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Long-Term Quality of Life of Kidney Transplant Recipients

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ABSTRACT

Introduction: The relevance of quality of life is increasingly evident in rising life expectancy and the prevalence of non-communicable chronic diseases like chronic kidney disease. Transplantation is the preferred treatment for end-stage chronic kidney disease, facilitated through living or cadaveric donors as per Brazilian legislation. However, limited literature compares long-term quality of life data and its correlation with graft origin. This study addresses this knowledge gap, focusing on patients who underwent kidney transplantation before 2012 at Hospital Universitário Evangélico Mackenzie. **Objectives:** The primary aim is to analyze kidney transplant recipients' long-term quality of life from living and cadaveric donors. **Methods:** The study was observational cross-sectional; the sample includes 24 female (61.5% cadaveric donor) and 19 male (38.5% cadaveric donor) patients who underwent transplantation before 2012. The Short Form-36 (SF-36) questionnaire was utilized, and data were statistically analyzed after tabulation in Excel®. **Results:** Cadaveric donor recipients experienced 39 additional months of dialysis ($p = 0.017$) and higher initial median creatinine levels than living donor recipients. Creatinine findings were more favorable for living donor recipients in the 7th and 8th years, indicating a temporal decline in the cadaveric donor group. In the SF-36 questionnaire, only the "mental health" domain showed a statistically significant difference, favoring the cadaveric donor group ($p = 0.008$). **Conclusion:** Long-term quality of life for living donor and cadaveric donor kidney transplant recipients did not significantly differ, except for the "mental health" domain, which favored cadaveric donor recipients. Creatinine levels exhibited a temporal decline in the cadaveric donor group, emphasizing the importance of considering graft origin in assessing transplant outcomes.

Descriptors: Quality of Life; Transplant; Donor; Corpse; Renal

Qualidade de Vida Tardia em Receptores de Transplante Renal

RESUMO

Introdução: Com o aumento da expectativa de vida, houve também crescimento da prevalência de doenças crônicas não transmissíveis, como a doença renal crônica (DRC). O tratamento de escolha da DRC terminal é o transplante renal (TR), via doador vivo (DV) ou falecido (DF). São escassos os dados na literatura sobre a qualidade de vida (QV) em pacientes transplantados e a correlação com a origem do enxerto. **Objetivos:** Analisar a QV em pacientes submetidos a TR antes de 2012, no Hospital Universitário Evangélico Mackenzie. **Métodos:** Este é um estudo transversal observacional. Foram selecionados pacientes submetidos a TR até 2012, sendo a amostra composta por 24 pacientes do sexo feminino (61,5% de DF) e 19 do sexo masculino (38,5% de DF). Foi aplicado o questionário Short Form-36 (SF-36). Os dados foram tabulados em Excel® e analisados estatisticamente. **Resultados:** Pacientes com DF apresentaram 39 meses excedentes de diálise ($p = 0,017$) e maiores níveis iniciais medianos de creatinina do que o grupo de DV (D1: $p = 0,001$, D3 e D7: $p < 0,001$), com maior decaimento mensal nos 8 anos de TR ($p < 0,001$) e menores níveis de creatinina nos 7º ($p = 0,008$) e 8º anos ($p = 0,037$). Com relação ao questionário SF-36, o único domínio estatisticamente significante foi "saúde mental", melhor no grupo de DF ($p = 0,008$). **Conclusão:** A QV de pacientes transplantados por DV e DF não apresentou diferença significativa, exceto em saúde mental, que foi melhor em DF. Os achados de creatinina foram melhores nos 7º e 8º anos em DF, com taxas maiores na 1ª semana pós-TR, apontando decaimento temporal no grupo de DF.

Descritores: Qualidade de Vida; Transplante; Doador; Cadáver; Renal.

INTRODUCTION

Chronic kidney disease (CKD) consists of slow and irreversible impairment of kidney shape or function.l[1,2]. It is considered a public health problem since, in Brazil, it is estimated that 1.2 to 1.5 million people are included in this situation[2].

Currently, population aging and increased life expectancy point to a greater prevalence of chronic diseases. The increased incidence of diabetes mellitus (DM) and systemic arterial hypertension (SAH), the main risk factors for CKD, contributed to the increased incidence of this condition, consequently leading to higher rates of related morbidity and mortality[2,3].

Kidney transplantation (KTx) is the treatment of choice for CKD. This complex and invasive procedure has excellent cost-benefit ratios. Its objectives include increasing longevity, reducing morbidity and improving quality of life (QoL)[4,5].

Immunosuppressive therapies have improved, increasing graft survival in patients undergoing KTx. Consequently, evaluating the long-term QoL of these patients is essential, as the Brazilian literature needs more data.

Factors closely related to QoL, such as emotional and psychosocial, are rarely observed in patients undergoing KTx. Furthermore, this procedure increases the patient's expectations and QoL. Therefore, studying and analyzing aspects related to these individuals' long-term QoL is essential.

METHODS

The present is an observational cross-sectional study. After approval by the Research Ethics Committee, the next step consisted of retrospectively collecting the medical records of transplant patients until 2012 at the Hospital Universitário Evangélico Mackenzie (HUEM). Data on age, transplant time, gender, comorbidities, creatinine, urea, blood glucose levels and contact telephone number were obtained.

Epidemiological data were collected from 100 patients over 18 years of age who underwent kidney transplants at HUEM from 2010 to 2012, with a functioning graft and without simultaneous transplantation of another organ, divided in half into kidney transplants from living donors (LD) and deceased donors (DD). After telephone contact, ten patients were excluded due to death, 15 due to failure and/or retransplantation, and 32 did not respond to any of the approaches. The final sample analysis comprised 43 patients, 30 LD and 13 DD.

Participants responded to the Short Form-36 (SF-36) questionnaire (attachments) with the help of researchers over the phone to clarify any doubts. All variables were described for the complete sample (n = 43) and compared between patients who received kidneys from LD or DD.

This research used the validated generic QoL assessment questionnaire SF-36. The SF-36 encompasses 36 items divided into eight domains for analyzing QoL: functional capacity, limitations due to physical aspects, pain, general health status, vitality, social factors, emotional aspects and mental health.

The scores for each question vary as indicated in the annexes (SCORE). The final Raw Scale value for each domain varies from 0 (worst) to 100 (best), following the following formula:

$$\text{Raw Scale} = \text{The value obtained in the corresponding questions} - \text{lower limit} \times 100 \,/\text{variation (score range)} \quad (1)$$

Data[6] were tabulated in Microsoft Excel and subjected to statistical analysis.

Qualitative variables were described by their absolute and relative frequencies, while quantitative variables were described by medians and interquartile range (first quartile; third quartile). Comparisons between groups were performed using Fisher's exact test for qualitative variables and the Mann-Whitney U test for quantitative variables. Correlations were calculated using Spearman's correlation coefficient.

The longitudinal creatinine profile over time was modeled using a mixed linear regression model with random intercept.

All analyses were conducted using the R software and always considered a 5% significance level.

RESULTS

The epidemiological sample consisted of 24 female patients (53.5% LD and 61.5% DD) and 19 males (46.5% VD and 38.5% DF). According to racial self-declaration, 36 patients were white, four were mixed race, and three were black.

Regarding patients' comorbidities, DM (n = 15), hypothyroidism (n = 3), hypertension (n = 32) and cardiovascular diseases (n = 22) were researched.

The etiology of CKD in the sample included undetermined causes (n = 14), glomerulonephritis (n = 15), hypertension (n = 6), polycystic kidney disease (n = 6) and diabetic nephropathy (n = 2).

The medical records contained data on dialysis. Six patients underwent peritoneal dialysis, and 30 underwent hemodialysis. The median dialysis time for each group was significantly different. Patients who received an LD kidney had a median dialysis time of 39 months less than patients who received DD ($p = 0.017$).

The difference between the median creatinine level of the two groups during the 1st week after transplantation was significant (D1: $p = 0.001$, D3: $p < 0.001$ and D7: $p < 0.001$) since, at all times, patients who who received a DD organ had a higher creatinine level. At the end of the follow-up period, the difference between the median creatinine level of the two groups was significant, given that both in the 7th ($p = 0.008$) and 8th year ($p = 0.037$) after transplantation, recipients of LD organs had higher creatinine levels than DD recipients.

The difference between the preoperative urea levels of the two groups was significant. At the same time, recipients of LD organs had a median of 29.5 mg/dL more urea than recipients of deceased organs ($p = 0.012$).

Regarding the SF-36 questionnaire, the only domain that showed a significant difference between the groups was mental health, in which recipients of LD organs scored a median of 22 points lower than recipients of DD organs ($p = 0.008$).

A significant negative correlation was found between the urea level and the limitation due to the emotional aspects domain ($p = 0.047$), indicating that higher urea levels were associated with lower scores in this domain. The same occurred between the blood glucose level and the domain limitations due to physical aspects ($p = 0.006$).

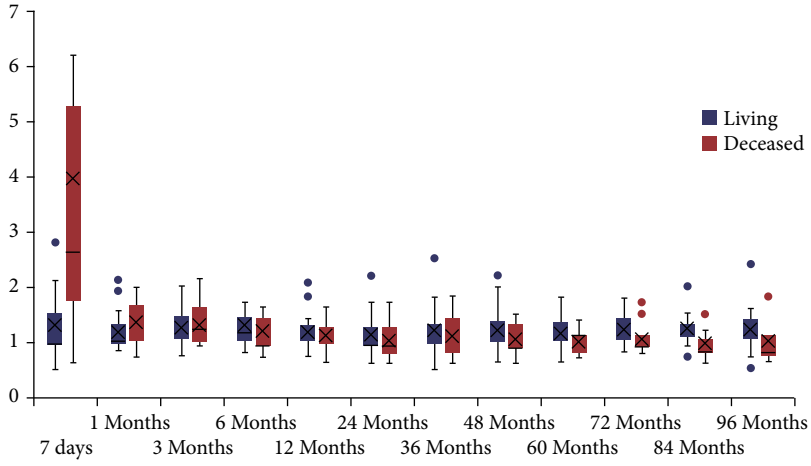
Through descriptive and bivariate analysis, it was possible to identify that, at the beginning of the follow-up period, immediately after transplantation, patients who received DD kidneys had higher creatinine levels than those who received LD kidneys. In contrast, at the end of the follow-up period, patients receiving LD had higher creatinine levels than the others (Fig. 1)

This behavior, in which a group has higher values at the beginning of the period but lower ones at the end, is consistent with the interaction between time and group variables.

Observations were considered for the model from the 7th day after transplantation (month 0) to the 8th year of follow-up. The type of donor, month and interaction between these variables were included as covariates in the model, significantly affecting the creatinine level.

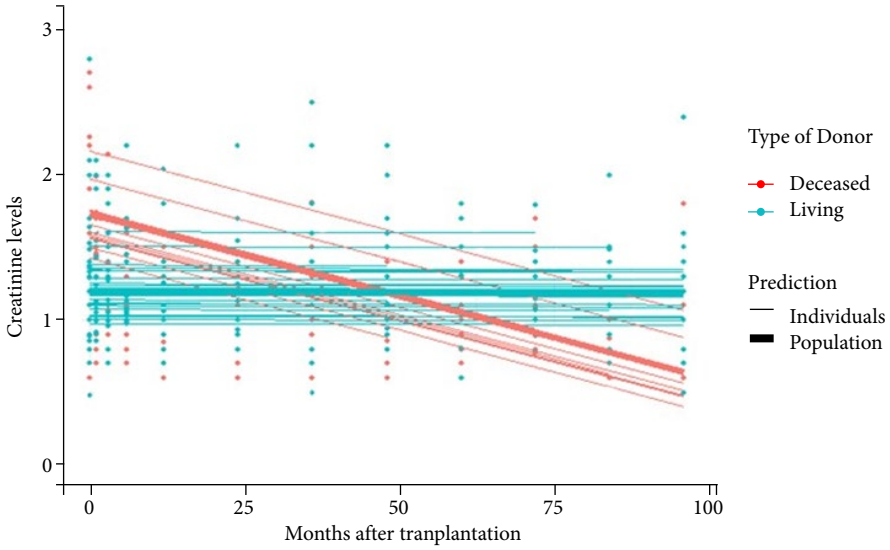
For patients with DD, the monthly effect was estimated at -0.011 ($p < 0.001$), indicating that the creatinine level decreased by 0.011 units each month after transplantation. For patients with LD, it was estimated that, at the beginning of follow-up, the creatinine level was lower by 0.525 units, on average, than for patients with DD ($p < 0.001$), and the effect of time cancels out with the impact of the interaction, indicating that the creatinine level remained constant over time.

This behavior can be observed in Fig. 2, where the thinner lines represent the regression model prediction for each individual, and the thicker lines represent the model prediction for the groups. In general, the DD group (red) decreased over time, starting above the LD group and ending below, while patients with LD (blue) had a constant creatinine level over time.



Source: Elaborated by the authors.

Figure 1. Evolution of creatinine in the living and deceased groups over time.



Source: Elaborated by the authors.

Figure 2. Creatinine prediction of patients and groups after transplantation

DISCUSSION

The leading causes of CKD worldwide are DM and SAH, but glomerulopathies, infection and exposure to toxic agents can also cause this condition[7]. In Brazil, according to epidemiological research between 2000 and 2004, the vast majority of the underlying causes of CKD were undetermined, followed by hypertension and other cardiovascular diseases, DM and glomerulonephritis.[2,3].

The shorter dialysis time of patients with LD correlates with literature data and can be explained by preemptive transplants and those recently started on dialysis[8]. Furthermore, the long waiting time for DD dialysis patients ends up worsening their clinical condition and reducing their chances of transplantation. This fact impacts post-transplant quality, mainly related to bone quality, with secondary hyperparathyroidism[9,10]. This highlights, once again, the advantage of KTx not only in reducing costs but also in the lower morbidity of the transplant patient compared to the dialysis patient.

After ten years of liver, kidney and heart transplantation, Karam et al.[10] found a QoL similar to that of the general population despite the side effects of immunosuppressive drugs, which would point to another advantage of KTx concerning dialysis in the literature.

The higher creatinine levels in the 1st week and the decline shown in the time analyzed post-KTx can be explained by the higher rate of late graft function in DD patients, which corroborates literature data due to the advanced age of the donor, prolonged cold ischemia and elevated terminal serum creatinine[11-13]. Other associated aspects are the origin of the unrelated graft (less compatibility), trauma resulting from the death of the donor[14] and the increase in expanded criteria donors and borderline donors[15].

Pehlivan et al.[16] cite possible aspects that lead to decreased QoL: stress, fear of dying, graft rejection and limitation of the patient's physical activities. A Polish study[17] cites the effects of polypharmacy as harming QoL, especially in the areas of pain and limitations due to physical aspects, in addition to the use of antidepressants[17,18] and complications of KTx, such as new-onset diabetes mellitus after transplantation (NODAT)[19].

Employment and income greater than three minimum wages4 indicate an improvement in the QoL of patients undergoing kidney transplantation. Specifically regarding the psychosocial burden, Milaniak et al.[20] point out personal and social factors, such as coping skills, optimism and social support.

The SF-36 is a widely used measure that promotes a score that aims to understand different aspects of a population's physical and mental health. It is also possible to comparatively evaluate the effects of treatments in the short, medium and long terms[21].

The definition of 10 years as late graft survival is justified by the statistics available in the literature[21] and due to the few national studies considering graft survival after five years.

Studies that analyze the QoL of transplant patients after three years point to a correlation between the results and the patient's pre-transplant situation, which may decrease when the study time is increased to 10 years[10].

The study by Ravagnani et al.[23] analyzed pre- and post-transplant QoL in Brazil and, despite not finding significant differences between the two samples, found that patients noticed improvements in pain and activities of daily living.

Regarding the SF-36 results, the mental health domain proved statistically significant, demonstrating better results in the DD group. This data may be related to the socioeconomic factors that separate the two groups (LD and DD). In practice, DD recipients wait long in the dialysis KTx queue to finally receive treatment. On the other hand, LD receivers wait a shorter time for such resolution. Furthermore, patients who receive a deceased kidney receive, according to the service's perception, better follow-up than the other group due to the greater appreciation of KTx. The lower creatinine results in DD kidney recipients after 8 years of transplantation can be explained by sample selection bias due to the inclusion criteria for analyzing patients' long-term QoL (mainly the absence of retransplantation and graft failure). Death as an exclusion criterion was higher in the DD group (n = 8), reducing it in relation to the LD group. This is due to the longer dialysis time in these patients, which leads to lower graft survival, and the relationship between this and the donor profile (expanded criteria)[24].

Data collection was limited due to outdated records, patients' lack of adherence to follow-up, and the difficulty of contacting them to conduct the study. Another point was the situation of immunosuppression as a risk factor in the coronavirus disease 2019 (COVID-19) pandemic, increasing the difficulty of obtaining data for research.

CONCLUSION

In the analyzed sample, the QoL of patients transplanted for LD and DD after ten years showed no significant difference between the groups, except in the mental health domain, where DD patients had higher scores. Furthermore, creatinine levels observed in the studied population were lower in DD patients 8 years after transplantation, with a tendency for a more significant decline over time than in LD patients.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Kimura RNY, Camargo PHHA, Jaworski PED; **Conception and design:** Kimura RNY, Camargo PHHA, Jaworski PED; **Data analysis and interpretation:** Kimura RNY, Camargo PHHA, Jaworski PED; **Article writing:** Kimura RNY, Camargo PHHA; **Critical revision:** Kimura RNY, Camargo PHHA, Jaworski PED; **Final approval:** Kimura RNY.

DATA AVAILABILITY STATEMENT

Data are available at: https://figshare.com/articles/online_resource/Anexos_pdf/26029540/1

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