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ORIGINAL PAPER

Chronic Kidney Dysfunction Prevalence after Liver Transplantation in a Service in Espírito Santo

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ABSTRACT

Introduction: The prevalence of chronic kidney disease (CKD) in post-liver transplant patients is high and widely variable, 35% to 77%, depending on the definition and methodology used in the studies. Despite the increase in the number of transplants performed worldwide, literature data on long-term post-transplant outcomes and complications remain scarce, especially in Brazil. **Objectives:** To evaluate a regional cohort after a minimum post-transplant follow-up of 2 years to verify the prevalence of CKD. **Method:** Retrospective, single-center, longitudinal descriptive study of the occurrences of CKD after liver transplantation. Patients were evaluated at the consultation immediately before the transplant (time 0) and at the consultation 2 years later (time 2). **Results:** Of the 163 records analyzed, it appears that the classification of CKD at time 0 and time 2 was, respectively, stage 1: 55.56% and 32.10%; stage 2: 34.72% and 46.91%; stage 3: 8.33% and 16.05%; stage 4: 1.39% and 2.47%; and stage 5: 0% and 2.47%. There was a significant association between creatinine at time 0 and time 2, with the cutoff point of 1.5 mg/dL. Regarding CKD, within 24 months, 20.99% of the sample had CKD itself. **Conclusion:** Creatinine increased from time 0 to time 2, with a cutoff point of 1.5 mg/dL, a significant value in the context of the patient's prognosis. There was a worsening of renal function and categorization of patients 2 years after transplantation into more severe categories of chronic renal dysfunction when compared to time 0. Prevention and early identification of renal dysfunction in transplant recipients have an impact on patient and graft survival, becoming an important measure to be taken in the follow-up of these patients.

Descriptors: Liver transplant; Chronic renal failure; Organ transplantation.

Prevalência de Disfunção Renal Crônica no Pós-Transplante Hepático em um Serviço no Espírito Santo

RESUMO

Introdução: A prevalência de doença renal crônica em pacientes pós-transplante hepático é alta e amplamente variável, 35% a 77%, dependendo da definição e da metodologia utilizada nos estudos. Apesar do aumento no número de transplantes realizados mundialmente, os dados da literatura sobre desfechos e complicações de longo prazo no pós-transplante permanecem escassos, principalmente no Brasil. **Objetivos:** Avaliar uma coorte regional após seguimento pós-transplante mínimo de 2 anos para verificar a prevalência de doença renal crônica. **Métodos:** Estudo retrospectivo, unicêntrico, descritivo e longitudinal das ocorrências de doença renal crônica no pós-transplante hepático. Os pacientes foram avaliados na consulta imediatamente anterior ao transplante (tempo 0) e na consulta 2 anos após (tempo 2). **Resultados:** Dos 163 prontuários analisados, verifica-se que a classificação de doença renal crônica no tempo 0 e no tempo 2 foram, respectivamente, em estágio 1: 55,56% e 32,10%; estágio 2: 34,72% e 46,91%; estágio 3: 8,33% e 16,05%; estágio 4: 1,39% e 2,47%; e estágio 5: 0% e 2,47%. Houve associação significativa entre a creatinina no tempo 0 e a no tempo 2, com o ponto de corte de 1,5 mg/dL. No que tange à doença renal crônica, em 24 meses, 20,99% da amostra apresentavam doença renal crônica propriamente dita. **Conclusão:** A creatinina aumentou do tempo 0 para o tempo 2, tendo como ponto de corte 1,5 mg/dL, valor significativo no contexto do prognóstico do paciente. Ocorreu piora da função renal e categorização dos pacientes 2 anos após o transplante em categorias mais graves de disfunção renal crônica quando comparadas ao tempo 0. A prevenção e identificação precoce da disfunção renal no transplantado têm impacto na sobrevida do paciente e do enxerto, tornando-se uma importante medida a ser tomada no seguimento desses pacientes.

Descritores: Transplante de fígado; Insuficiência renal crônica; Transplante de órgãos.

INTRODUCTION

Chronic kidney disease (CKD) is a frequent and clinically significant complication after liver transplantation (LT), with reported prevalence rates ranging from 35% to 77%, depending on the diagnostic criteria and study design.[1-2] Long-term follow-up studies estimate that approximately 30% of LT recipients will develop CKD within 10 years post-transplant.[1,3] The onset of CKD in this population is associated with a substantially increased risk of cardiovascular events, higher hospitalization rates, a fourfold increase in all-cause mortality, and an elevated likelihood of liver allograft dysfunction.[1,3]

Established risk factors for post-LT CKD include advanced age, female sex, hepatitis C virus (HCV) infection, calcineurin inhibitor (CNI) exposure, acute kidney injury (AKI) in the early post-transplant period, elevated pre-transplant Model for End-Stage Liver Disease (MELD) score, and the development of post-LT systemic arterial hypertension (SAH) or diabetes mellitus (DM) – the latter recently identified as the most prominent risk factor in a systematic review.[4–6]

The pathogenesis of CKD after LT is multifactorial. Pre-existing renal dysfunction and CNI-induced nephrotoxicity are major contributors.[1] CNIs are associated with acute nephrotoxicity, mediated primarily by renal vasoconstriction, and chronic nephrotoxicity through incompletely defined mechanisms that ultimately result in tubulointerstitial fibrosis. Additional adverse effects, such as hypertension, hyperlipidemia, and post-transplant DM, further accelerate renal deterioration, making CNI-related toxicity the leading cause of progressive renal failure in solid organ transplant recipients.[2]

Despite the increasing number of LT procedures performed worldwide, data on the long-term outcomes and risk factors for post-LT CKD remain limited,[7] particularly in Brazil. This study aimed to determine the prevalence of CKD in a cohort of LT recipients with a minimum follow-up of 24 months and to identify clinical and demographic factors associated with its development.

METHODS

We conducted a retrospective cross-sectional study including patients who underwent LT at a single transplant center in Espírito Santo, Brazil, from January 2005 to February 2019. Eligible participants had a minimum post-transplant follow-up of 24 months. Two time points were assessed: baseline (T0), defined as the pre-LT evaluation or, if unavailable, the earliest documented follow-up visit, and 24 months post-LT (T2).

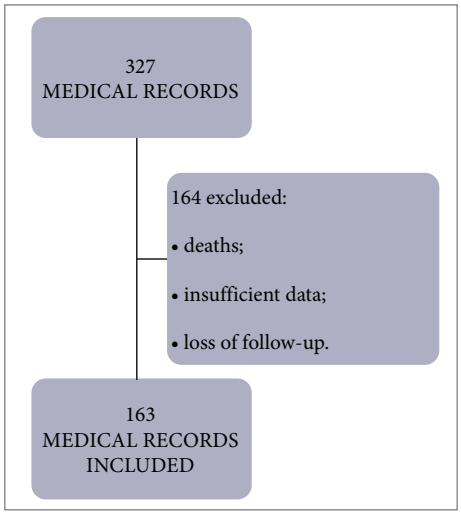
Of 327 medical records screened, 163 patients met the inclusion criteria. Patients who had died before the 24-month follow-up, those with incomplete medical records, or those lost to follow-up were excluded.

Demographic, epidemiological, clinical, and laboratory data were abstracted from medical records using a standardized form. The estimated glomerular filtration rate (eGFR) was calculated using the Cockcroft-Gault equation. Renal function stages were classified according to the Kidney Disease: Improving Global Outcomes (KDIGO) Clinical Practice Guidelines[8]: stage 1, ≥ 90 mL/min/1.73 m²; stage 2, 60–89 mL/min/1.73 m²; stage 3, 30–59 mL/min/1.73 m²; stage 4, 15–29 mL/min/1.73 m²; and stage 5, < 15 mL/min/1.73 m² or dialysis. CKD was defined as stages 3–5.

Data were entered into Microsoft Excel and analyzed using IBM SPSS Statistics, version 27. A $p < 0.05$ was considered statistically significant. The study protocol was approved by the institutional ethics committee (CAE 3947914).

RESULTS

Of the 327 medical records reviewed, 163 patients were included (Fig. 1). The cohort was predominantly male (76.1%) with a mean age of 52.9 ± 10.4 years. The leading indications for LT were alcohol-related cirrhosis (19%) and HCV infection (12.3%). Renal replacement therapy (RRT) was required in three patients prior to LT and in 13 patients post-LT, with two patients remaining on RRT at T2. Sociodemographic and clinical characteristics are summarized in Table 1.



Source: Elaborated by the authors.

Figure 1. Flowchart of patient inclusion in the study.

Table 1. Sociodemographic data and baseline clinical characteristics.

Characteristics	Numbers
Age at LT, years (mean ± SD)	52.9 (± 10.4)
Sex (%)	
Male	76.1
Female	23.9
MELD (mean ± SD)	17.6 ± 6.2
Child Pugh (%)	
A	10.4
B	20.2
C	12.3
Lack information	57.1
LT indication (%)	
Alcohol	19.0
HCV	12.3
HBV	7.4
MASH	6.1
FK level at time 2 (mean)	7.42 ng/mL

Source: Elaborated by the authors. HBV: hepatitis B virus; MASH: metabolic dysfunction-associated steatohepatitis; SD: standard deviation.

Comparison of comorbidity prevalence between T0 and T2 demonstrated a statistically significant increase in SAH and DM (both $p < 0.001$) (Table 2).

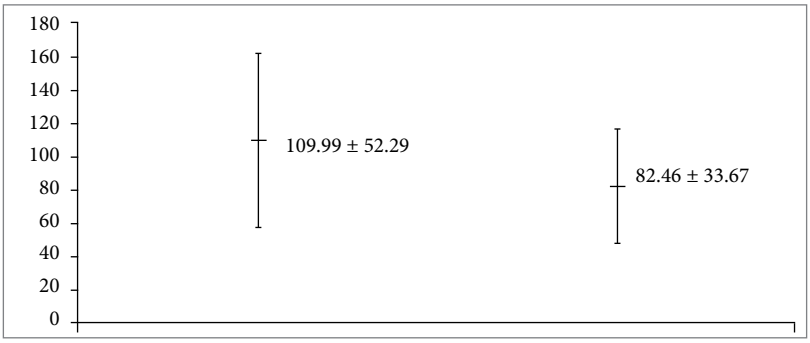
Table 2. Comorbidities at T0 and T2

Comorbidities	Time 0	Time 2
DM	26.4%	48.5%*
Dyslipidemia	9.2%	19.0%*
Arterial hypertension	26.4%	55.8%*
Obesity	6.2%	9.8%*

Source: Elaborated by the authors. *Spearman coefficient ($p = 0.000$).

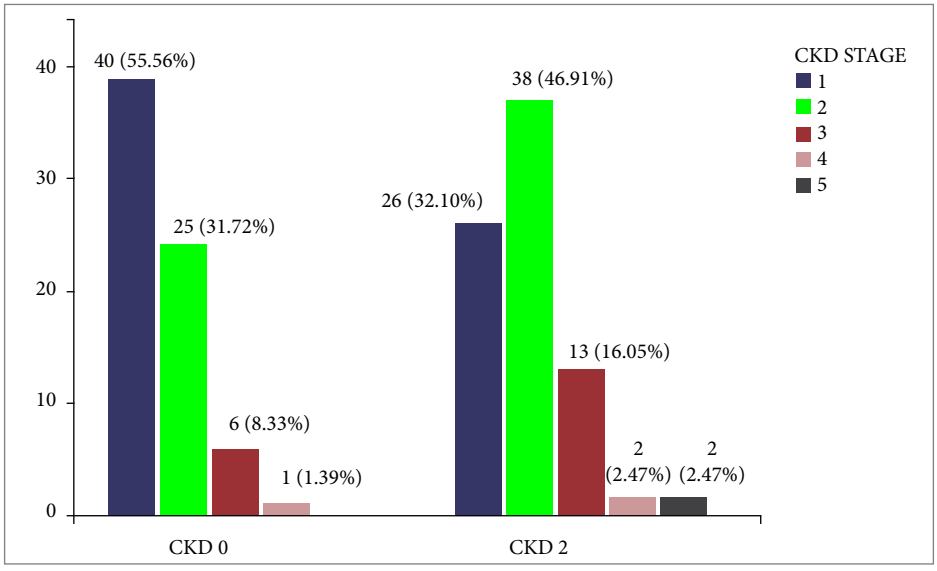
At T0, 8.92% of patients had a serum creatinine (sCr) ≥ 1.5 mg/dL, rising to 15% at T2. The association between sCr ≥ 1.5 mg/dL at T0 and T2 was statistically significant ($p = 0.009$), with a weak positive Spearman correlation ($r = 0.377$, $p < 0.001$). Using an sCr threshold of 2.0 mg/dL, the association was not statistically significant ($p = 0.152$).

Mean eGFR declined significantly from T0 to T2. At T0, 55.56% of patients were in stage 1, 34.72% in stage 2, 8.33% in stage 3, and 1.39% in stage 4. At T2, the distribution shifted to 32.10% in stage 1, 46.91% in stage 2, 16.05% in stage 3, 2.47% in stage 4, and 2.47% in stage 5 (Fig. 3). Overall, 21% of patients met CKD criteria (stages 3–5) at 24 months post-LT.



Source: Elaborated by the authors.

Figure 2. Mean glomerular filtration rate values at T0 and T2.



Source: Elaborated by the authors.

Figure 3. Distribution for CKD at T0 and T2.

DISCUSSION

This study assessed the prevalence and associated factors of CKD in 163 LT recipients at a Brazilian transplant center. The mean age corresponded to the fifth decade of life, consistent with reports from international series.[9-11] Male predominance was observed, reflecting the epidemiological profile of LT indications in Brazil. Unlike European and Chinese cohorts, where viral hepatitis predominates, alcohol-related cirrhosis was the leading etiology in this sample, aligning with Latin American epidemiology.[12] Meta-analytic data suggest worse renal outcomes in alcohol- and virus-related cirrhosis, while autoimmune etiologies appear to confer more favorable renal prognoses.[13] In our sample, no significant association between etiology and CKD was observed.

The MELD score is a validated predictor of waitlist mortality but remains less reliable for post-LT prognosis.[14] In a Chinese cohort, advanced age, AKI, and elevated MELD score were associated with CKD within 1 year post-LT, with adverse survival outcomes.[4] Our mean MELD score was 17.6, but incomplete records (30.1% missing) and the exclusion of deceased patients limited analysis of its prognostic role.

SAH and DM emerged as important factors in post-LT CKD pathogenesis, consistent with prior studies.[15,16] In our cohort, the prevalence of SAH and DM nearly doubled between T0 and T2 (26.4% to 55.8% and 26.4% to 48.5%, respectively; $p < 0.001$), similar to rates reported in the literature.15,17 Notably, CKD prevalence was approximately twice as high among patients with DM compared to those without.[17]

CNIs remain the backbone of post-LT immunosuppression but are a well-established cause of nephrotoxicity, even at low tacrolimus (FK) trough levels.[17] In this study, the mean tacrolimus level at T2 was 7.42 ng/mL; however, no direct comparative analysis was performed regarding CNI exposure and CKD.

While sCr is an imperfect early biomarker for CKD, baseline sCr remains one of the most widely used predictors of post-LT survival.[1] Using 1.5 mg/dL and 2.0 mg/dL thresholds, only the lower cutoff demonstrated a significant association with CKD development. Limitations of sCr interpretation in LT recipients include the influence of muscle mass, nutritional status, age, and protein intake, potentially leading to an overestimation of eGFR.[19]

Mean eGFR decreased significantly from 109.99 ± 52.29 mL/min/1.73 m² at T0 to 82.48 ± 33.57 mL/min/1.73 m² at T2, paralleling findings from Polish and Spanish cohorts.[9,17] International studies consistently demonstrate a substantial decline in renal function within the first year post-LT, with CKD prevalence reaching 30% at 12 months and 37% at 24 months.[19] In our sample, CKD prevalence at T2 (21%) exceeded that of the general Brazilian population, particularly for advanced stages (stages 4 and 5).[20]

Study limitations include the retrospective design, single-center data, exclusion of deceased patients, incomplete medical records, and relatively short follow-up (24 months). Nevertheless, our cohort reflects real-world clinical practice in Espírito Santo, and the paucity of Brazilian data on post-LT CKD underscores the need for further prospective studies.

CONCLUSION

CKD is a frequent complication within 24 months after LT, often accompanied by new-onset comorbidities such as hypertension and DM, which further accelerate renal decline. In our cohort, stage 2 renal dysfunction became the most prevalent category post-LT, while CKD (stages 3–5) was present in 21% of patients at 24 months. Early identification and proactive management of renal dysfunction are essential to improve patient and graft survival in LT recipients.

CONFLICT OF INTEREST

Nothing to declare.

AUTHOR'S CONTRIBUTION

Substantive scientific and intellectual contributions to the study: Lucas ACM, Miossi LS, Venturini L; **Conception and design:** Pacheco MP, Trindade LZ; **Data analysis and interpretation:** Lucas ACM, Miossi LS, Venturini L; **Article writing:** Pacheco MP, Lucas ACM, Miossi LS; **Critical revision:** Pacheco MP, Trindade LZ; **Final approval:** Pacheco MP.

DATA AVAILABILITY STATEMENT

All data were generated or analyzed in this study.

FUNDING

Not applicable.

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