Reply

Sir,

Zitta et al. presented an argument that questions the precision of constant infusion of inulin to measure GFR. They suggested that the technique is extremely impractical from a clinical standpoint, and is also principally error prone, since attainment of a steady state is much more insecure and requires much more time than suggested. In addition, they suggested that this method might underestimate the real GFR. They referenced their criticism on their previous published work.

We agree that a steady state must be attained before valid conclusions are drawn. We also agree that achievement of a steady state must be stressed in the results of published work on inulin clearances. We, in fact, were surprised to see only few papers discussing attainment of a steady state in their protocols. We believe, however, that with the method we used, which includes a loading dose, it was sufficient to produce a steady state in most patients as documented in our paper. A constant infusion of inulin without a loading dose will certainly require several hours before attainment of a steady state. We also wish to point out that we measured serum creatinine at the outset, as well as at the end of our experiment. A comparison of the equations based on creatinine/cystatin C measured at the two points was not significantly different (data were not shown). We believe that the simultaneous measurement of these indigenous molecules was more important for the comparative analysis. Our interest was to compare performances of equations rather than measurement and assessment of GFR for other epidemiological or clinical reasons. After all, GFR can change from 1 min to the next, based on what we eat and drink.

Conflict of interest statement. None declared.

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doi: 10.1093/ndt/gfm928

Advanced Access publication 17 December 2007

About CKD stage-3 subdivision proposal

Sir,

I have read very carefully the paper published in a recent issue of NDT about DOQI-NKF classification of CKD stage-3 related [1]. In short, Abutaleb et al. proposed subdividing CKD-3 into two stages: 3a and 3b, respectively. There is no doubt that CKD is increasing in a dramatic way, and is recognized as a global public health problem, representing a heavy burden not only for the patients, but also for their families and for the society [2,3]. On the other hand, CKD patients are more likely to die, mainly from cardiovascular disease (CVD) before progressing to stage 5 [4].

On this theme, it would be good to remember the Hoorn study, which demonstrated that mild renal function impairment was associated with a significant CV mortality when glomerular filtration rate (GFR) was <70 ml/min/1.73 m²/bs with an important increase in the risk of CV death by each 5 ml/min/1.73 m² decrease [5]; this might be a plausible explanation for the highly different death rates among CKD stages 3 and 4.

I agree with the use of two subdivisions of 15 ml/min/1.73 m²/bs ranged components, 3a (GFR 59–45 ml/min/1.73 m²/bs) and 3b (GFR 44–30 ml/min/1.73 m²/bs) because it seems logical to think this would help to define more accurately the level within CKD stage 3 at which mortality becomes a real problem for the international nephrology community, health authorities and of course, patients and their relatives.

However, as a current point of view, renal transplantation must continue to be considered as a form of renal replacement therapy (RRT), because even though successful kidney transplantation results in an improved quality of life and is certainly a better therapeutic option than haemodialysis or peritoneal dialysis, unfortunately it is not always possible to reach complete renal recovery. Besides, the transplant recipient will require a permanent immunosuppressive regimen and close medical control; furthermore, nowhere in the world are there sufficient human kidney donors for patients with CKD-5, waiting for a renal transplantation.

For those reasons among others, we believe it impossible to develop a global strategy to recommend kidney allograft as a standard modality of treatment for CKD stage 3 or 4.

We believe that the cornerstone in the global struggle against CKD, especially for developing countries, is PREVENTION.

Conflict of Interest Statement: None declared.

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1. Abutaleb N. Why we should subdivide CKD stage 3 into early (3a) and late (3b) components. *Nephrol Dial Transplant* 2007; 22: 2728–2729
Sir,

I appreciate Professor SantaCruz’ support for the idea of dividing CKD stage 3 into a and b components, and its related reasoning.

However, there should be no reason to refuse the suggestion that we need to study the possibility of offering renal transplantation (TX), as a measure to save patients’ health and lives. Regardless of the mechanisms and pathological processes responsible for morbidity and mortality in CKD stages 3 and beyond, we are faced with a disease process that is more fatal than many malignancies treated by more dangerous chemotherapies. Despite the recognized side effects of immunosuppressive therapy and despite the fact that the received nephron mass is often suboptimal and is currently given only after losing native nephrons, the benefits to health and survival remain dramatic. The USRDS 2006 indicates that, compared to transplant patients, mortality rates in the dialysis population are 9.6–13.8 times higher for heart disease, 5.2–6.3 times higher for cerebrovascular disease and 6.1–8.4 times higher for septicemia. During a 5-year follow-up of CKD stage 3 patients, Keith et al., while reporting that only 1.3% reached end-stage renal disease (ESRD) stage, described a mortality of 24.3% among the same cohort [1]. Recent data have shown that CKD patients are 5–10 times more likely to die than to reach ESRD [2].

With no hesitation, offering earlier renal TX would theoretically result in even higher gains. Total post-transplant nephron mass (and so GFR) would be much higher than the current levels achieved by offering renal TX as a RRT modality (i.e. in stage 5). In fact I have made this suggestion, in an unpublished letter in 1995, as an alternative approach to the idea of dual kidney transplantation that had been offered as a means to prevent non-immunological self-perpetuating chronic allograft dysfunction [3]. Early supplement of nephrons is likely to help preserve renal tissue in both native and transplanted kidneys, provided calcineurin inhibitor (CNI) drugs can be avoided. In addition, early transplantation would save hearts and other organ systems from significant and irreversible damage that results in the loss of life of 90% of the CKD population prior to reaching ESRD [2]. What is the logic in insisting that patients ‘must’ complete this fatal CKD journey, when we can abort it by transplantation? Or on insisting on keeping this therapy for this ‘happy’ minority? Extrapolation from the well-known beneficial effects on grafts and patients’ lives gained by pre-emptive transplantation and from simply reducing the time on dialysis should raise the question as to how far backward (i.e. earlier) within CKD stages this benefit would continue to occur. As opposed to what is stated by Professor SantaCruz, many of the early transplant patients are likely to reach even stage 1, far from uraemia-related pathologies.

Organ feasibility should not block scientific research and analysis. If benefits became proven, ‘loving’ related donors who donate for their beloved patients at stage 5 would continue to do so regardless of the CKD stage, as long as science and medicine indicate its appropriateness.

I admit however that the nephrotoxicity of CNI would interfere with the benefit of protecting mainly one native organ system. Despite the potential anti-hyperfiltration haemodynamic effect on the native kidneys, such an early TX approach would further stress the trends to avoid CNI drugs and start the discussion about preservation of residual renal function among transplant patients as we do among dialysis patients. However, even accelerating the loss of residual renal function post-transplantation by using CNI drugs, the benefits on health and patients’ survival from aborting the ‘CKD’ journey are unlikely to be touched.

Conflict of interest statements. None declared.

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Vasculitis and anti-thyroid medication

Sir,

We appreciate the opportunity to respond to the comments made by Woywodt et al., regarding our evaluation of the association of thyroid disease and vasculitis [1]. Their major concern is that our study does not support our statement that the use of anti-thyroid agents does not account for many cases of ANCA-Small Vessel Vasculitis (ANCA-SVV) in the general population, a contention we continue to support.

Undoubtedly the relationship between thionimides, particularly propylthiouracil (PTU), and ANCA-SVV is well recognized with numerous cases reported in the literature, as well as a description and review of drug-induced vasculitis by our own group [2]. However, an abundance of publications does not translate to a high attributable risk of the disease from any specific cause. Continuous efforts to explore the aetiopathogenesis of ANCA-SVV require studies...