

## LETTER TO THE EDITOR

## Does kidney transplantation influence a form of discrimination for antihypertensive drugs prescriptions?

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Cardiovascular (CV) diseases are the leading cause of death worldwide [1] and in Europe [2]. Arterial hypertension is the leading preventable risk factor for CV disease and mortality [3] and was present in >30% of the global adult population in 2010 [4]. For patients with early chronic kidney disease (CKD), the risk of dying from CV disease is greater than that of reaching the dialysis stage [5]. After transplantation, CV disease remains a major cause of morbidity and mortality. Functional graft death is a common cause of graft loss and CV disease represents a leading cause of functional graft death after transplantation. Moreover, hypertension is common in patients with CKD, being present in 60–90% of this population [6]. Blood pressure (BP) control is frequently not achieved among patients with CKD. A high pill burden may negatively influence BP control. In kidney transplant recipients (KTRs) the drug burden is very high [7].

Recent decades have been marked by a significant reduction in CV mortality in the majority of industrialized countries. This survival benefit is largely associated with improved screening, prevention and therapeutic management strategies of CV diseases, such as the use of renin-angiotensin system (RAS) blockers. RAS blockers improve BP control and provide

nephroprotection and cardioprotection. For instance, CKD progression is associated with the rate of proteinuria and reducing proteinuria has been shown to slow CKD progression.

We recently reported the results of two studies comparing the risk of mortality and CV events [8] and the level of arterial stiffness [9] between non-transplanted CKD patients and KTRs, matched on several CV risk parameters including glomerular filtration rate (GFR). These studies were based on the successive analysis of two cohorts of CKD patients (Chronic Kidney Disease–Renal Epidemiology and Information Network, NephroTest) and two cohorts of KTRs [Données Informatisées et Validées en Transplantation (DIVAT), TransplanTest]. KTRs were matched to non-transplanted CKD patients according to a propensity score based on six variables evaluated at inclusion, which was at 1 year post-transplantation for KTRs. In the first study [8], the variables were estimated GFR, gender, diabetic status, history of CV event, interaction between diabetic status and history of CV event and initial nephropathy type. In the second [9] study, the variables were measured GFR, age, sex, mean BP, body mass index and heart rate. This provided propensity score-matched sets of 945 [8] and 363 patients [9] with a median GFR of 42 mL/min/1.73 m<sup>2</sup> and 52 mL/min/1.73 m<sup>2</sup>, respectively.

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Both studies revealed differences between the prescribed drugs according to whether or not they were kidney transplanted, despite the matching. Indeed, RAS blockers were less often prescribed among KTRs than among non-transplanted CKD patients (19% versus 72%,  $P < 0.001$  [8] and 52% versus 79%,  $P < 0.001$  [9]), to the benefit of calcium channel blockers (CCBs) (50% versus 39%,  $P = 0.002$  [8] and 60% versus 34%,  $P < 0.001$  [9]) and  $\beta$ -blockers (54% versus 35%,  $P < 0.001$  [8] and 42% versus 23%,  $P < 0.001$  [9]).

We were astounded by the relatively scarce prescriptions of RAS blockers at 1 year after renal transplantation, although the involved teams were widely different. To our knowledge, no previous large randomized trial has actually demonstrated a positive effect of RAS blockers on mortality or CV events among KTRs [10–14]. This could be explained, at least in part, by the potential absence of overactivation of the RAS system, low levels of proteinuria or improved CV diseases among KTRs. Hiremath *et al.* [12] reported in 2016 a meta-analysis of eight trials (1502 patients) and found that their results neither support nor refute the hypothesis that RAS blockade improves clinical outcomes in KTRs. They concluded their work by saying that a study of >10000 patients would be needed to definitively answer the question of whether RAS blockade reduces graft loss in KTRs and that, in the meantime, clinicians should discuss with their patients the risks and benefits of using these drugs on a case-by-case basis. This case-by-case approach is often necessary in nephrology and/or kidney transplantation and further highlights the necessity of including KTRs among large randomized trials. In any case, the recently published Kidney Disease: Improving Global Outcomes Practice Guideline for the Management of BP in CKD recommended the use of a CCB or an angiotensin II receptor blocker as the first-line antihypertensive agent in adult KTRs based on their previously reported renoprotective effects [14].

## DATA AVAILABILITY STATEMENT

No new data were generated or analysed in support of this research.

## CONFLICT OF INTEREST STATEMENT

None declared. This article has not been published previously in whole or part.

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