



# Your Kidneys May Outlive You

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Since the introduction of estimated glomerular filtration rate (eGFR) as a measurement for kidney function and the staging of chronic kidney disease, referral to nephrology for evaluation of chronic kidney disease has increased significantly.<sup>1</sup> Recently I saw a Mrs. Jones (not her real name), who was referred for eGFR of 55 mL/min. She is an 80-year-old with controlled hypertension and otherwise healthy. She was very concerned because she was told that her kidney function is only 55% and that she has stage 3 chronic kidney disease. She searched the Internet and found out that if she advanced to stage 5, she would need dialysis. Her history and physical examination results were not remarkable, and her laboratory results showed stable eGFR without hematuria, proteinuria, or other significant renal abnormalities. I told her 2 things. First, starting at age 40 years, eGFR should decrease approximately 1 mL/min per year owing to normal aging,<sup>2</sup> so that the best eGFR for a woman her age is roughly 60 mL/min and she was only 5 points off. Second, with the help of the big chronic kidney disease chart on the wall of my clinic, I told her that if she continues to lose 1 mL/min per year, she will probably need dialysis at age of 120. She asked me to repeat. I did and she laughed and said, "Doctor, I will not take on dialysis when I am 120." I said, "I agree with you," then went on to tell her how to prevent a loss of eGFR of more than 1 mL/min/year. She went out happy and told my assistant that her doctor told her that she would live to 120. Well, I did not say so; what I meant was that her kidneys might outlive her.

Obviously, not all elderly patients with chronic kidney disease are the same. Presently the most rapid growing dialysis population is patients aged >70 years. When to refer elderly patients with chronic kidney disease to a nephrologist has been controversial. In this issue, practice guidelines for detecting and managing patients with chronic kidney disease for primary care physicians are published.<sup>3</sup> These guidelines were developed by a panel of nephrologists and internists aiming at

strengthening the collaboration between nephrologists and primary care physicians and shifting some responsibility of chronic kidney disease care to primary care physicians.

The major impact of the guidelines on current practice is that for patients with stable eGFR without other renal abnormalities, they should be referred to a nephrologist only when eGFR is <30 mL/min. This is quite appropriate for a patient such as Mrs. Jones, whose reduced eGFR is mainly due to the aging process.<sup>4</sup> A recent meta-analysis including almost 2 million patients with chronic kidney disease provides risk prediction for mortality and end-stage renal disease in patients of different ages, eGFR, and albuminuria.<sup>5</sup> **Figures A and B** are based on the data from this study, to illustrate the relative risk of mortality and end-stage renal disease (ESRD), respectively, for young (aged 18-54 years) and elderly (aged >75 years) patients with chronic kidney disease compared with the same age group with normal eGFR and no microalbuminuria. The elderly patients with eGFR of 45-59 mL/min and no microalbuminuria, such as Mrs. Jones, have a relative risk of mortality and ESRD of 1.20 and 2.51, respectively. Both risks increase when the severity of albuminuria or proteinuria worsens (**Figures A and B**).<sup>5</sup> If Mrs. Jones's chronic kidney disease is truly due to the aging process, why is her risk of ESRD so substantial? One possibility is that elderly patients are prone to development of acute kidney injury. James et al<sup>6</sup> reported that in patients with eGFR 45-59 mL/min without proteinuria (including all age groups), the relative risk for mortality and ESRD is 1.0 and 1.7, respectively, when compared with those with eGFR >60 mL/min without proteinuria. However, if they developed acute kidney injury requiring hospitalization, their risk for mortality and ESRD increases to 7.2 and 21, respectively. Therefore, the prevention of acute kidney injury or rapid progression of chronic kidney disease is critical for the care of Mrs. Jones, as recommended in the guidelines.<sup>3</sup>

Is the 30 mL/min eGFR cutoff for nephrology referral in elderly patients without proteinuria too low? Although the risk for mortality is not substantial (**Figure A**), the risk for ESRD is as high as 9.83 in elderly patients with eGFR 30-44 mL/min without microalbuminuria, when compared with patients of the same age with eGFR >60 mL/min.<sup>5</sup> These patients are most likely to have pathologic changes

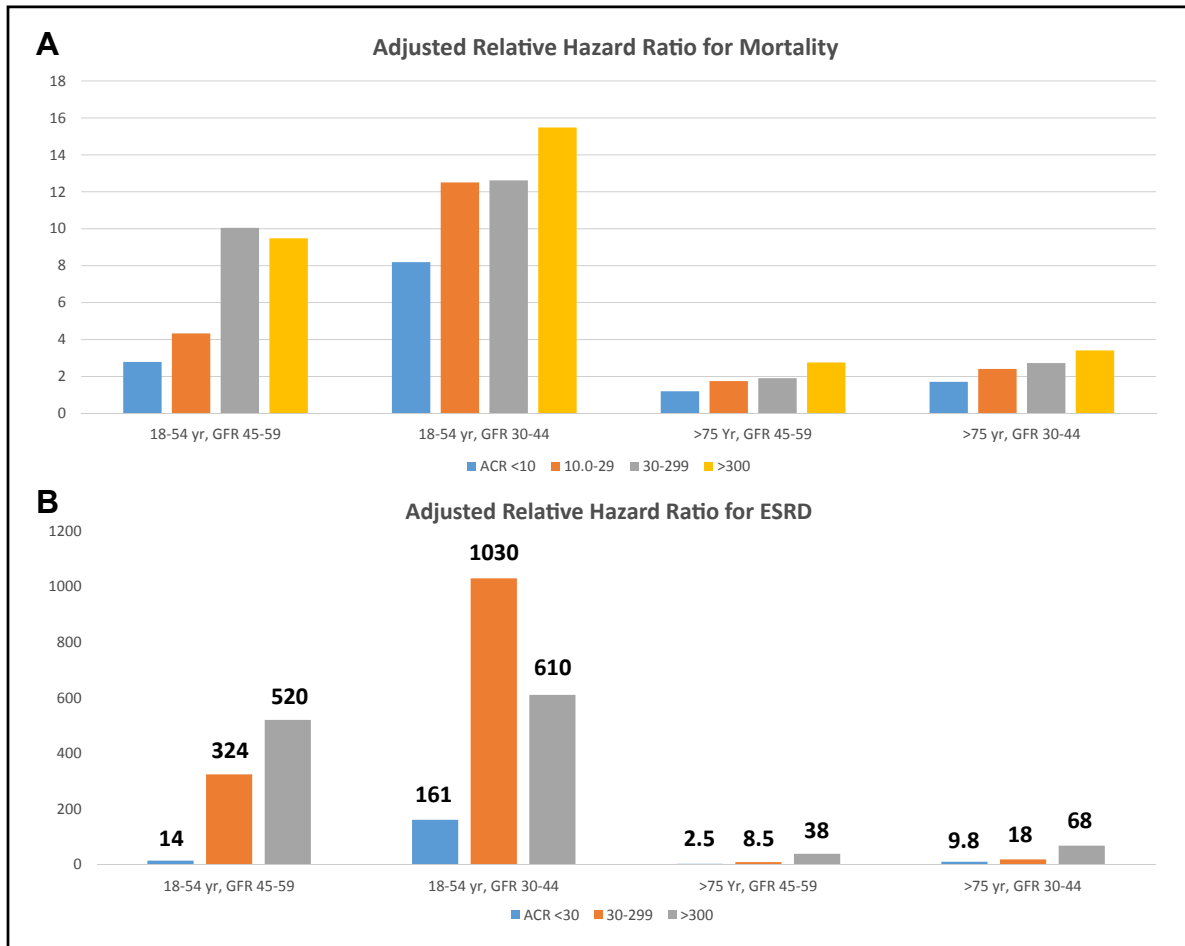
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**Figure** (A) Relative hazard ratio for mortality in young (aged 18-54 years) and elderly (aged >75 years) patients with chronic kidney disease. Data are taken from Figure 3 published by Hallan et al.<sup>5</sup> Four categories of urine albumin-to-creatinine ratio (ACR) are <10, 10-29, 30-299, and >300. Two categories of estimated glomerular filtration rate (eGFR) are 30-44 and 45-59 mL/min. The reference groups are the respective age group with urine ACR <10 and eGFR 75-89 mL/min. (B) Relative hazard ratio for end-stage renal disease (ESRD) in young (aged 18-54 years) and elderly (aged >75 years) patients with chronic kidney disease. Data are taken from eFigure 22 published by Hallan et al.<sup>5</sup> Three categories of urine ACR are <30, 30-299, and >300. Two categories of eGFR are 30-44 and 45-59 mL/min. The reference groups are the respective age group with urine ACR <30 and eGFR >60 mL/min. The relative risk is listed on top of each bar.

in their kidneys and would progress faster to end-stage or renal disease. In addition, their renal reserve is limited because of existing renal pathologies, so if they developed acute kidney injury, the chance to recover their renal function is much smaller. For these patients, raising the eGFR cutoff point for nephrology referral to 45 mL/min seems to be appropriate.

The eGFR cutoff at 30 mL/min for nephrology referral for younger patients (aged 18-54 years) without proteinuria is also concerning. Compared with the same age group with eGFR >60 mL/min, the relative risk for mortality for young patients without microalbuminuria is 2.79 and 8.19 (Figure A), and for ESRD is 13.78 and 160.95 (Figure B), for eGFR of 45-59 and 30-44 mL/min, respectively. The effects of albuminuria on renal and patient outcomes are more dramatic in younger patients than elderly patients (Figures A and B).<sup>5</sup> Excepting individuals with a single

kidney for various reasons, most younger patients with chronic kidney disease stage 3 are likely to have pathologic changes in the kidneys. As suggested in the guidelines, primary care physicians should consider nephrology referral when the cause of kidney disease is not apparent.<sup>3</sup> These patients may have renal vascular disease, tubulointerstitial diseases, or other renal pathologies, which may be treatable if referred to a nephrologist earlier.

In conclusion, with rapid growth of the population with chronic kidney disease, the publication of chronic kidney disease detection and management guidelines for primary care physicians is timely and provides a framework for co-management of chronic kidney disease by primary care physicians and nephrologists.<sup>3</sup> The eGFR criteria for nephrology referral should be adjusted according to the risks for mortality and progression of chronic kidney disease, as well as the causes of chronic kidney disease. The shifting of care from primary

care physicians to nephrologists for high-risk patients will serve patients with chronic kidney disease best.

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