

Reply to Letter to the Editor

Resposta a Carta ao Editor

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Many thanks to Dr. Moura Neto for the letter commenting on our paper on “When Kidneys Get Old- an essay on Nephro-geriatrics”.¹ The point raised about risk of all-cause mortality (ACM) in the elderly associated with an estimated or measured GFR of between 45 and 59ml/min/1.73m² is an important but controversial one. We suggested that such levels of renal function in an elderly subject (say over 70 years of age), when unaccompanied by any abnormal proteinuria, is not associated with any significant reduction in remaining life expectancy nor does it consistently or reliably predict an excess of mortality (compared to similarly aged subjects with eGFR of > 60ml/min/1.73m² and no abnormal albuminuria).

In the cited Nagai *et al.* study,² the fully adjusted Hazard Ratio (HR) for eGFR of 45-59ml/min/1.73m² was not increased in 70-80 year old men, but it was in women relative to an eGFR of > 60ml/min/1.73m². The HR for ACM was increased in both men and women 70-80 years old at an eGFR of 30-44ml/min/1.73m². In the cited study of Roderick *et al.*,³ the age-adjusted HR (adjusted for dipstick proteinuria) for ACM in subject > 75 years was increased in men but not in women. In the landmark study of Go *et al.* in 2004,⁴ the fully adjusted HR for ACM was not increased in a sub-set of patients (average age 65 years) who had multiple measures of eGFR 45-59ml/min/1.73m² (MDRD) during follow-up.

More recently Malmgren *et al.*⁵ in longitudinal study of elderly women in Sweden found no increase in HR for ACM in a study of elderly women with an

eGFR of 45-59ml/min. calculated by various estimating formulas. Also, Warnock *et al.*⁶ have shown an HR of 1.62 (1.34-1.95) for ACM in males and 1.30 (1.05-1.62) in elderly females with an eGFR of 45-59ml/min/1.73m² (CKD-EPI) and no abnormal albuminuria, using a reference value of 80-100ml/min/1.73m².

There seems to be little doubt that advancing age attenuates the age-specific risk of mortality⁷ and a stable or slowly declining eGFR of 45-ml/min/1.73m² in an elderly subject without albuminuria has little impact on shortening remaining life expectancy.⁸ We believe that the evidence supports the view that a *stable* eGFR of 45-59ml/min/1.73m² (calculated by a variety of formulas using serum creatinine) in the absence of abnormal albuminuria does not consistently associate with an overall increased risk for ACM in the elderly, although gender, ancestry, non-GFR related determinants of eGFR and unmeasured comorbidity may significantly influence such outcomes.⁹ Thus, it has been suggested that gender- and ancestry- specific stratification needs to be considered in addition to age in constructing “heat maps” of the relationship of eGFR (and albuminuria) and mortality risk.⁶

The claim that a decline in renal function with normal healthy aging is not universal is based largely on a single longitudinal study conducted in 1985¹⁰ using endogenous creatinine clearance as the measure of renal function that included patients with Type 2 Diabetes, a disorder known to influence GFR. Other longitudinal studies have not uniformly confirmed this observation.⁵

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We do not disagree that a “diagnosis” of CKD based on a stable or very slowly declining eGFR of 45-59ml/min/1.73m² without albuminuria in an elderly person might have some theoretical benefits, by bringing attention to potential risks of use of water-soluble nephrotoxic drugs, but is it necessary to label such patient with a “chronic disease” in order to accomplish this aim? Why not simply use the information about eGFR, with due recognition of its inaccuracies, to make appropriate clinical decisions without adding the anxiety provoking label of CKD?

One should also not assume that “Early detection” of stable or slowly declining eGFR of 45-59ml/min/1.73m² (normal organ senescence) in the absence of albuminuria in an elderly subject will directly translate in cost-effective benefits and not material harms. We certainly would not object to better control of glycemia in diabetes, management of hypertension obesity, treating dyslipidemia or stopping smoking, but do these steps need to be taken via an “early diagnosis” of CKD. In so far as the elderly, non-albuminuric adult is concerned, we think not. In our view, the future approach to the diagnosis of CKD based on eGFR values should be refined to take into account the expected decline with normal healthy aging and the variations observed in associated outcomes relating to demographic features such as gender and ancestry rather than a “one-size fits all” schema.

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