

Fasting Urinary Osmolality, CKD Progression and Mortality: Brief Report

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Introduction

Today, interstitial fibrosis and tubular atrophy (IF/TA) are the main contributing factors to the failure of long-term renal allografts. It results from complex processes involving both alloantigen-dependent and -independent components. Histopathological abnormalities can be used to detect IF/TA early on, prior to the development of clinical symptoms, which are late signs of the illness. The use of screening renal biopsies (RB) to find and characterise the main causes of renal damage is growing [1]. Chronic tubulointerstitial lesions have already been shown to advance quickly during the first month following transplantation, with lesions already present at three months. Additionally, it has been demonstrated that IF is correlated with long-term graft function and renal graft survival, raising the possibility that early histological detection of IF could be used to predict the risk of subsequent graft function deterioration and, possibly, as a surrogate marker to determine the effectiveness of particular therapeutic interventions.

Description

The objectives of this study were to determine the relative importance of IF and its evolution at various times after transplantation, to identify key determinants of IF, and to precisely describe the evolution of IF during the initial period after transplantation using sequential screening biopsies. We used automatic image analysis as a sensitive and quantitative way to quantify renal fibrotic damage in order to reduce bias.

In autosomal dominant polycystic kidney disease, the vasopressin-cAMP-osmolality axis is aberrant (ADPKD). In the Management of Autosomal Dominant Polycystic Kidney Disease and Its Outcomes with Tolvaptan Efficacy and Safety Tolvaptan, a vasopressin V2 receptor antagonist, reduced the progression of ADPKD in individuals with intact GFR in the 3:4 Trial, a 3-year randomised, placebo-controlled trial in adults [2,3]. Here, we looked into what causes baseline urine osmolality (Uosm) and its significance as a measure of ADPKD severity, what influences how tolvaptan responds, and whether changes in Uosm are related to important trial end points. At the outset, higher total kidney volume (TKV) and older age were independently associated with lower Uosm as well as female sex, the presence of hypertension, lower eGFR, and higher eGFR.

After transplantation, the results of these screening biopsies are critical for diagnosis. Numerous studies have shown how important they are for separating the toxicity of IF/TA and calcineurin inhibitors from the genuine incidence of allograft nephropathy. The Banff classification's semiquantitative grading method may prove invaluable for standardising diagnostic procedures,

however the assessment of IF exhibits a large interobserver variation that renders comparisons across centres useless. In a research, the Fleiss Kappa score for the IF grade was 0.29. Furthermore, in the early stages of IF/TA, when intervention is most likely to protect graft function, the few grades available in the Banff system to indicate the seriousness of certain histological abnormalities are not sensitive enough. Since IF is not treated as a continuous variable but rather as a semiquantitative score in the Banff classification, many delicate statistical analysis techniques cannot be used. Additionally, even if the 'actual' difference between biopsies with different categories of interstitial fibrosis is slight [4], this is possible because the 1-3 scale is not linear. This impact, in particular, might be deceptive when evaluating sequential biopsies. In fact, Banff criteria to assess two successive biopsies results in the misdiagnosis of almost 25% of patients.

Over the course of 36 months, tolvaptan regularly decreased Uosm by 200–300 mOsm/kg. The baseline eGFR and Uosm had an impact on the Uosm response to tolvaptan. Clinical progression events were significantly reduced in subjects with larger Uosm alteration. Patients using tolvaptan who had more Uosm suppression saw a slower loss in renal function. Both the placebo and treatment groups both had a significantly lower Uosm when assessed at the follow-up visit without the use of medication. Plasma osmolality was markedly elevated by tolvaptan but recovered to normal at follow-up. To sum up, baseline Uosm in ADPKD reflects age, renal function, and TKV, and baseline Uosm, eGFR, and TKV affect how tolvaptan affects Uosm [5]. The individuals with greater Uosm suppression, or those with higher baseline eGFR, saw the most renal benefit.

Clinical practise guidelines created under the Kidney Disease Outcomes Quality Initiative (KDOQI) of the National Kidney Foundation, which divides CKD into five stages of disease severity based on glomerular filtration rate, have made CKD detection and management easier in recent years (GFR). These recommendations have been adopted and put into practise in numerous nations, leading to the usual automatic reporting of estimated GFR (eGFR) from blood creatinine readings using the MDRD Study equation's four variables. 10 Isotope-dilution mass spectrometry (IDMS), which was later adopted as the international reference standard for serum creatinine measurement was created for IDMS-aligned assays in order to further refine the MDRD Study equation in order to account for the impact of variation in serum creatinine measurements between laboratories [6,7].

However, there are questions about the MDRD Study equation's reliability when used in contexts other than the initial clinical environment in which it was created. It has been demonstrated that the MDRD Study equation consistently overestimates genuine GFR over the high-normal range of renal function, which is particularly relevant to its application in the general population.

Conclusion

In order to address these constraints of bias and imprecision, the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) recently created a new equation for the calculation of GFR based on pooled research and clinical populations with a variety of clinical features. The CKD-EPI equation appears to be more accurate than the MDRD Study equation, especially for higher GFRs, according to preliminary validation.

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Conflict of Interest

There is no conflict of interest by author.

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