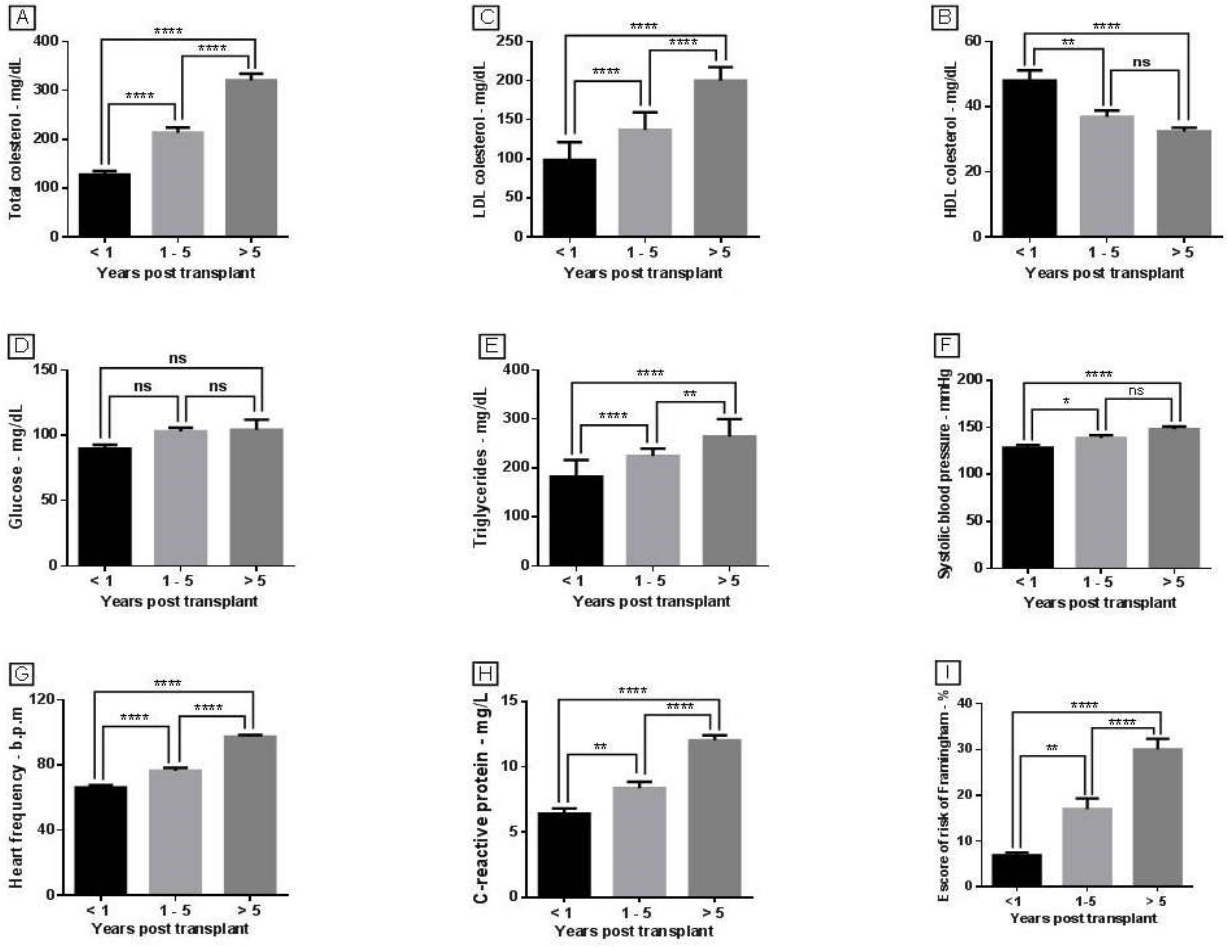
	Years After Kidney Transplantation		
Variable	<1 year	1-5 years	>5 years
WC (cm)	85,9±15,3	86,6±16,8	88,5±14,3
CP (cm)	40,7±3,8	40,8±4,7	40,5±3,7
WC (cm)	96,8±11,9	93,1±14,6	100,2±8,9
BMI (kg/m2)	26,1±2,9	25,8±3,7	27,6±4,0

Regarding the analysis of the lipid profile of the patients in this study, the variables analyzed were, CT, LDL-C, HDL-C, Glc, TG and PCR (figure 1). From the above, we can observe the variable CT, in which patients with less than one year of transplantation obtained a significantly lower mean (128.22 ± 34.73) when compared to groups aged one to five years (213 , 90 ± 46.53) and more than five years of transplantation (320.5 ± 64.18) (Figure 1-A). Regarding the LDL-C variable, we can observe that the group with less than one year TR obtained a mean (98.68 ± 22.56) significantly lower in relation to the other groups, which presented an average of (137.14 ± 23.31) and (200.18 ± 17.08) respectively, showing that there was a statistically significant difference between the groups (Figure 1-C). Regarding HDL-C levels, the group with less than one year of RT presented a mean (48 ± 14.56) significantly higher than the other groups, which presented an average of (36.85 ± 9.13) and (32.40 ± 5.46) respectively, (Figure 1-B). Furthermore, regarding the levels of TG, we observed that the group under the age of one year of RT presented a mean (182.09 ± 34.50) significantly lower than the other groups, which exhibited an average of (224.57 ± 14.89) and (262.80 ± 36.40), respectively, showing a significantly greater difference in the group with more than five years after transplantation when compared to the other groups (Figure 1-E). Still on the biochemical parameters, with regard to blood Glc levels, the levels were not significant, the mean of Glc did not differ significantly between the groups, being its presentation, respectively, according to the years of RT (89.76 ± 13.890), (102.95 ± 13.34) and (104.19 ± 36.88) (Figure 1-D). In addition to the biochemical parameters, we can observe the CRP values, in which significant results were obtained, since the group with the highest average (12.04 ± 1.85) was the group with more than five years of RT, which differed significantly when compared to the other groups that presented an average, respectively, for the group under one year of RT (6.47 ± 1.63) and (8.38 ± 2.15) for the group of one to five years of age. post-transplant (Figure 1-H).

Regarding the blood pressure variable, we chose to work only with Systolic Blood Pressure (SBP), respecting its imposing contribution to CVD when it is high. Looking at the groups after kidney transplantation, it is possible to understand that there was a significant increase in SBP when compared to the group under one year of transplantation (128.18 ± 15.33) with those transplanted more than five years ago (148.13 ± 13.04), demonstrating the elevation of SBP simultaneously at the age of transplantation (Figure 1-F). Among the variables analyzed, patients with less than one year of transplantation had a significantly lower heart rate (HR) (66.22 ± 6.64) compared to the group with more than five years of transplantation (97.22 ± 5, 24). The patients belonging to the group from one to five years after transplantation, presented a HR (76.33 ± 8.63) higher when compared to the group with transplant age less than one year and lower, when compared to the group with more than five years of transplantation. In summary, patients less than one year after transplantation had a significantly lower HR when compared to the other groups (Figure 1-G). Still in relation to the variables analyzed in this study, we can conclude that the group with more than five years of transplantation had a higher risk of developing CVD in the next ten years of life when compared to the other groups. Because the patients in this group had a significantly high mean (30.05 ± 10.30) when compared to the one to five year RT group (16.97 ± 10.60) as well as when compared to the group with less one year after transplant (6.89 ± 2.58) (Figure 1-I).

DISCUSSION

The presence of central obesity is defined by the measurement of the waist, considering waist circumference above 88 cm for women and above 102 cm for men, as an increased risk factor for CVD. Obesity, particularly visceral, is related to the coronary risk in the development of left ventricular hypertrophy. Our data demonstrate that there was no significant difference in variables between the weighted groups. According to de Martins *et al*. (2016), who perform an assessment of kidney recipient patients, it can be observed that the variables BMI and WC have no significance for the study. In another study by Pereira *et al*. (2015), who analyzed the nutritional profile of patients with RT, it was observed that the WC variable also did not differ significantly between the groups, these studies being in agreement with the findings in this research. CVD is the main cause of death in patients with chronic kidney disease (CKD) undergoing renal replacement therapy (RRT), being the greatest risk factor for mortality to arterial hypertension. Our data demonstrate that patients with less than one year of RT had significantly lower HR when compared to the other groups.



Source: Elaborated by the author, 2020.

Figure 1. Biochemical parameters of kidney transplant patients

Findings similar to those presented in this work were found in a research carried out by Oliveira *et al*. (2014). In light of the above, most patients with a history of CKD have a slight decrease in sensitivity to changes in HR modulation due to reduced blood vessel distensibility, which can result in the development of heart failure (Chesterton *et al*., 2005). In our study, there was a significant increase in the PAS variable simultaneously with age after kidney transplantation. The findings are in line with a study developed by Stabouli *et al*. (2016), who evaluated the change in SBP in the long term in patients with RT, revealing that SBP increased significantly in the long term, reaching an average of 150mmHg in patients with RT for more than six years. Together, it is evident that high SBP is a frequent problem among renal patients after RT. According to Liberman *et al*. (2013), patients with chronic renal failure, hypertension, diabetes mellitus and atherosclerosis are predisposed to develop vascular calcification, which results in decreased blood vessel elasticity, causing compromised adaptation of baroreflex sensitivity to changes in blood pressure, pre ordering these patients to develop cardiac arrhythmias. Dyslipidemias are cited as one of the main risk factors for the development of coronary artery disease. Regarding the total cholesterol variable, it can be highlighted that, the value suggested by the Brazilian Consensus for the Standardization of the Laboratory Determination of the Lipid Profile (2016), is that the TC is less than 190mg / dL for people aged greater than or equal 20 years, which was observed in the present study, especially in the group with less than one year of RT. The results obtained were similar to that observed in a study by Spinelli *et al*. (2011), which has an average of 159mg / dL CT. Regarding LDL-C, it was observed that the group with less than one year TR had a significant reduction in relation to the others, which is in line with the research developed by Spinelli *et al*., Where the lipid profile of patients before and after RT. Still, it was possible to verify the data referring to HDL-C. From a study by Fazal *et al*. (2014), with patients in the first year of RT, it was possible to observe that the average HDL-C of the participants was 45mg / dL, in which this value is similar to that found in this study.

Regarding the group with RT age over five years, it can be noted that it had the lowest average when compared to the others. This result corroborates the research developed by Pannu *et al*. (2009), who evaluated patients with RT for a period of ten years, and found an average HDL-C of 36.87mg / dL. The author associates this finding with the significant decrease in medication when compared to patients in the first months of RT. In addition, with regard to biochemical parameters, it can be observed that the TG levels in the group under the age of one year of RT presented a significantly lower average in relation to the other groups. Spinelli *et al*. (2011), when analyzing the biochemical parameters of patients during the first year of transplantation, obtained as a result an average TG rate of 184mg / dL, acquiescing with the findings of the present study. A study carried out in São Paulo, Brazil, observed that the first year of RT is considered a period of caution and attention to care among patients, mainly due to the euphoria of the independence of dialysis machines and the increased survival expectation, directly resulting in decrease in

some indexes of evaluation of these parameters described above (Campos, 2012). On the other hand, some studies indicate that dyslipidemia is frequent after one year of RT. Dyslipidemia deserves special attention, and its influence on the development of cardiovascular diseases is known, relevant to atherosclerosis. Disorder of fats present in the blood, can be triggered when increased values of LDL-C (> 160mg / dL) and TG (> 150mg / dL) or reduction of HDL-C (men <40mg / dL and women <50mg / dL) alone or in association with an increase in LDL-C or TG (Walker, Edwards, 2003; Sposito *et al*., 2007; Spinelli *et al*., 2011). The absence or deficiency of treatment related to these and other factors can lead to the development of comorbidities, with CVD being an example, which directly or indirectly affects the graft, which may result in the loss of the transplant or even in the death of the patient (Ito, Yoshida, 2014). Elevated TG and HDL-C values are a high predictor of the risk of developing coronary artery disease. In addition, high TG levels and low HDL-C levels are also predictors of coronary artery disease (Moraes *et al*., 2017). A study developed by Alencastro *et al*. (2013), carried out in the city of Porto Alegre, Brazil, evaluated patients with RT age between one and ten years, in which they obtained results in relation to the Glc parameter, respectively, an average of 91mg / dL and 102mg / dL, being the results are not significant for the research, which is similar to the findings in this study. A study by Cippa *et al*. (2015), analyzed the factors of rejection and infection in 630 patients with RT for five years. This study revealed a mean CRP of 9mg / dL in patients with more than four years of RT, which was possible to assimilate with the data obtained in the study in question. The author associates the increase in CRP due to the conditions of immunosuppression due to the medications used by these patients, thus resulting in an "affected" immunity, as well as an increased risk of contracting infections (such as some CVD) that may directly affect the graft. . Our study shows that the CRP values show significant results, since the group with the highest average (12.04 ± 1.85) was the group with more than five years of RT, which differed significantly when compared to the other groups, which presented an average, respectively, (6.47 ± 1.63) and (8.38 ± 2.15). From the data obtained in this study and in relation to the application of the ERF, it can be seen that the group with more than five years of RT had a higher risk of developing CVD in the next ten years of life when compared to the other groups. This is because, the patients in this group had a significantly high average when compared to the group of one to five years of RT, as well as when compared to the group with less than one year of RT. Data similar to those obtained in the study in question were acquired in a research carried out in São Paulo, Brazil, by Leite and Campos (2010), in which the authors counted on the participation of 300 recipients of RT, which analyzed the risk factors for develop CVD through the application of the ERF and with interventions according to the result of the calculation. This study also found that patients with more than five years of RT are at high risk (58%) to develop CVD in the next decade of life. Another work developed in Canada, carried out by Mansell *et al*. (2013), found a significant result after the application of the ERF in patients with more than three years of RT, with a high risk prevalence in 40.7% of patients.

Conclusion

We concluded that patients with more than five years of kidney transplantation present an alarming average for the development of dyslipidemia, contributing to the risk factors for the development of CVD. The application of the ERF is extremely important for this group of patients in question. Its application, through the expressed result, will contribute for the intervention to be assertive in relation to the risk parameters for CVD, thus reflecting in the improvement of the quality of life as well as in the increased survival of patients with kidney transplantation.

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