

ORIGINAL CONTRIBUTION

2,611 Liver Transplants: Indications and Survival Rates of a High-Volume Latin American Center

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ABSTRACT

Introduction and Objectives. The liver transplantation program at the Centro de Transplante de Fígado do Ceará (CTFC), one of the largest centers in Northern and Northeastern Brazil, was evaluated over a 23-year period to describe indications, recipient characteristics, and survival outcomes.

Materials and Methods. This retrospective cohort included 2611 liver transplants performed in 2491 patients between 2002 and 2025. Demographic, clinical, surgical, and laboratory data were collected from medical records and managed using REDCap. Survival was estimated using Kaplan−Meier analysis.

Results. Most recipients were middle-aged men, predominantly from outside the state, and nearly all procedures were funded by the public health system. The main indications for transplantation were decompensated cirrhosis, hepatocellular carcinoma, and alcohol-related liver disease, reflecting global epidemiological shifts. Overall survival rates were 88% at one month, 79% at one year, and 71% at 5 years, with progressive improvement over time. Donor characteristics and ischemia times were consistent with international standards.

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Conclusions. These results show that a high-volume public transplant center can achieve outcomes comparable to major international programs while serving a socioeconomically diverse population.

LIVER transplantation represents the only curative therapy for patients with end-stage liver disease and primary hepatic malignancies, having led to substantial improvements in long-term survival. The standard immunosuppression regimen used in liver transplantation consists of a calcineurin inhibitor (most commonly tacrolimus) as the backbone, often combined with mycophenolate mofetil or everolimus and corticosteroids for early post-transplant management [1,2].

Over the past 2 decades, the indications for liver transplantation have changed markedly. There has been a significant decline in transplants performed for viral hepatitis (hepatitis B and C), primarily due to the widespread use of direct-acting antivirals for hepatitis C and improved management of hepatitis B. In contrast, there has been a substantial increase in liver transplants performed for metabolic dysfunction-associated steatotic liver disease (MASLD, formerly known as nonalcoholic steatohepatitis [NASH]) and alcohol-associated liver disease. Recent registry data from North America and Europe confirm that MASLD and alcohol-associated liver disease have now become the leading indications for liver transplantation, surpassing viral etiologies [3−5].

In the United States, the proportion of liver transplants for chronic hepatitis C declined from 28% in 2013 to 4% in 2022, while transplants for MASLD (NASH/MASH) increased from 19% to 27% over the same period. Alcohol-associated liver disease also rose sharply, now representing the most common indication among patients without hepatocellular carcinoma. Similar trends are observed in Europe and Spain, although the increase in MASLD-related transplants has been less pronounced outside North America [3,6].

Brazil ranks fourth globally in the absolute number of liver transplants, with nearly 90% of the procedures funded by the public health system (Sistema Único de Saúde − SUS). The liver transplantation program at CTFC has been active since 2002 and serves as the principal referral center for liver transplantation in the North and Northeast regions of Brazil, performing approximately 160 transplants annually. National data consistently show that Brazil performed 2449 liver transplants in the year 2024, the vast majority financed by SUS − reflecting the country's commitment to universal access and public investment in high-complexity healthcare [7]. Nonetheless, regional disparities persist, and specialized centers such as HUWC play a crucial role in expanding access and mitigating inequities in transplantation services. The national liver transplant waiting list in Brazil has evolved according to federal regulations: from 2002 to 2006, organ allocation was based on the chronological order of registration; from 2007 to 2018, the Model for End-Stage Liver Disease (MELD) score was adopted (resolutions 1.160 of 05/29/2006 and 2.600 of 10/21/2009 from the Minister of Health); and since 2019 the MELD-Na score has been implemented, incorporating serum sodium for improved mortality prediction. (Resolution 2.049 of 08/09/2019 from the Minister of Health) [8−10].

The aim of this study was to describe the indications, epidemiological profile, and survival outcomes of liver transplantation at 2 reference centers over 2 decades of clinical practice.

MATERIALS AND METHODS

Study Design and Ethical Considerations

This retrospective cohort included patients who underwent LT at 2 tertiary reference center in Brazil from May 2002 to May 2025. This study was approved by the institutional ethics committee of HUWC-UFC, with the number 7.229.434, being conducted in accordance with the Declaration of Helsinki.

Demographic, Clinical, Surgical and Laboratorial Data

Data were collected from medical records and securely stored in the RedCap® database, ensuring maximum data security and confidentiality [11,12]. Demographic variables included gender, age at LT, race, body-mass index (BMI), education level, origin, indication for liver transplantation, etiology of liver disease, staging according to the Child classification, blood type, calculated and corrected Model for End-Stage Liver Disease MELD-Na score, special situations (exceptions to MELD-NA), Child Classification, comorbidities, alcohol and smoking habits, and prior drug use. Biochemical tests (blood count, liver function, renal function, alpha-fetoprotein levels), pre-LT staging of hepatocellular carcinoma (HCC) according to BCLC, donor (age, sex, cause of death, blood type, organ origin), warm ischemia time, cold ischemia time, explant biopsy, type of immunosuppression, clinical outcome, causes of death, 1, 12, and 5-month survival.

Surgery, Immunosuppression and Hepatocellular Carcinoma

The team's standard technique for liver transplantation is the piggyback technique with end-to-end anastomoses of the portal and common bile ducts. Arterial anastomosis is usually performed between the donor's hepatic artery and the recipient's hepatic artery, enlarged by joining the gastroduodenal artery with interrupted sutures. The immunosuppression protocol consists of the use of tacrolimus 0,1 mg/kg/day associated with prednisone (20 mg in the first month with progressive reduction to 5 mg from the fourth month after liver transplantation, followed by discontinuation. The serum tacrolimus level is maintained between 6 and 8 ng/mL in the first 6 months and 4 to 6 ng/mL indefinitely after liver transplantation. Mycophenolate sodium (average dose 720-1440 mg/day) or everolimus (level 3

to 8 ng/mL) are associated in patients with renal dysfunction. Post-LT complications were assessed by our multidisciplinary liver transplantation team. The end of follow-up corresponded to death, date of loss to follow-up or last medical examination. Brazilian legislation adopts the Milan-Brazil criteria for hepatocellular carcinoma, where only measuring 2 cm or larger are counted, and up to 3 nodules measuring up to 3 cm or 1 nodule measuring up to 5 cm are accepted. The alpha-fetoprotein level must be less than 1000, and downstaging is assessed using M-recist [13,14].

Statistical Analysis

Continuous data were summarized as mean ± standard deviation (SD) or median ± interquartile range (IQR), based on the distribution's normality, as determined by the Kolmogorov-Smirnov test. Categorical variables were expressed as percentages. In the survival analysis for patient and graft outcomes, these were considered as time-dependent events and were analyzed as a fixed event. Kaplan-Meier (KM) curves were used for visual assessment of time-dependent patterns. Statistical significance was set at a 2-tailed P-value < .05. All analyses were conducted using R software (version 4.3.2, R Foundation for Statistical Computing, Vienna, Austria).

RESULTS

From May 2002 to May 2025, a total of 2,611 liver transplants were performed in 2,491 patients, including 120 retransplants (4.8%). The majority of patients (57.3%) originated from other Brazilian states, predominantly from the North (23.1%) and Northeast (28.8%) regions. Regarding race/ethnicity, most patients were mixed-race (n = 1308; 76.4%), followed by White (n = 304; 17.8%), Black (n = 60; 3.5%), Asian (n = 24; 1.4%), and unknown (n = 15; 0.9%). With respect to educational level (data available for n = 857), most patients had completed or partially completed primary education (n = 421; 49.1%), followed by secondary education (n = 290; 33.8%) and technical or higher education (n = 146; 17.1%).

Clinical and epidemiological data of the patients are found in Table 1. Indications by etiology can be seen in Fig 1.

Regarding survival estimates, the overall survival curve for the entire period was 88%, 79%, and 71% at 1, 12, and 60 months, respectively. When grouped by time period, survival rates at the same time points were 84%, 78%, and 64% for 2002−2007; 88%, 78%, and 71% for 2007−2018; and 91%, 82%, and 71% for 2019−2025 (Figure 2), with $P < .05$. In the first period (2002 to 2006), the liver transplant list followed a chronological order of registration. In the second period (2007 to 2018), the MELD score was adopted, and in the third period (2019-present), the MELD-Na score was adopted.

The main causes of donor death were trauma brain injury (TBI) (294; 53.7%), hemorrhagic stroke (150; 27.4%) and ischemic stroke (37; 6.8%). The mean age was 40.8 (n = 657) years and 66% (n = 406) were male. The mean warm ischemia time was 30 minutes and the mean cold ischemia time was 340 minutes.

DISCUSSION

This study provides a comprehensive overview of more than 2 decades of experience with liver transplantation (LT) at a high-volume reference center in Northeastern Brazil, encompassing over 2,600 procedures. The findings reveal key demographic, clinical, and survival trends that mirror global changes in LT epidemiology, while also highlighting regional particularities shaped by Brazil's public healthcare system and geographic disparities.

The largest published Latin American case series of liver transplantation are concentrated in Brazil and Argentina, with additional significant data from Colombia and Chile. Few studies have published the experience of a single liver transplant center. In Brazil, a center in the Midwest reported outcomes from 500 consecutive deceased donor liver transplants, with 1-year and 5-year patient survival rates of 85% and 80%, respectively. Early mortality was primarily associated with higher MELD scores, and outcomes were comparable to international benchmarks despite regional disparities in access [15].

The demographic profile of this cohort − predominantly male patients in their sixth decade of life − is consistent with worldwide LT trends, where male predominance and middle to older age at transplantation remain typical [5,16]. The relatively low mean pre-transplant MELD-Na score and short waiting list time observed reflect both the efficiency of organ allocation in this region and the accessibility provided by the SUS-funded transplant system. However, this finding also suggests a potential regional imbalance in organ distribution, with Northeastern centers benefiting from relatively higher organ availability compared to more densely populated regions in the Southeast.

The etiological distribution of LT indications has undergone marked shifts over the 23-year study period. Alcohol-associated liver disease and metabolic dysfunction-associated steatotic liver disease (MASLD, formerly NASH) have progressively overtaken viral hepatitis as leading causes of transplantation. This trend parallels data from North America and Europe, where the introduction of direct-acting antivirals (DAAs) for hepatitis C and improved hepatitis B management have drastically reduced transplant listings for viral etiologies [3,4,6]. The increasing burden of alcohol-related and metabolic liver disease in this Brazilian cohort highlights an urgent need for public health interventions addressing alcohol consumption, obesity, diabetes, and other metabolic risk factors.

Despite the epidemiological transition, hepatitis C virus (HCV) and hepatocellular carcinoma (HCC) remain significant contributors to the transplant burden, as seen in other large cohorts [5]. The persistent relevance of HCC likely reflects the late presentation of cirrhosis in Brazil, limited access to surveillance programs, and regional disparities in early detection. The rise in retransplantation (4.8%) underscores ongoing challenges related to graft dysfunction and post-transplant complications, though this rate remains within the range reported by major international centers [1,17].

Ashok et al. from the University of Pittsburgh published a series of 4,000 liver transplants performed between 1981 and 1998, showing that the last series, coinciding with the

Table 1. Baseline Characteristics of Patients Undergoing LT.

Male gender	(n = 1663; 67,1%)
Median age (n = 2429)	55 (3-76)
LT indication (n = 2431)	Decompensated cirrhosis (81.8%; n = 1988)
	Hepatocellular carcinoma (26.2%; n = 638)
	Acute Liver failure (2.7%; n = 65)
	Others (3.9%; n = 95)
Blood type (n = 2.098)	A (736, 35,1%),
	O (1.034, 49,3%),
	B (261, 12,4%),
	AB (67, 3,2%)
Double transplant Liver + Kidney (n = 1790)	n = 40 (2.2%)
BMI (n = 1486)	25 kg/m^2 (12.5-39)
MELD or MELD-NA (n = 1861)*	18 (6-72)
Special situations of LT** (n = 1.758)	Yes (895, 50.9%)
What special situation?	Hepatocellular carcinoma (532, 60.1%), Refractory ascites (217, 24.5%),
	Persistent hepatic encephalopathy (60, 6.8%),
	Hepatopulmonary syndrome (22, 2.5%), Familial polyamyloidiasis (FPA) (10, 1.1%),
	Intractable pruritus (7, 0.8%),
	Recurrent cholangitis (8, 0.9%),
	Neuroendocrine tumor (13, 1.5%),
	Other (28, 3.2%)
CHILD (n = 1930)	A (316, 16,4%),
	B (986, 51,1%),
	C (548, 28,4%),
	Non-cirrhotic (80, 4.1%)
Comorbidities (n = 1021)	Hypertension (307, 30.1%),
	Diabetes (298, 29.2%),
	Obesity/Overweight (107, 10.5%),
	Chronic Kidney Disease (80, 7.8%),
	Dyslipidemia (46, 4.5%),
	Thyroid Disease (32, 3.1%),
	IBD (32, 3.1%),
	Heart disease (27, 2.6%),
	HIV+ (5, 0.5%)
Time on waiting list (n = 1750) (months)	3 (0-164)
Financing (n = 1718)	SUS (1651; 96.1%)
	Health plan or insurance company (58, 3.4%)
	Private (9, 0.5%)
Survival time (n = 2376)	66 months (0-274)

Abbreviation: BMI (body mass index); HIV (human immunodeficiency virus); IBD (inflamatory bowel disease); SUS (Sistema Único de Saúde/Unified Health System).

* MELD-Na was adopted in Brazil starting in 2019.

** Exceptions to MELD.

introduction of tacrolimus into the immunosuppression regimen, showed increased survival rates of 1, 5, and 10 years to 86%, 72%, and 60%, respectively [18]. Since then, with refinements in surgical technique, advances in anesthesiology and intensive care, coupled with more appropriate selection of donors and recipients, several international centers have reported 1-year survival rates exceeding 90% and 5-year survival rates of 75%.

A study comparing survival rates in the United States and the United Kingdom showed similar results at 90 days, but overall 5-year survival was higher in the United Kingdom, at 75.6% and 81.9%, respectively. The authors suggest that international comparisons of liver transplantation can highlight differences in healthcare delivery and aid in comparative evaluation by identifying modifiable factors that may facilitate better overall outcomes in liver transplantation [19].

One of the main difficulties to be overcome is early mortality, which can be assessed over a period of 90 days and 1 year. Fabio Baganate et al., evaluating 64,977 liver transplants performed in the USA, found 90-day and 1-year mortality rates of 5% and 10%, respectively. Death associated with cardiovascular / cerebrovascular / pulmonary / hemorrhage was the most cause of death within the first 21 days. Infections were the most frequent cause of death during 30-180 days after liver transplantation [20].

The average survival rate of the recipient in Brazil at 1 and 5 years is 75% and 66%, respectively, according to records from the Brazilian Association of Organ Transplants [7]. Survival outcomes in this series are encouraging. The overall survival probability of 91.6% at one month, 81.0% at 12 months, and 73.4% at 5 years surpasses the national average and aligns closely with outcomes from high-performing international

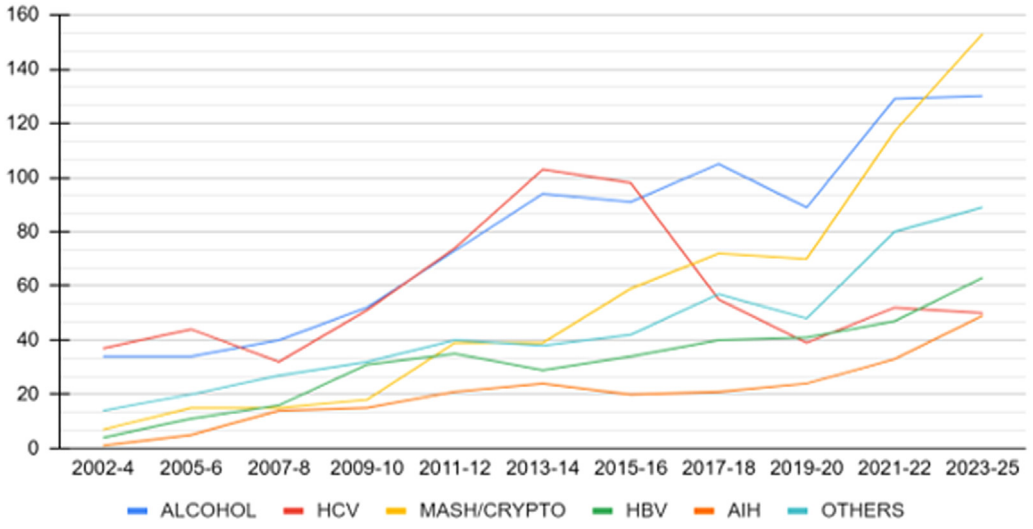


Fig 1. Indications for liver transplantation over two decades in a referral center in Brazil.

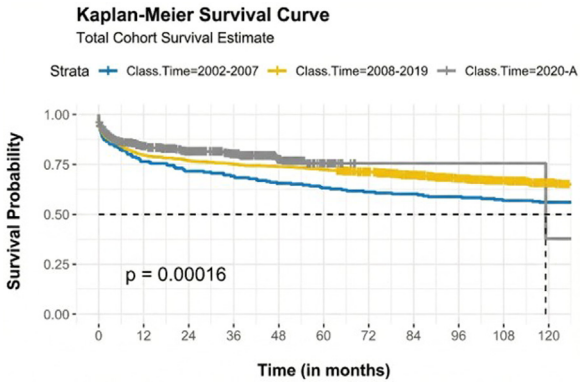


Fig 2. Survival rates according to period of time Kaplan-Meier Survival Curve.

centers [21,22]. Kaplan-Meier analysis demonstrated a significant improvement in survival over time ($p = .042$), reflecting continuous progress in perioperative care, immunosuppressive management, and long-term patient follow-up. This trend mirrors the global evolution of liver transplantation outcomes driven by advancements in surgical techniques, organ preservation, and multidisciplinary management. In recent years, following the implementation of quality criteria – including monthly evaluations and systematic discussions with the multidisciplinary team regarding postoperative complications and mortality – we have achieved an increase in patient survival to 92% by 2025.

CONCLUSIONS

This program's sustained activity and good outcomes are particularly notable given its role as a public, high-volume transplant center serving predominantly low-income patients from Brazil's North and Northeast. Nearly 60% of recipients originated from outside the state, emphasizing the center's role in reducing regional inequities in access to complex healthcare. These data underscore the importance of maintaining robust public investment in transplantation infrastructure and reinforcing referral networks across Brazil's geographically diverse regions.

Some limitations of this study should be acknowledged. Its retrospective design relies on secondary data collection, which may introduce incomplete records or reporting bias. Additionally, long-term follow-up beyond 5 years was limited for a subset of patients, reflecting the challenges of maintaining consistent post-transplant monitoring across broad geographic areas. Nevertheless, the large sample size, long observation period, and comprehensive dataset strengthen the reliability of these findings.

DATA AVAILABILITY

Data will be made available on request.

DECLARATION OF COMPETING INTEREST

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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