# ANTIPROTEINURIC EFFECT OF SPIRONOLACTONE IN KIDNEY TRANSPLANT RECIPIENTS DURING A 5-YEAR FOLLOW-UP

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***Keywords: Proteinuria, Graft Function, Graft Survival, kidney Transplantation, Aldosterone.***

Abstract No: **WCN24-AB-2699**

## INTRODUCTION

Post-transplant proteinuria is a biomarker of renal injury that negatively affects graft function and survival and has a multifactorial cause [1]. Aldosterone contributes to chronic allograft dysfunction injury, resulting in renal fibrosis and proteinuria, which reduces survival and organ function [2]. Aldosterone triggers inflammation, oxidative stress, and endothelial dysfunction, causing interstitial fibrosis, vasculopathy, and glomerulosclerosis. This leads to proteinuria and reduced GFR [3, 4]. Blocking the renin-angiotensin-aldosterone system (RAAS) is considered the gold standard therapy for non-transplant patients with proteinuria [5], but there is a lack of data to determine its effect in kidney transplantation. Studies suggest that blocking RAAS through treatment with aldosterone antagonists effectively controls proteinuria and has a protective effect on the progression of renal fibrosis, leading to less graft loss [6, 7]. This study aims to evaluate the effect of spironolactone, an aldosterone antagonist and RAAS inhibitor, on proteinuria and renal function after kidney transplantation.

## METHODS

Retrospective unicentric cohort study, approved by the UNICAMP ethics committee (CAAE 6.076.8289).

*Inclusion criteria:*

• Patients older than 18 years who received a kidney from deceased or living kidney transplant donor between January/1991 and December/2015, undergoing regular outpatient follow-up at the UNICAMP Clinical Hospital;

• Treatment with spironolactone for persistent proteinuria ≥ 0.5 g/day during a 5-year follow-up.

For analysis, the included patients were grouped according to the amount of proteinuria (protein-to-creatinine ratio) at the beginning of therapy: (1) mild: <1; (2) moderate: 1-3; and (3) nephrotic: >3. Numerical data were expressed as mean and standard deviation and analyzed with the Student's t-test. Categorical data were expressed as percentages and analyzed with Pearson's chi-square test. Values of $P < 0.05$ were considered significant.

## RESOULTS AND DISCUSSION

167 patients fulfilled the inclusion criteria, most male (n=122, 73%), with a mean age of 40.7 ± 14.5 years. Most (n=135, 80.8%) received a kidney from a deceased donor. Most frequent etiologies of chronic kidney disease were unknown (n=38, 23%), chronic glomerulonephritis (n=37, 22%) and hypertensive nephrosclerosis (n=33, 20%). Considering the amount of proteinuria at the beginning of therapy, 47 (28%) were classified as mild, 90 (54%) moderate, and 30 (18%) nephrotic. The evolution of proteinuria during the follow-up is presented in Figure 1. The estimated graft function during follow-up is shown in Figure 2.

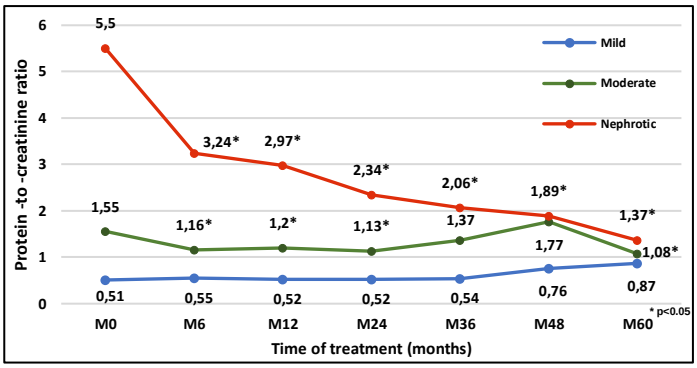


**Figure 1**: Proteinuria of kidney transplant recipients treated with spironolactone, according to the groups, during a 5-year follow-up.

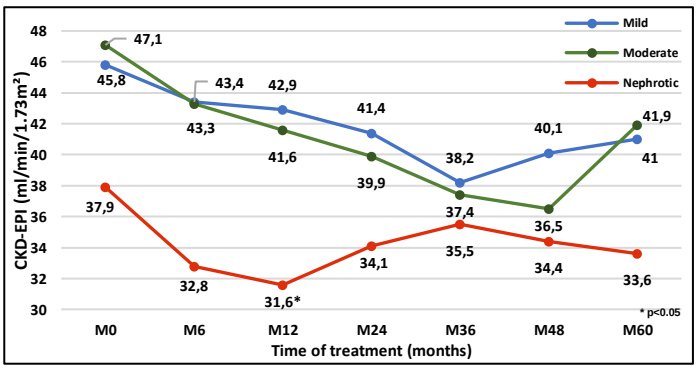


**Figure 2**: Estimated glomerular filtration rate (CKD-EPI) of kidney transplant recipients treated with spironolactone, according to the groups, during a 5-year follow-up.

Recipients with nephrotic proteinuria treated with spironolactone presented significant and consistent reduction of proteinuria in a 5-year follow-up. Renal function remained stable in all groups. Most patients received spironolactone without ACE inhibitors or ARBs. Four patients discontinued the medication - three due to gynecomastia and one due to hyperkalemia. No hypotension was observed in any group.

## CONCLUSIONS

Kidney transplant recipients with nephrotic proteinuria treated with spironolactone presented a significant and persistent reduction in proteinuria. Proteinuria remained stable in the other groups, and graft function remained stable in all groups.

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**SUPPORT**