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ORIGINAL PAPER

Factors Associated with Hospital Readmission in the First Year After Liver Transplantation

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ABSTRACT

Objectives: Liver transplantation is the primary treatment for various cases of advanced liver disease. The occurrence of complications within the first year post-transplant influences patient survival and quality of life, in addition to increasing healthcare costs. This study aims to analyze potential factors associated with the incidence of hospital readmission after liver transplantation. **Methods:** A retrospective study was conducted using data from liver transplant recipients at Hospital Felício Rocho who underwent transplantation between July 1, 2018, and June 30, 2022. The study assessed their readmissions and one-year survival, as well as the relationship between these outcomes and donor and recipient data, surgical procedure details, and hospitalization duration for transplantation. **Results:** The sample comprised 128 cases, with a median age of 57.5 years. Most patients experienced at least one readmission within the first year, totaling 141 readmissions during the period, with infection being the leading cause. In univariate analysis, risk factors for readmission included the need for renal replacement therapy (p = 0.038), intensive care unit (ICU) stay > 8 days (p = 0.023), and hospital stay exceeding 20 days (p = 0.029). In multivariate analysis, ICU stay > 8 days remained associated with readmission, while readmission frequency and underlying liver disease were linked to survival at the end of the period. **Conclusion:** An ICU stay longer than 8 days is the primary risk factor associated with readmissions within the first year post-transplant. Additionally, readmission frequency and underlying liver disease are factors related to reduced one-year survival.

Descriptors: Liver Transplantation; Readmissions; Survival.

Fatores Associados à Reinternação Hospitalar no Primeiro Ano Pós-Transplante Hepático

RESUMO

Objetivos: O transplante hepático é o principal tratamento em diversos casos de doença hepática avançada. A ocorrência de complicações no 1º ano pós-transplante é fator influenciador na sobrevida e na qualidade de vida dos pacientes, além de aumentar os custos em saúde. O objetivo do presente estudo é analisar potenciais fatores relacionados à incidência de reinternação após transplante hepático. **Métodos:** Estudo retrospectivo com informações de receptores de fígado do Hospital Felício Rocho transplantados no período de 1 de julho de 2018 a 30 de junho de 2022, avaliando suas reinternações e sobrevida ao final de 1 ano, além da relação desses desfechos com dados dos doadores e receptores, do procedimento cirúrgico e do período de internação para o transplante. **Resultados:** Amostra de 128 casos, com mediana de idade de 57,5 anos. A maioria apresentou pelo menos uma reinternação no 1º ano, sendo 141 o total de reinternações no período, com infecção como principal causa. Em análise univariada, foram fatores de risco para reinternação a necessidade de terapia de substituição renal (p = 0,038), tempo de permanência no centro de terapia intensiva (CTI) > 8 dias (p = 0,023) e permanência hospitalar de mais de 20 dias (p = 0,029). Na análise multivariada, a permanência no CTI > 8 dias permaneceu associada à reinternação, enquanto a frequência de reinternações e a doença hepática de base se relacionaram com a sobrevida ao final do período. **Conclusão:** A permanência no CTI por mais de 8 dias é o principal fator de risco associado às reinternações no 1º ano pós-transplante. A frequência de reinternações e a doença hepática de base, por sua vez, são fatores relacionados à redução da sobrevida em 1 ano.

Descritores: Transplante Hepático; Reinternações; Sobrevida.

INTRODUCTION

Liver transplantation is the primary therapeutic option for patients with advanced liver disease, whether acute or chronic. Currently, in Brazil, the average survival rate in the first year after transplantation is approximately 70%[1]. The highest occurrence of complications and hospitalizations after the procedure occurs in the 1st postoperative year, with a tendency to reduce over time[2]. There are several causes of hospitalization in the first year after transplantation, including infections, surgical complications, vascular events and graft rejection, increasing healthcare costs for the care of these patients[3,4]. Overall, 1-year readmission rates after liver transplantation range from 15% to 69%[5,6].

Regarding risk factors related to readmissions, there are some differences in the factors currently linked to readmissions in the first year, in the first 90 days and in the first 30 days. In the first year, the main ones are abdominal surgery before the transplant, liver neoplasia as an indication for the transplant and the occurrence of any complication after the transplant[5].

In the first 90 days, the etiology of liver disease, specifically hepatitis caused by the hepatitis C virus, is the main factor described[7]. In the first 30 days, the need for hospitalization up to 90 days before the transplant, portal vein thrombosis before the procedure, creatinine levels greater than 1.9, albumin less than 2.6, and surgical complications are factors related to the subsequent need for readmission[8].

Hospitalizations worsen recipients' quality of life, bringing higher costs to the hospital and the Unified Health System (Sistema Único de Saúde-SUS) and potentially reducing patient survival[3,4]. By identifying prognostic factors related to the donor, recipient, or procedure, it is possible to act against modifiable risk factors and optimize treatment and monitoring of complications in patients in the postoperative period to reduce the occurrence of complications. A lower rate of complications also tends to reduce the frequency of hospitalizations, improve recipients' quality of life, with potential gains in survival, and minimize costs to the health system.

The objective of this study was to identify the occurrence of readmissions in the first year after liver transplantation in patients transplanted between 2018 and 2022 and to identify related demographic, clinical, and laboratory characteristics. In addition, the objective was to analyze the impact of readmissions on survival at the end of one year and other potential risk factors for death in the first year after transplantation.

METHODS

This retrospective study used information from liver recipients of both sexes from Hospital Felício Rocho (HFR), whose transplant was performed between July 1, 2018, and June 30, 2022. Information regarding the surgical procedure, donors, and readmissions in the first year after transplantation, recorded in medical records and the database of the HFR liver transplant service, were used.

Patients who were lost to follow-up in the service less than 1 year after liver transplantation, as well as those who died during hospitalization for transplantation, were excluded from this study since, in these cases, it would not be possible to analyze readmissions in 1 year after hospital discharge.

For patients retransplanted early, during the same hospitalization as the first transplant, the first procedure and its complications were excluded for the same reason. In this case, data relating only to the second procedure were considered, as well as characteristics relating to the donor of this event and the clinical conditions of the recipient at that time.

Electronic research in the HFR medical records obtained data on the recipients and procedures. Donor information was provided by the National Transplant System (Sistema Nacional de Transplantes-SNT) database.

The study's dependent variable is the occurrence of hospital readmissions of transplant patients in the 1-year post-transplant period or until the date of death if this occurs less than 1 year after the procedure.

Readmissions were grouped according to their etiology into the following groups: cytomegalovirus (CMV) infection, other infections, biliary complications – such as fistulas and bile duct stenosis requiring intervention – rejection requiring pulse therapy, vascular complications – such as a portal vein or hepatic artery thrombosis – and others – such as renal dysfunction, hydroelectrolytic disorders and cardiovascular events.

During this period, the diagnosis of CMV infection was made through antigenemia testing so that a result greater than or equal to 7 cells was considered an indication for preemptive CMV treatment. In the service in question and during the period considered, there was no availability for oral or intravenous medication infusion treatment in a day hospital. Therefore, patients with an indication for preemptive treatment required hospitalization to receive the medication.

Potential prognostic factors associated with post-transplant readmission were used as independent variables, including age and sex of the donor and recipient, laboratory tests of the recipient, and underlying liver disease. All variables considered are listed in Tables 1 and 2.

Table 1. Characteristics of the recipient and the surgical procedure.

Recipient variables		Distribution
Sex	Male	95 (74.2%)
	Female	33 (25.8%)
Age (years)		57.5 (I49.5-63.8)
Underlying liver disease	NASH/cryptogenic	33 (25.8%)
	Ethanolic	41 (32.0%)
	Viral	15 (11.7%)
	Autoimmune	21 (16.4%)
	Others	18 (14.1%)
MELD calculated		20.0 (16.0-24.0)
MELD assigned		21.0 (20.0-25.0)
Special situation		44 (34.4%)
Type of special situation	HCC	25 (56.6%)
	Refractory ascites	15 (34.1%)
	Hepatic encephalopathy	0 (0.0%)
	Recurrent cholangitis	1 (0.1%)
	Refractory pruritus	0 (0.0%)
	Hepatic artery thrombosis	2 (0.1%)
	Hepatopulmonary syndrome	1 (0.1%)
Comorbidities	DM	35 (27.3%)
	SAH	34 (26.6%)
	CKF	4 (3.1%)
Previous abdominal surgery		41 (32.0%)
Negative CMV serology		5 (3.9%)
Nutritional status	Normal or risk	57 (44,5%)
	Malnutrition	26 (20,3%)
	Severe malnutrition	35 (27,3%)
	Overweight or obesity	8 (6,3%)
CIT (minutes)		390,0 (330,0-480,0)
Retransplantation		7 (5,5%)

Source: Elaborated by authors. HCC = hepatocellular carcinoma; DM = diabetes mellitus; SAH = systemic arterial hypertension; CKF = chronic kidney failure.

Table 2. Characteristics of liver graft donors.

Donor variables		Distribution
Sex	Male	83 (64.8%)
	Female	45 (35.2%)
Age (years)		44.5 (30.3-56.0)
Cause of brain death	CVA	63 (49.2%)
	TBI	47 (36.7%)
	Others	18 (14.1%)
Use of antibiotics at the time of donation		78 (60.9%)
Noradrenaline use at the time of donation		103 (80.5%)
Length of hospital stay (days)		4.0 (2.0-6.75)

Source: Elaborated by authors. CVA = cerebrovascular accident; TBI = traumatic brain injury.

Regarding the patient's underlying liver disease, etiology groups were created to facilitate analysis: ethanol, non-alcoholic steatohepatitis (NASH)/cryptogenic, viral, autoimmune, and others. Regarding the assessment of nutritional status by nutrologists, patients were grouped into four categories: standard or at risk of malnutrition, malnourished, severely malnourished, and overweight or obese.

Finally, variables related to hospitalization for transplantation were also evaluated: total length of hospital stay, length of stay in the intensive care unit (ICU), and occurrence of complications during hospitalization for transplantation.

Descriptive frequency analysis was performed for nominal variables. Comparisons involving these variables were analyzed using the chi-square test. Data were presented by the median and interquartile range (IQR) to analyze quantitative variables with non-normal distribution, and the Mann-Whitney test was used for comparisons.

The associations between donor, recipient and procedure-related variables and the occurrence of readmissions for different causes were analyzed. The same variables were also correlated with the recipient's status at the end of 1 year. This analysis identified statistically significant variables at a significance level less than or equal to 0.05. Finally, variables potentially related to the outcomes in the univariate analyses were included in the multivariate analysis. Statistical calculations were performed using IBM SPSS Statistics version 29.0.2.0.

RESULTS

During the period analyzed, 188 liver transplants were performed at the institution. Of these, 60 cases were excluded: five due to loss of clinical follow-up, eight due to the need for retransplantation during the same hospitalization, and 47 due to death while still hospitalized for transplantation. The sample analyzed, therefore, contains a total of 128 cases.

The median age was 57.5 years (IQR 49.5-63.8), and 74.2% were male. In most cases, the indication for transplantation was due to cirrhosis of ethanol etiology – 41 cases (32%) – followed by NASH or cryptogenic – 33 cases (25.8%). The group designated as other etiologies included patients with hemochromatosis, Wilson's disease, alpha-1 antitrypsin deficiency, secondary biliary cholangitis, drug-induced cirrhosis, hepatic artery thrombosis, or Budd-Chiari syndrome. Patients had a median model for end-stage liver disease (MELD) calculated sodium of 20.0 (IQR 16.0-24.0) and a MELD attributed sodium of 21.0 (IQR 20.0-25.0). Other clinical characteristics of the recipient, such as comorbidities and nutritional status, are described in Table 1.

Regarding donors, the median age was 44.5 years (IQR 30.3-56.0), and most of the sample was male (64.8%). Most donors (60.9%) were using antibiotics, and 80.5% were using vasoactive amines at the time of donation. Donor characteristics are described in Table 2.

Regarding the procedure, only seven (5.5%) were retransplants, and the median cold ischemia time (CIT) was 390.0 minutes (IQR 330.0-480.0) (variables also described in Table 1).

When analyzing hospitalization for transplantation, it was possible to note a median length of stay in the ICU of 5.5 days (IQR 4.0-8.0) and a total length of hospital stay of 17.0 days (IQR 12.0-24.8).

Regarding complications occurring during hospitalization for transplantation, the primary etiology was a bacterial infection in 45 cases (35.2%), followed by the need for renal replacement therapy (16.4%), bleeding (10.9%) and preemptive CMV treatment (10.2%). More rarely, biliary complications (3.9%), vascular complications (2.3%) and acute cellular rejection (2.3%). The survival rate at the end of 1 year of follow-up in the sample studied was 91.4%.

Most patients (56.3%) had at least one readmission within 1 year after hospital discharge from the transplant, and the median number of readmissions per patient was 1.0 (IQR 0.0-2.0), with a maximum of 6. The time elapsed between hospital discharge and the first readmission occurred with a median of 61.0 days (IQR 38.0-131.3), and the median time until the 6th (and last) readmission was 257.0 days (IQR 142.8-345.8).

The analysis of the main indications for hospitalizations identified the following as the main etiologies: infection in 23.4% of cases (33 patients), preemptive treatment for CMV in 20.6% (29), and biliary complications in 12.8% (18) (Table 3).

Table 3. Main causes of hospital readmission in each readmission event.

Causes	Readmissions						
	1ª	2ª	3ª	4ª	5ª	6ª	Total n (%)
Infection	11	11	3	3	3	2	33 (23.4)
CMV Treatment	22	3	2	2	0	0	29 (20.6)
Biliary complications	6	4	2	4	1	1	18 (12.8)
Rejection	9	5	1	0	0	1	16 (11.3)
Vascular complications	4	4	3	2	0	0	13 (9.2)
Others	20	9	3	0	0	0	32 (22.7)
Total hospitalizations	72	36	14	11	4	4	141 (100.0)

Source: Elaborated by authors

Initially, it was possible to identify an association between the need for hospital readmission and survival at the end of 1 year: patients who had some readmission had a higher risk of death than those who did not ($p = 0.002$) (Table 4). More specifically, readmissions for preemptive CMV treatment ($p = 0.006$) and those caused by other infections were associated with a higher risk of death ($p < 0.001$) (Table 5). In addition, the total number of readmissions in 1 year influences survival. Patients with two or more readmissions had lower survival than those with none or only

one hospitalization (p = 0.011). The etiology of liver disease was also related to survival; patients grouped into "other etiologies" had lower survival (p = 0.011). Other characteristics of the donor, recipient or procedure alone did not constitute risk factors for death in 1 year.

Table 4. Factors associated with status at the end of 1 year.

Variables		Living	Death	*p*-value
Post-transplant readmissions		61 (52.1%)	11 (100.0%)	**0.002**
Number of readmissions	Up to 1 readmission	88 (75.2%)	4 (36.4%)	**0.011**
	2 or more readmissions	29 (24.8%)	7 (63.6%)	
Recipient's sex (M/F)		88 (75.2%)/29 (24.8%)	7 (63.6%)/4 (36.4%)	0.473
Age of the recipient		58.2 (50.1-64.1)	53.6 (44.1-60.0)	0.282
MELD calculated		19.0 (16.0-23.5)	23.0 (19.0-28.0)	0.122
MELD assigned		21.0 (20.0-24.5)	24.0 (20.0-28.0)	0.119
Retransplantation		6 (5.1%)	1 (9.1%)	0.475
DM		32 (27.4%)	3 (27.3%)	1.000
Arterial hypertension		30 (25.6%)	4 (36.4%)	0.481
CKD		4 (3.4%)	0 (0.0%)	1.000
Previous abdominal surgery		37 (31.6%)	4 (36.4%)	0.744
Liver disease	NASH/cryptogenic	29 (24.8%)	4 (36.3%)	**0.011**
	Ethanolic	39 (33.3%)	2 (18.2%)	
	Viral	12 (12.8%)	0 (0.0%)	
	Autoimmune	21 (17.9%)	0 (0.0%)	
	Others	13 (11.1%)	5 (45.5%)	
Presence of HCC		24 (20.5%)	2 (18.2%)	1.000
Refractory ascites		13 (11.1%)	2 (18.2%)	0.617
Special situation		37 (31.6%)	4 (36.4%)	0.744
Negative serology for CMV		3 (2.6%)	2 (18.2%)	0.058
Nutritional status	Normal or risk	51 (44.3%)	6 (54.5%)	0.793
	Malnutrition	24 (20.9%)	2 (18.2%)	
	Severe malnutrition	32 (27.8%)	3 (27.3%)	
	Overweight or obesity	8 (7.0%)	0 (0.0%)	
Complications during transplant hospitalization	Kidney replacement therapy	20 (17.1%)	1 (9.1%)	0.691
	Bacterial infection	42 (35.9%)	3 (27.3%)	0.746
	Preemptive CMV treatment	13 (11.1%)	0 (0.0%)	0.602
	Vascular complications	3 (2.6%)	0 (0.0%)	1.000
	Bleeding	13 (11.1%)	1 (9.1%)	1.000
	Biliary complications	4 (3.4%)	1 (9.1%)	0.367
	Rejection	3 (2.6%)	0 (0.0%)	1.000
	Cardiovascular event	5 (4.3%)	0 (0.0%)	1.000
	Neurological event	4 (3.4%)	0 (0.0%)	1.000
CIT		390.0 (325.0-480.0)	390.0 (360.0-540.0)	0.548
Donor sex (M/F)		75 (64.1%)/42 (35.9%)	8 (72.7%)/3 (27.3%)	0.746
Donor age		44.0 (30.0-56.0)	45.0 (36.0-51.0)	0.892
Cause of brain death	CVA	57 (48.7%)	6 (54.5%)	0.776
	TBI	44 (37.5%)	3 (27.3%)	
	Others	16 (13.7%)	2 (18.2%)	
Antibiotic use – donor		69 (59.0%)	9 (81.8%)	0.200
Noradrenaline use – donor		94 (80.3%)	9 (81.8%)	1.000
Donor hospitalization time		4.0 (2.0-6.0)	4.0 (2.0-10.0)	0.894
Length of stay in ICU > 8 days		22 (18.8%)	3 (27.3%)	0.448
Length of hospital stay > 24 days		30 (25.6%)	2 (18.2%)	0.730

Source: Elaborated by authors. Bold p-values indicate statistically significant differences. F = female; M = male.

Table 5. Relationship between the different causes of readmission and the status at the end of 1 year.

Causes of readmission	Living n (%)	Death n (%)	*p*-value
CMV	22 (25.0)	6 (31.5)	**0.060**
Other infections	18 (20.4)	7 (36.9)	**< 0.001**
Rejection	8 (9.1)	3 (15.7)	0.052
Biliary complications	10 (11.4)	0 (0.0)	0.171
Vascular complications	5 (5.6)	1 (5.4)	0.514
Other causes	25 (28.5)	2 (10.5)	0.801

Source: Elaborated by authors. Bold *p*-values mean statistically significant differences.

When analyzing potential risk factors for readmissions, the factors associated with a greater need for readmission were the need for renal replacement therapy in the postoperative period ($p = 0.038$), ICU stay for more than 8 days ($p = 0.023$), and hospital stay for more than 20 days ($p = 0.039$). In the sample analyzed, negative pre-transplant CMV serology showed a tendency for a greater need for readmissions ($p = 0.067$) and higher mortality at 1 year (p = 0.058), but without reaching statistical significance ($p < 0.05$). Other characteristics of the recipient, donor, procedure, and complications during hospitalization for transplantation were not related to the need for readmission, as explained in Table 6.

Table 6. Factors related to the need for readmission within 1 year.

Variables		Post-transplant readmission		*p*-value
		No	Yes	
Recipient's sex (M/F)		40 (71.4%)/16 (28.6%)	55 (76.4%)/17 (23.6%)	0.524
Recipient's age		57.2 (49.5-63.8)	58.4 (49.1-64.2)	0.439
MELD calculated		19.0 (15.0-23.0)	20.0 (16.3-24.0)	0.100
MELD assigned		21.0 (20.0-25.8)	21.0 (20.0-24.0)	0.981
Retransplantation		4 (7.1%)	3 (4.2%)	0.698
DM		18 (32.1%)	17 (23.6%)	0.283
Arterial hypertension		17 (30.4%)	17 (23.6%)	0.391
CKD		0 (0.0%)	4 (5.6%)	0.131
Previous abdominal surgery		21 (37.5%)	20 (27.8%)	0.242
Liver Disease	NASH/cryptogenic	14 (25.0%)	19 (26.4%)	0.464
	Ethanolic	19 (33.9%)	22 (30.6%)	
	Viral	7 (12.5%)	8 (11.1%)	
	Autoimmune	8 (14.3%)	13 (18.1%)	
	Others	8 (14.3%)	10 (13.8%)	
Presence of HCC		13 (23.2%)	13 (18.1%)	0.472
Refractory ascites		7 (12.5%)	8 (11.1%)	0.809
Special situation		21 (37.5%)	20 (27.8%)	0.242
Negative serology for CMV		0 (0.0%)	5 (6.9%)	0.067
Nutritional status	Normal or risk	25 (45.5%)	32 (45.1%)	0.556
	Malnutrition	9 (16.4%)	17 (23.9%)	
	Severe malnutrition	16 (29.1%)	19 (26.8%)	
	Overweight or obesity	5 (9.1%)	3 (4.2%)	
Complications during hospitalization for transplant	Kidney replacement therapy	5 (8.9%)	16 (22.2%)	**0.044**
	Bacterial infection	18 (32.1%)	27 (37.5%)	0.529
	Preemptive CMV treatment	4 (7.1%)	9 (12.5%)	0.387
	Vascular complications	1 (1.8%)	2 (2.8%)	1.000
	Bleeding	7 (12.5%)	7 (9.7%)	0.617
	Biliary complications	1 (1.8%)	4 (5.6%)	0.385
	Rejection	0 (0.0%)	3 (4.2%)	0.256
	Cardiovascular event	1 (1.8%)	4 (5.6%)	0.385
	Neurological event	2 (3.6%)	2 (2.8%)	1.000
CIT		367.5 (300.0-450.0)	405.0 (330.0-510.0)	0.145
Donor sex (M/F)		38 (67.9%)/18 (32.1%)	45 (62.5%)/(27 (37.5%)	0.529
Donor age		44.0 (30.0-55.8)	45.0 (31.3-56.8)	0.658

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Table 6. Continuation...

Variables		Post-transplant readmission		*p*-value
		No	Yes	
Cause of brain death	CVA	26 (46.4%)	37 (51.4%)	0.656
	TBI	23 (41.1%)	24 (33.3%)	
	Others	7 (12.5%)	11 (15.3%)	
Antibiotic use – donor		35 (62.5%)	43 (59.7%)	0.749
Noradrenaline use – donor		46 (82.1%)	57 (79.2%)	0.674
Donor hospitalization time		4.0 (2.0-6.0)	3.5 (2.0-7.0)	0.915
Length of stay in ICU > 8 days		6 (10.7%)	19 (26.4%)	**0.026**
Length of hospital stay > 24 days		9 (16.1%)	23 (31.9%)	**0.040**

Source: Elaborated by authors. Bold *p*-values mean statistically significant difference.

Finally, clinically relevant variables that presented $p < 0.20$ in the univariate analysis were included in the multivariate analysis. In the search for association with the occurrence of readmissions, the following variables were included: length of hospital stay longer than 24 days, length of ICU stay greater than 8 days, renal replacement therapy in the initial post-transplant period, and negative serology for CMV. The only significant variable related to readmission remained the length of ICU stay greater than 8 days ($p = 0.031$).

Regarding the status at the end of 1 year, the variables included in the multivariate analysis were the occurrence of readmissions, the number of readmissions, liver disease, and negative serology for CMV. The relevant factors were the number of readmissions ($p = 0.004$) and the underlying liver disease – other etiologies group with lower survival ($p = 0.019$).

DISCUSSION

Liver transplantation is a highly complex surgical procedure performed on potentially serious patients, especially those with advanced liver cirrhosis or acute liver failure. Therefore, it is understandable that this is a procedure with a high frequency of associated complications and, consequently, a high rate of long-term readmission.

Several studies have shown the relationship between the occurrence of hospital readmissions and the reduction in survival of transplant patients[5,6,9]. However, there are other studies in which this relationship has not been established[10]. Furthermore, multiple readmissions tend to increase the costs related to liver transplantation[3,4]. All these factors justify the analysis of readmissions and their association with the characteristics of the recipient and donor, intending to enable interventions that help reduce hospital readmissions.

This study analyzes the context of a private hospital serving SUS patients. The period from July 1, 2018, to June 30, 2022, was chosen due to the greater ease of access to hospital record data. As already explained, the sample size of this study contains 128 cases. The sample was similar to other studies in the literature concerning the median age of the recipients, the predominance of males, and other clinical data, such as the median MELD score at transplantation and the occurrence of previous abdominal surgery[5,7,9,10].

At least one readmission was identified in 56.3% of the cases analyzed. Readmission rates vary widely in the literature, from 18 to 69%, in periods ranging from 30 days to 1 year of follow-up[5-8].

Infections were the leading cause of readmission in this study (23.4% of cases), followed by hospitalization for preemptive CMV treatment. In other studies, infections are the main indication for readmission, with an incidence ranging from 19.5 to 48%[5,6,10,11]. Less frequently, other studies highlight other leading causes of readmission, such as surgical complications and rejection[12].

Regarding the infection sites identified in readmissions, abdominal infection was recognized as the most frequent (12 cases), corresponding to 36.37% of the infections considered, followed by respiratory (27.27%) and urinary (15.15%) infections. Less frequently, other infections were detected (21.21% of cases): catheter infection, skin infection, neurotuberculosis, oral candidiasis and herpes zoster. A recent study developed in China describes respiratory infections as the most common causes of post-transplant readmissions, unlike what was found in the current case series[11].

This study's high need for hospitalization for preemptive CMV treatment is noteworthy, unlike what is usually seen in the literature. This is because, during the period analyzed, it was not possible to perform outpatient CMV treatment with valganciclovir or in a day hospital with intravenous ganciclovir for transplant patients admitted by the SUS. Therefore, these patients with an indication for preemptive treatment needed to be hospitalized to receive the medication.

It is also important to emphasize that the relatively low frequency of biliary, vascular and acute cellular rejection complications found in the study does not reflect the total number of complications of this type that generally occur in the service. Many of these complications occur early, during the same hospitalization for transplantation. Since, in this study, patients who died or required retransplantation during the same hospitalization for transplantation were excluded from the analysis, some complications that occurred early in the postoperative period were disregarded. The data presented clearly show the association between the occurrence of readmissions and the reduction in 1-year survival ($p = 0.002$) and, mainly, the relationship between hospitalization due to infections or preemptive CMV treatment and death within 1 year. More specifically, there was also a relationship between the higher frequency of readmissions (two or more) and lower survival. This reduction is also found in other studies[5,6].

Another characteristic that proved relevant in the current analysis was the etiology of liver disease. In comparison, some studies have shown hepatitis C as a factor related to readmissions[7,9]. This study demonstrated lower survival rates in patients included in the group with other etiologies ($p = 0.019$). One possible explanation for this relationship is that part of this group comprises retransplant patients, whose etiology of the second procedure was hepatic artery thrombosis. These are usually more severe patients, which may explain their unfavorable outcomes.

Concerning risk factors associated with a higher risk of readmissions, the main variables identified in the literature were the diagnosis of liver neoplasia[5], previous abdominal surgery[5], postoperative complications[5,8] and chronic kidney disease (CKD) before transplantation, mainly requiring renal replacement therapy[13,14]. Prolonged transplant hospitalization also appears as an essential factor related to the risk of readmissions[9,10,11,15]. Regarding the length of hospital stay, Yataco et al.[10] concluded that hospitalization lasting longer than 7 days increased the risk of readmissions, while Patel et al.[9] showed that hospitalization for more than 14 days was a risk factor. In the present study, prolonged hospitalization was associated with a higher readmission rate. In univariate analysis, hospitalization for more than 24 days and ICU stay for more than 8 days were statistically significant, while in multivariate analysis, ICU stay was the variable that remained significant ($p = 0.031$).

The limitations of this study include its retrospective nature and the fact that it was conducted in a single center. Therefore, it is necessary to develop other prospective and multicenter studies.

CONCLUSION

The main factor associated with the need for hospital readmissions in the first year after liver transplantation is the length of stay in intensive care for more than 8 days. The frequency of readmissions, mainly secondary to infections and preemptive CMV treatment, and the etiology of liver disease harm survival after 1 year of liver transplantation.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Pereira BB; **Conception and design:** Pereira BB; **Data analysis and interpretation:** Pereira BB; **Article writing:** Pereira BB; **Critical revision:** Martins GM, Andrade AMF; **Final approval:** Pereira BB.

DATA AVAILABILITY STATEMENT

All dataset were generated or analyzed in the current study.

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