Acute kidney injury following liver transplant is independent of Tacrolimus trough concentrations. A single-centre retrospective cohort study.

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Introduction

Acute kidney injury (AKI) occurs frequently after liver transplantation (LT) and is associated with adverse outcomes. While several risks factors for AKI have been identified, the role of Tacrolimus, a key immunosuppressive agent in preventing graft rejection, remains a matter of debate, in particular in low-dose immunosuppressive regimens. Therefore, this study aimed to evaluate the risk factors for AKI after LT, with a particular focus on Tacrolimus trough concentrations.

Methods

This retrospective monocentric study assessed 412 patients who underwent LT between April 2008 and May 2020 in Cliniques universitaires Saint-Luc (Brussels), where low-dose Tacrolimus is routinely used for immunosuppression post-LT. Patients were followed up to 30 days from LT, or until ICU discharge, whichever came first. The occurrence of AKI, based on AKIN criteria, and trough tacrolimus concentrations (measured daily during the whole ICU and hospitalization stay) were retrieved from electronic medical recordings.

Results

AKI occurred in 139 patients (33.7%) and was associated with higher 30-day mortality (12.2 vs 2.9%).

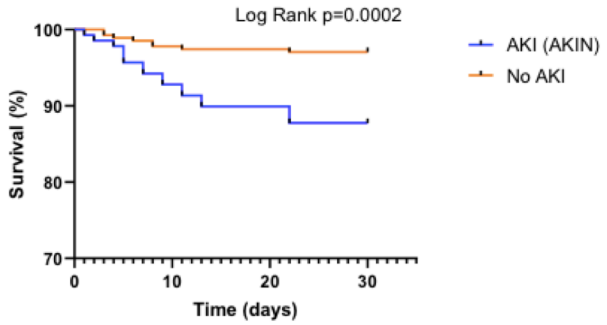

Figure 1. Survival curves of patients who developed AKI or not after liver transplantation (according to AKIN criteria).

In multivariate analysis, pre- LT Meld Score, "warm ischemia" duration, volume of red blood cell and of crystalloids administered during LT were independently associated with AKI, whereas no association was found with maximal Tacrolimus trough concentration.

	Multivariate		
Variables	Adjusted odd Ratio	IC 95	p
Age	0.99	0.97-1.02	0.90
CKD before OLT	1.44	0.72-2.87	0.32
Meld Score	1.05	1.009-1.09	0.016
Child Pugh Category C	2.19	0.96-5	0.064
Duration of OLT (min)	1.00	0.99-1.001	0.60
Warm ischemia time (min)	1.026	1.003-1.05	0.024
Volume of RBC transfusion during OLT (L)	1.60	1.11-2.31	0.013
Volume of crystalloids infused during OLT (L)	1.26	1.08-1.48	0.004
Maximum Tacrolimus trough concentration (ng/ml)	1.00	0.93-1.07	0.99

Table 1. Multivariate regression analysis for variables associated with AKI (AKIN) > OLT (139 patients/412). OLT = Orthotopic liver transplantation, CKD = chronic kidney desease, RBC = red blood cells.

Mixed model analysis (fig 2) revealed different time trends in Tacrolimus trough concentrations (C0), which were lower in patients with AKI (A). This difference was probably explained by lower daily doses in the AKI group (B), rather than by differences in Tacrolimus metabolism, with similar values of the C0/daily dose ratio between groups (C).

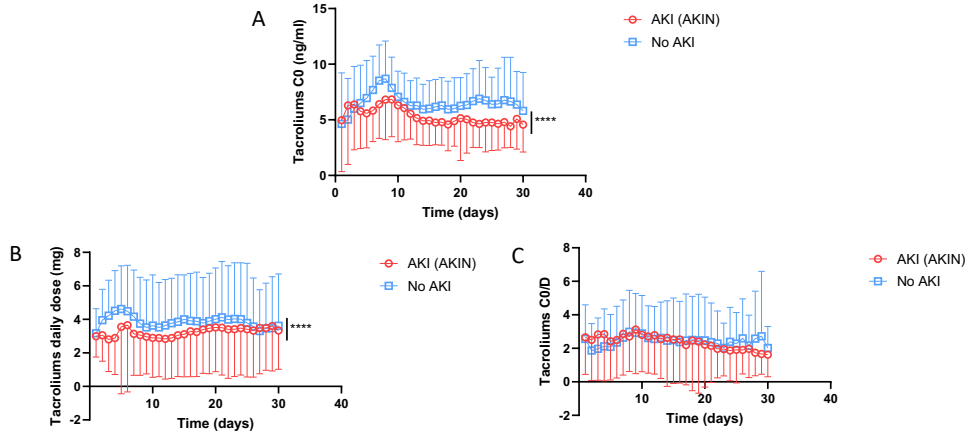

Figure 2. Time trends of Tacrolimus trough concentrations (A), Tacrolimus daily dose (B) and Tacrolimus trough concentration/daily dos ratio (C0/D, panel C) between patients with AKI vs no AKI using generalized linear mixed models with the group as a fixed factor and time as a random repeated factor. **** indicates p<0.0001 (group factor).

Conclusion

In this retrospective study from a single center in which low-dose Tacrolimus is used as sole immunosuppressive therapy after LT, AKI frequently occurred after LT and was not associated with Tacrolimus trough concentrations.

- Ciria R, Gómez-Luque I, Cortés M, Khorsandi SE, Ayllón MD, Rodríguez-Perálvarez M, et al. Interaction between tacrolimus, MELD score and acute kidney injury after liver transplantation. Analysis on a large contemporary bicenter meld-era series. Clinical Transplantation. 2020;34(9):e13890.