





Admissions Within the First Year After Kidney Transplantation: Evaluation of Risk Factors, Causes, and Outcomes

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ABSTRACT

Objectives: The aim of this study was to evaluate causes of hospital admission within the 1st year after kidney transplantation in a public hospital. **Methods:** This is a retrospective cohort. Data were collected by medical record review. Inclusion criteria were age older than 18 years and kidney transplant. Exclusion criteria were double transplant, primary graft failure, and in-hospital death after transplant procedure. Outcomes included 4-year patient survival (primary outcome), 1-year graft failure, and graft function in 1 year. **Results:** A total of 130 patients were evaluated. There was a predominance of male sex, glomerulonephritis, history of hemodialysis, first kidney transplant, and deceased donor kidneys. Hospital admission in the 1st year occurred in 71.5%. There were three deaths at the first admission (two had cardiovascular causes). The most frequent causes of admission were infections, rejection, and surgical complications. Less common causes included elective procedures such as peritoneal dialysis catheter removal. There was no statistically significant association between categorical and continuous variables studied and the occurrence of hospital admission. Also, hospital admission did not influence primary outcome or 1-year graft failure rate. However, it was associated with lower graft function at 1 year (both by serum creatinine and by estimated glomerular filtration rate – $p < 0.05$). **Conclusion:** There was a high incidence of hospital admission, and first admissions resulted in death in three patients (noninfectious causes). Considering the contribution of elective procedures to the high incidence of admission, we propose that hospital managers focus on improving the ability to solve such problems in the outpatient setting.

Descriptors: Kidney Transplantation; Hospitalization; Opportunistic Infections.

Internações no Primeiro Ano Após o Transplante Renal: Avaliação de Fatores de Risco, Causas e Desfechos

Objetivos: Este estudo objetivou avaliar as causas de internação no 1º ano após o transplante renal em um hospital público. **Métodos:** Trata-se de coorte retrospectiva feita por meio da revisão de prontuários médicos. Os critérios de inclusão foram 18 anos de idade ou mais e transplante renal. Os critérios de exclusão foram transplante duplo, falência primária do enxerto e óbito durante a internação para transplante. Os desfechos avaliados incluíram sobrevida global em 4 anos (desfecho primário), falência do enxerto em 1 ano e função do enxerto em 1 ano. **Resultados:** Dentre os 130 pacientes, predominavam o sexo masculino, glomerulonefrite como etiologia, histórico de hemodiálise, primeiro transplante renal e rim de doador falecido. A taxa de internação no 1º ano após o transplante foi de 71,5%. Houve três óbitos na primeira internação (dois por eventos cardiovasculares). As principais causas de internação foram infecções, rejeição e complicações cirúrgicas. Causas menos comuns incluíam procedimentos eletivos, como a retirada do cateter de diálise peritoneal. Nenhuma das variáveis avaliadas teve associação estatisticamente significativa com risco aumentado para internação. Além disso, a ocorrência de internação não teve impacto na sobrevida global em 4 anos após o transplante (desfecho primário) e tampouco no risco de falência do enxerto em 1 ano. Porém, houve impacto negativo na função do enxerto ao final do 1º ano (tanto com o valor de creatinina quanto pela taxa de filtração glomerular estimada, com $p < 0,05$). **Conclusão:** Houve elevada frequência de internações, tendo a primeira resultado em óbito em três casos, nenhum de causa infecciosa. Considerando a contribuição de procedimentos considerados eletivos para tal estatística, propõe-se o investimento em resolutividade no nível ambulatorial em situações como retirada de cateter de Tenckhoff, tratamento dos casos leves de infecção pelo citomegalovírus (CMV) e biópsia do enxerto renal.

Descritores: Transplante de Rim; Hospitalização; Infecções Oportunistas.

INTRODUCTION

Historically, kidney transplantation was the first modality of renal replacement therapy (RRT) to be successfully performed and is currently the method of choice for the vast majority of patients with end-stage renal disease (ESRD)¹. Compared to hemodialysis, it dramatically impacts patients' survival and quality of life^{2,3}. Regarding peritoneal dialysis, there is also a proven benefit in survival⁴, with higher rates of progression to transplantation in patients using this method when compared to those on hemodialysis^{5,6}. Furthermore, the healthcare costs for kidney transplant recipients are lower than those inherent to dialysis patients¹.

However, the survival benefit only occurs after an initial period in which there is a transient increase in the risk of death attributed to surgical complications, graft dysfunction and induction immunosuppression⁷. Surveys conducted in the United States (US) [United States Renal Data System (USRDS)], Europe [European Renal Association-European Dialysis and Transplantation Association (ERA-EDTA)], Australia and New Zealand [Australian and New Zealand Dialysis and Transplant Registry (AZNDATA)], Japan [Japanese Renal Transplant Registry (JRTR)] and Brazil [*Registro Brasileiro de Transplantes* (RBT)] describe infection, cardiovascular disease and malignancy as the leading causes of death after kidney transplantation. Still, new studies highlight changes in the epidemiological scenario due to the coronavirus disease 2019 (COVID-19) pandemic⁸⁻¹⁴.

Hospitalization and early mortality rates in kidney transplant recipients are favored by factors inherent to the donor (deceased donor, especially those with expanded criteria), perioperative events [absence of induction therapy, acute rejection, delayed graft function (DGF), length of hospital stay] and the recipient [advanced age, pre-transplant diabetes, chronic obstructive pulmonary disease, dialysis time, pre-transplant cytomegalovirus (CMV) serology, socioeconomic status, adherence to immunosuppressive therapy and graft failure]¹⁵⁻¹⁸.

Several publications from the last two decades have collected data on hospital admission after kidney transplantation^{15,16,19-21}, but Brazil lacks surveys of this type. This study aims to evaluate the causes of hospitalization in the first year after kidney transplantation in a public hospital in Belo Horizonte, Minas Gerais.

METHODS

Study design

An observational analytical retrospective cohort study with a quantitative approach was carried out. As mentioned, the research was conducted in a public hospital in Belo Horizonte. Data collection took place from December 2022 to January 2023. We identified patients who underwent kidney transplantation at this hospital between January 2019 and December 2021. Subsequently, a review of medical records was performed.

Sample selection

The inclusion criteria covered patients over 18 who had undergone a kidney transplant from a deceased or living donor (related or not). The exclusion criteria were the following: double transplant (e.g., liver-kidney, heart-kidney or pancreas-kidney), primary graft failure and death during the hospitalization in which the transplant was performed.

Outcomes

Patient survival four years after transplantation was evaluated as the primary outcome. Secondary outcomes were graft failure one year after transplantation and graft function one year after transplantation [with glomerular filtration rate estimated by the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) formula].

Statistical analysis

The incidence of hospitalization, graft survival, and patient survival were expressed using Kaplan-Meier curves, while the causes of hospitalization were described as percentages. The associations between the occurrence of hospitalization, graft survival, and patient survival were analyzed using the Cox linear regression model.

The remaining variables were evaluated as possible risk factors for hospitalization. Categorical variables were analyzed using Fisher's exact test and expressed as percentages. Continuous variables were analyzed according to their normality: Mann-Whitney test (expressed as median) for those with normal distribution and unpaired t-test (expressed as mean and standard deviation) for those with normal distribution.

Ethical aspects

This research involved consulting the hospital's electronic medical records in a closed environment. It was carried out only by the responsible researchers, with individual access, to ensure anonymity, complying with Federal Law No. 13,709 rules of August 14, 2018 - General Data Protection Law. The research was submitted to the institution's Research Ethics Committee for evaluation

and approved under protocol 65311122.2.0000.5138. The Free and Informed Consent Form was also applied to all participants. This form details the study procedure, focusing on preserving anonymity and explaining the risks and benefits of participating in the research.

RESULTS

Many 130 medical records were analyzed, with a median age of 51, and most of the patients were male (Table 1). Among the transplanted patients, the most common etiology of CKD was glomerulonephritis (29.2%), followed by diabetic kidney disease (13.8%) and polycystic kidney disease (9.2%). A significant proportion (26.1%) had CKD of undetermined etiology.

The primary modality of RRT used before transplantation was hemodialysis (78.4%), and the majority of transplanted organs were from deceased donors (80%). Only five patients (3.8%) had a history of prior kidney transplantation.

Table 1. General characteristics of the patients.

Characteristics	n (%)
Age (median)	51 (minimum 18, maximum 73)
Recipients gender	
Male	73 (56.1)
Female	57 (43.8)
Etiology of kidney disease	
Glomerulonephritis	38 (29.2)
Diabetic kidney disease	18 (13.8)
Polycystic kidney disease	12 (9.2)
Congenital abnormalities	7 (5.3)
Atherosclerotic nephropathy	3 (2.3)
Others	21 (16.1)
Undetermined	34 (26.1)
RRT Modality	
Hemodialysis	102 (78.4)
Peritoneal dialysis	26 (20.0)
Preemptive transplant	2 (1.5)
Previous kidney transplant	
Yes	5 (3.8)
No	125 (96.1)
Donor type	
Living	26 (20.0)
Deceased	104 (80.0)

Source: Elaborated by the authors

Ninety-three patients (71.5%) were hospitalized in the first year after transplantation, with three cases of death during the first hospitalization (2.3% of the sample) from different causes (acute pancreatitis, aortic dissection and acute myocardial infarction). Among those hospitalized, the average number of hospitalizations in the first year was 2.6.

The causes of hospitalization were grouped as follows (Table 2): infections (48.3%, among which the most common agent was CMV), rejection (15%, with a predominance of cellular rejection), surgical complications (10.7%, with a predominance of lymphocele and surgical site infection) and others (9.5%). Only two cases (2.1%) of hospitalization were due to coronavirus infection.

Four continuous variables were evaluated as possible risk factors for hospitalization, two of which were inherent to the recipient (age, discharge creatinine level at admission for transplant) and two inherent to the donor [final creatinine, Kidney Donor Profile Index (KDPI)] (Table 3). Eight categorical variables were also evaluated for this purpose (type of donor, recipient gender, dialysis modality, diabetes, cardiovascular disease, previous transplant, use of "double J" catheter and DGF). None showed a statistically significant association with the occurrence of hospitalization (Table 4).

Table 2. Causes of hospitalization in the first year after kidney transplantation.

Causes	n (%)
Infections	45 (48.3)
Cytomegalovirus	23 (24.7)
Urinary tract infection	14 (15)
Presumably infectious diarrhea	2 (2.1)
Coronavirus	2 (2.1)
Herpes zoster	1 (1.0)
Cellulitis	1 (1.0)
Bacterial pneumonia	1 (1.0)
Infected diabetic foot	1 (1.0)
Rejection	14 (15.0)
Cellular	9 (9.6)
Antibody-mediated	1 (1.0)
Mixed	4 (4.3)
Surgical complications	10 (10.7)
Lymphocele	2 (2.1)
Surgical site infection	2 (2.1)
Surgical site pain	1 (1.0)
sigmoid volvulus	1 (1.0)
Incarcerated incisional hernia	1 (1.0)
Perigraft hematoma	1 (1.0)
Graft urethroplasty	1 (1.0)
Elective removal of Tenckhoff catheter	3 (3.2)
Noninfectious esophagitis	2 (2.1)
Deep vein thrombosis	2 (2.1)
Recurrence of underlying kidney disease	2 (2.1)

Source: Elaborated by the authors.

Table 3. Continuous variables evaluated as possible risk factors for hospitalization.

Variables	Hospitalization	No Hospitalization	p-value
Recipient age (years, median)	50	50	0.92
High creatinine at admission for transplant (mg/dL, median)	2.08	1.80	0.42
Final donor creatinine (mg/dL, median)	0.89	1.10	0.37
KDPI (% , median)	51	49	0.67

Source: Elaborated by the authors

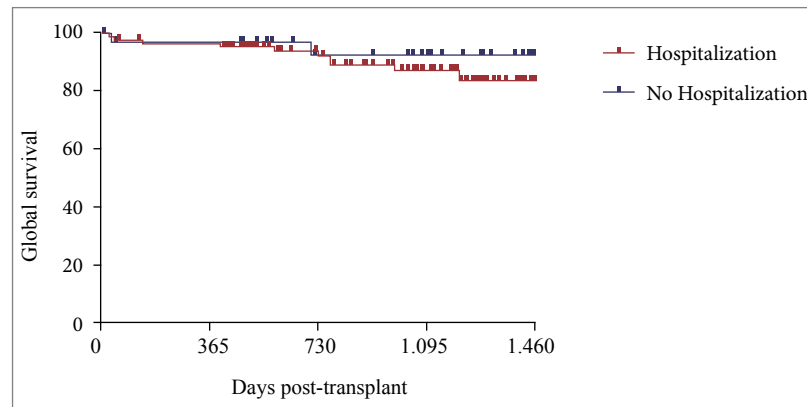
Table 4. Categorical variables evaluated as possible risk factors for hospitalization.

Variables	RR	IC95%	p-value
Deceased donor	1.04	0.68-1.21	0.80
Male gender	0.99	0.79-1.24	> 0.99
Hemodialysis	0.84	0.69-1.13	0.33
Pre-transplant diabetes	1.07	0.78-1.33	0.80
Pre-transplant cardiovascular disease	0.96	0.68-1.21	0.80
Previous kidney transplant	1.12	0.69-1.90	> 0.99
Use of "double J" catheter	1.10	0.88-1.40	0.41
Delayed graft function	1.03	0.92-1.30	0.84

Source: Elaborated by the authors.

In the analysis of patient survival four years after transplantation (primary outcome) (Fig. 1), no statistically significant impact was identified due to the occurrence of hospitalization (83.7% among patients with a history of hospitalization, 92.6% among those without hospitalization, $p = 0.41$). Regarding the graft failure rate one year after transplantation, the result was similar [relative risk (RR) 0.90, reliability index (CI) 0.40-1.27, $p = 0.65$].

In the analysis of graft function at the end of the first year after transplantation, a statistically significant impact was identified due to the occurrence of hospitalization, both with the mean creatinine value (1.54 vs. 1.28 mg/dL, $p = 0.02$) and with the glomerular filtration rate estimated by the CKD-EPI formula (47.2 vs. 60,3 mL/min/1.73 m², $p = 0.01$).



Source: Elaborated by authors.

Figure 1. Kaplan-Meier curve showing the comparison of overall survival until the end of follow-up (1,460 days) between patients with and without a history of hospitalization in the first year after transplantation. Nine patients were excluded from the survival analysis due to loss of follow-up.

DISCUSSION

In this study, the rate of hospitalizations in the first year after kidney transplantation (71.5%) was higher than that reported in previous surveys: 54.3 to 57.5% in the USA^{20,22}; 45,5% in Tunisia¹⁹; 38.2 to 65.9% (in and out of the coronavirus pandemic) in Thailand²³. This is possibly due to the rate of elective hospitalizations due to the difficulty, in our scenario, of performing specific procedures on an outpatient basis, such as removal of the Tenckhoff catheter, prophylaxis of opportunistic infections, treatment for CMV (low availability of oral therapies) and renal graft biopsy.

As for the causes of hospitalization, this study's findings agree with two national studies in which infections predominated (with CMV as the leading cause), followed by surgical complications.^{24,25}

A study conducted in Tunisia also showed infections as the leading cause of hospitalization¹⁹. In contrast, studies conducted in the USA found different results, predominately of surgical complications or graft dysfunction^{20,26-28}.

The national surveys cited here demonstrated that factors such as age, negative pre-transplant CMV serology, DGF and induction therapy with rabbit antithymocyte globulin are correlated with a higher risk of hospitalization^{24,25}. International studies have shown similar findings, adding to the risk factors: female gender, obesity, diabetes, time on dialysis before transplant, length of hospitalization for transplant, organ from deceased donor, CMV infection and use of mycophenolate or cyclosporine¹⁹⁻²¹. However, in the present study, none of the factors evaluated had a statistically significant association with an increased risk of hospitalization. This is likely due to the small sample size assessed compared to the other studies cited.

Regarding the evaluated outcomes, hospitalization had no significant impact on long-term patient survival or the incidence of graft failure. These findings agree with the results of a Brazilian study in which both outcomes were influenced by early hospitalization²⁵, similar to data from the US^{20,26}. However, a study conducted in Tunisia (with a 12-year follow-up) and another in the USA also found no such association^{19,21}. Such analysis may be influenced by the sample size and follow-up time, which were limited in this study.

On the other hand, this study demonstrated a negative impact of hospitalization on graft function at the end of the first year, which agrees with findings from studies in different countries^{29,30}. This relationship could be justified by the risk of acute kidney injury during hospitalizations and the need for adjustments in immunosuppressant doses (increasing the risk of rejection when doses are reduced and infection when doses are increased).

Finally, this study shows that among the three deaths that occurred in the first year after kidney transplantation, two were attributed to cardiovascular events, a common cause of death among transplant recipients in several studies^{15,19,20,25,31}. None, however, were attributed to infections, which are the leading causes in some surveys with the same follow-up time^{19,20,25}.

It is worth highlighting some of the limitations of this study. First, because it is an observational study, the causal relationship between the variables studied cannot be established with certainty. Furthermore, the single-center nature of this study limits the application of the results to the reality of other regions of Brazil and other countries. In addition, some relevant variables were

not included in the analysis of risk factors for hospitalization (such as immunosuppressive regimen in use and adherence to treatment). Although these variables influence the incidence of hospitalizations in the first year after transplantation, such data were unavailable for collection during the study.

CONCLUSION

This study identified a high frequency of hospitalizations in the first year after transplantation, with the first hospitalization resulting in death in three cases, none of which were due to infectious causes. Considering the contribution of procedures considered elective to this statistic, the first step towards improvement may be to invest in outpatient resolution in situations such as Tenckhoff catheter removal, renal graft biopsy and treatment of mild cases of CMV infection (a situation in which the greater availability of oral antiviral medication would be of great benefit, eliminating the need for hospitalization).

Future studies, with the analysis of more extensive, multicenter samples and with a more extended follow-up period, may provide greater statistical power and identify modifiable risk factors for the occurrence of hospitalization, causing a positive impact on short- and long-term outcomes for this population.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Ferreira VM, Sarcinelli CCS, Alvarenga AS; **Conception and design:** Ferreira VM, Sarcinelli CCS, Alvarenga AS; **Data analysis and interpretation:** Ferreira VM, Sarcinelli CCS, Alvarenga AS; **Article writing:** Ferreira VM, Sarcinelli CCS; **Critical revision:** Alvarenga AS; **Final approval:** Ferreira VM, Sarcinelli CCS, Alvarenga AS.

DATA AVAILABILITY STATEMENT

Data will be available upon request.

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