The Conundrum of Chronic Kidney Disease Classification and End-Stage Renal Risk Prediction in the Elderly – What Is the Right Approach?

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Chronic kidney disease (CKD) has been found to be very common worldwide\cite{1–3}. The prevalence is particularly high in elderly subjects. The fact that this system is mainly based on estimated glomerular filtration rate (eGFR), subdividing the severity of CKD into five stages, is a matter of debate. A main issue is that although a reduced eGFR is often encountered in elderly subjects, most of these subjects do not have a renal disease leading to an increased risk of ESRD, i.e. the predictive power of ESRD is unsatisfactory. Recent advances have been put forward to improve (1) estimation of GFR and (2) prediction of ESRD. In this review, we discuss the currently available data with a focus on the elderly and propose an improved classification system of CKD which is characterized by a substantially better diagnostic accuracy for progression to ESRD. This is simply and cost-effectively accomplished by subdividing stage 3 CKD into two groups (eGFR 30–44 and 45–59 ml/min/1.73 m\textsuperscript{2}) and by complementing all levels of eGFR with information about urinary albumin excretion, i.e. whether normoalbuminuria, microalbuminuria, or macroalbuminuria is present. The consequence should be a revision of the 2002 KDOQI CKD classification system according to these findings, which would be a significant step forward, particularly for elderly CKD patients.

Chronic kidney disease (CKD) has been found to be very common worldwide\cite{1–3}. The prevalence is particularly high in the elderly with 47, 35 and 28% of subjects above age 70 in US, European, and Chinese general populations, respectively, diagnosed as having CKD according to the current Kidney Disease Outcomes Quality Initiative (KDOQI) definition\cite{1–3}. Although a large proportion of new end-stage renal disease (ESRD) cases today comes from this age group, it has become apparent that the risk for progression to kidney failure among elderly CKD patients is low\cite{4}. This has lead to a vivid debate whether or not the current KDOQI definition of CKD is valid and appropriate\cite{5–9}. A major concern is...
that a large proportion of CKD cases, especially among the elderly, may be misclassified and that their low estimated glomerular filtration rate (eGFR) is just a 'normal' reduction of kidney function with increasing age.

**Current CKD Classification**

The 2002 KDOQI classification system for CKD is mainly based on degrees of reduction in GFR [10]. Stages 1–5 are defined as eGFR ≥90, 60–89, 30–59, 15–29 and <15 ml/min/1.73 m², respectively, and the findings should be consistent for more than 3 months. For stages 1–2 signs of kidney damage (albuminuria, hematuria or sonographic abnormalities) are also required. GFR should be estimated with formulas based on serum creatinine taking age, sex, and other demographics into account. The first publications using the KDOQI system were hampered by estimation formula problems [11, 12]. The first Modification of Diet in Renal Disease (MDRD) study formula was based on an unusually low calibrated serum creatinine method [13], and the use of the Cockcroft-Gault formula results in a too steep decline of kidney function with age [14]. Both problems lead to a substantial underestimation of GFR thereby overestimating the CKD prevalence.

A recalibration of the MDRD formula based on isotope dilution mass spectroscopy traceable serum creatinine values improved performance substantially, and recently the Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was published with even better performance [15]. By using the CKD-EPI equation, the mean systematic underestimation at GFR 60 ml/min/1.73 m² and upwards has been reduced from −10.6 to −3.5 ml/min/1.73 m² and precision has increased, resulting in 88.3% of the results being within ±30% of the true GFR (as measured by radiolabeled tracers) compared to 84.7% with the recalibrated MDRD formula [15]. However, for the individual patients there is still a clinically inaccurate (e.g. errors of ±20% are not unusual), and this can – especially in eGFR-dominant systems – lead to misclassification. When using this new equation, the median eGFR in the general population shifts from 85 to 95 ml/min/1.73 m², and a substantial proportion of subjects is reclassified from the 30–59 ml/min/1.73 m² category to the 60–89 ml/min/1.73 m² category, i.e. from stage 3 to stage 2 of the current KDOQI CKD classification [15].

The CKD-EPI equation should be well suited for use in the elderly, because a total number of 1,592 subjects above age 65 was enrolled during development, internal and external validation of this formula [15]. In contrast to middle-aged subjects, there is no shift of the median eGFR in elderly subjects using the CKD-EPI equation. Table 1 shows the prevalence of CKD stages 1 through 4 in elderly subjects from two large population-based studies using the MDRD and the CKD-EPI equations. Independent of the formula used, the CKD prevalence is consistently found to be very high.

**Table 1. Prevalence of CKD among the elderly in the USA and in a European population**

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td></td>
<td>MDRD</td>
<td>CKD-EPI</td>
</tr>
<tr>
<td>Stage 1</td>
<td>1.2</td>
<td>0.6</td>
</tr>
<tr>
<td>Stage 2</td>
<td>7.6</td>
<td>8.5</td>
</tr>
<tr>
<td>Stage 3</td>
<td>35.5</td>
<td>35.3</td>
</tr>
<tr>
<td>Stage 4</td>
<td>1.9</td>
<td>2.4</td>
</tr>
<tr>
<td>Total</td>
<td>46.3</td>
<td>46.8</td>
</tr>
</tbody>
</table>

Data are percentages of the general population. Prevalence estimates were based on eGFR in subjects aged >70 years. GFR was estimated with the MDRD study equation for use with calibrated serum creatinine values and the CKD-EPI equation. The prevalence estimates for the Norwegian HUNT 2 study were based on the same study sample as previously published [2].

**Controversies over the Current CKD Classification**

There has been a brisk debate over the last couple of years whether the CKD epidemic is fact or fiction. In a series of articles, Glassock and Winearls [7–9, 16, 17] put forward strong critiques about the current eGFR-focused CKD classification, which in turn, has been strongly defended by the KDOQI chairpersons [5, 6]. The main critique has been related to ‘the improbable high prevalence estimates’, a fixed cutoff for abnormality for all ages, and omission of the possibility that a decline in kidney function may be a normal part of the aging process. The KDOQI 2002 classification system definitely has shortcomings as a renal risk score, but the above mentioned critiques, which are clearly interrelated, also have deficits. First, we have repeatedly learnt over the past 40 years that normality and percentiles are not always the optimal approach for diagnostics and risk stratification. Cutoffs for blood pressure and cholesterol have repeatedly been low-

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Hallan/Orth
 Reduced Kidney Function in the Elderly

The reduction of GFR with increasing age deserves special attention. Studies have shown that there is a gradual decline in measured GFR with age [21–23]. The classical work by Davies and Shock [21] showed that mean GFR (measured using the gold standard of inulin clearance) decreased from 123 (SD 16) ml/min/1.73 m² at age 20–29 years to 65 (SD 20) ml/min/1.73 m² at age 80–89 years. This indicates that there is a true reduction in kidney function among the elderly and that this may not only be a phenomenon created by inaccurate or biased equations for estimating GFR. However, the majority of participants in the previous studies were in-hospital patients with acute or chronic infections, atherosclerosis or other diseases and treatments that potentially could influence kidney function although patients with obvious cardiovascular diseases were excluded. On the contrary, there are good indications that the reduction of GFR at higher age is only modest, as long as the subjects investigated are healthy. For instance, Fliser et al. [24] found that this was the case when comparing 10 healthy subjects with a median age of 70 years (range 61–82) with a group of 15 subjects with a median age of 26 years (range 23–32). They also documented that at least until the age of 80 years renal functional reserve, i.e. the increase in GFR after an amino acid load, was preserved in these subjects independent of gender. Thus, age-related changes of renal function are less severe than previously thought. However, the arterial wall is substantially remodeled with increasing age even in the healthiest subjects. These normal changes caused by the joint effects of biomolecular, cellular and matrix modifications are significantly aggravated by classical cardiovascular risk factors such as hypertension, diabetes and smoking, i.e. conditions often encountered in elderly subjects [20, 25]. One of the consequences is increased arterial stiffness, and significant associations have been found even to small reductions of eGFR and to low-grade albuminuria. The kidneys are, as a low resistance organ, thought to be especially prone to the resulting high pulse pressures, and resulting microcirculation changes lead to kidney dysfunction through ischemia. Decreasing kidney function could then lead to calcium-phosphate depositions and increased oxidative stress setting up a vicious circle as indicated in figure 2 [26, 27].

To separate the effect of toxins and diseases that may injure the kidneys over time and the 'natural aging' caused by replicative senescence and oxidative stress, we must study a population that is very unlikely to have any kind of kidney disease and no cardiovascular risk factors. Kidney donors are probably the most valid study group to analyze this problem. These subjects undergo all available noninvasive tests to ensure that donation will have
no negative influence on their future health. A pooled analysis of measured GFR in 1,040 kidney donors showed that there was only a modest reduction of kidney function over time [14]. Median GFR (2.5th and 97.5th percentiles) was 110 ml/min/1.73 m² (80–150) at age 25, 95 ml/min/1.73 m² (70–125) at age 50, and 80 ml/min/1.73 m² (60–110) at age 75, which corresponds to a reduction in GFR of 0.6 ml/min/1.73 m² per year. Figure 3 shows that estimation of GFR using the CKD-EPI formula in 1,027 subjects from the HUNT 2 study eligible for kidney donation gave very similar results. Inclusion criteria for this healthy group were absence of macroalbuminuria, cardiovascular disease (CVD), diabetes mellitus and malignancy as well as presence of normotension, normal serum creatinine, body mass index <35 and the self-reporting of good or excellent general health [14]. The median eGFR at age 75 was exactly the same as measured GFR in kidney donors reported in the literature (80 vs. 81 ml/min/1.73 m²), while the eGFR values at younger ages were slightly higher (97 vs. 94 ml/min/1.73 m² at age 50). In this cohort, the 5th percentile, which has been suggested as a lower limit of normal kidney function, was above 60 ml/min/1.73 m² even for 80-year-old subjects. Clearly, the 5th percentile is substantially lower if estimated in the general population versus a very healthy population like potential kidney donors, and it would be principally wrong to use percentiles derived from the total general population for decision making. Therefore, it seems clear indeed that there is a normal decline in kidney function with age, but the decline is not as steep as had often been claimed in the past. The important conclusion is that even among the elderly an eGFR below 60 indicates a pathological reduction in kidney function!

Cardiovascular Disease Risk in Elderly CKD Patients

CVD is the most imminent threat for patients with CKD. It is not until CKD patients have progressed to stage 4 that the risk for future ESRD exceeds the risk of cardiovascular death [28]. The reason for this extremely increased CVD risk is both an increased prevalence of traditional cardiovascular risk factors in elderly subjects and several novel risk factors associated with CKD [29]. Anemia, electrolyte disturbances, hyperparathyroidism, metabolic acidosis, and others contribute to the increased risk. In a substantial number of CKD patients one or more of these risk factors start to appear at a GFR of 60 ml/min/1.73 m² [30]. However, the relative risk associated with traditional risk factors like hypertension and hypercholesterolemia is lower in the elderly compared with younger subjects [31, 32]. In the oldest, there are even indications of a reversed causation for several traditional CVD risk factors (body mass index, blood pressure, and cholesterol) [33]. In this context, it also has to be kept in mind that the major risk equations used today, i.e. the U.S. Framingham Score and the European System for Cardiac Operative Risk Evaluation (or SCORE), are based on data derived from populations below the age of 70 years.

Albuminuria has long been recognized as an important predictor of increased cardiovascular mortality in the general population as well as in different subgroups including the elderly [34, 35]. Since eGFR emerged as an important CVD risk factor the combined assessment of these two parameters seems prudent. Several studies have found that both lower eGFR and increasing albuminuria
are significant independent cardiovascular risk factors. Table 2 shows data from some studies based on elderly subjects. These, as well as other general population-based studies [36–41], are quite heterogeneous regarding study design and patient characteristics. Thus, it is not possible to give good pooled estimates of the association between CKD and cardiovascular mortality.

Such research is, however, underway in the Kidney Disease Improving Global Outcomes (KDIGO) organization [6], and it is likely that more than 100,000 elderly subjects with data on eGFR and albuminuria will be included into a meta-analysis. The presence of CKD has already been included as a new major risk factor for CVD in general clinical guidelines [42], and the data

**Table 2.** Data from the literature on the association between eGFR and albuminuria and cardiovascular mortality risk in elderly subjects

<table>
<thead>
<tr>
<th>Study</th>
<th>Age group</th>
<th>Variable</th>
<th>Relative risk</th>
<th>Study conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK [53] (general practice)</td>
<td>≥75 years</td>
<td>proteinuria (dipstick neg./pos.)</td>
<td>NS</td>
<td>GFR is an independent strong risk factor, especially in men</td>
</tr>
<tr>
<td></td>
<td></td>
<td>eGFR (&gt;60, 45–59, 30–44, &lt;30)</td>
<td>1.0, 1.6, 1.7, 4.5</td>
<td></td>
</tr>
<tr>
<td>Japan [54] (general population)</td>
<td>≥80 years</td>
<td>eGFR (&gt;60, &lt;60)</td>
<td>1.0, 4.6</td>
<td>CKD increases CVD risk in very elderly individuals</td>
</tr>
<tr>
<td>US (Cardiovascular Health Study) [55]</td>
<td>≥65 years</td>
<td>albuminuria (quintiles)</td>
<td>1.0, 1.2, 1.4, 1.6, 2.1</td>
<td>albuminuria and GFR are graded independent risk factors for CVD</td>
</tr>
<tr>
<td>Japan (general population)</td>
<td></td>
<td>eGFR (quintiles)</td>
<td>1.0, 1.1, 1.6, 1.8, 2.5</td>
<td></td>
</tr>
<tr>
<td>Taiwan (Elderly Health Examination Program study) [56] (general population)</td>
<td>≥65 years</td>
<td>eGFR (&gt;60, 45–59, 30–44, &lt;30)</td>
<td>1.0, 1.3, 2.4, 3.6</td>
<td>late-stage CKD is a significant risk factor in the elderly</td>
</tr>
<tr>
<td>Norway (HUNT study) [39] (general population)</td>
<td>≥70 years</td>
<td>albuminuria (quintiles)</td>
<td>1.0, 1.4, 2.1, 2.4, 2.7</td>
<td>albuminuria and GFR are strong independent risk factors, especially when combined and in the elderly</td>
</tr>
<tr>
<td></td>
<td></td>
<td>eGFR (&gt;60, 45–59, 30–44, &lt;30)</td>
<td>1.0, 1.4, 2.6, 2.5</td>
<td></td>
</tr>
</tbody>
</table>

Relative risk given for albuminuria and GFR are adjusted for each other and age, sex, diabetes, hypertension, and other relevant cardiovascular risk factors. NS = Nonsignificant.

* Unpublished data from reference [39], new categorization to improve comparison with other studies.
shown in table 2 very consistently document that low eGFR and increasing albuminuria are strong independent cardiovascular risk factors. It has also been shown that the additional predictive power of a combined eGFR-albumin:creatinine ratio (ACR) variable is especially high among the elderly [39]. This is probably due to the reduced risk associated with traditional risk factors and CKD working as a marker of subclinical atherosclerosis in the elderly. Indeed, there are substantial experimental, epidemiological and clinical data suggesting that CKD is a marker of subclinical atherosclerosis [20].

Inclusion of kidney function and damage, i.e. eGFR and albuminuria, in future CVD risk equations seems reasonable, and a close collaboration with the cardiology societies will be very important.

### Risk of Progression to Kidney Failure in Elderly CKD Patients

The risk of progression to kidney failure is of major interest for CKD patients and nephrologists. Developing renal risk scores are therefore urged by nephrology leaders [43]. In this process, we should ensure that the risk scores to be developed are also suitable for use among the elderly. The largest proportion of incident dialysis patients comes from this group of CKD patients, which also is the most difficult to evaluate concerning the need of intensive prophylactic treatment and follow-up. The currently available knowledge for the specific subgroup of the elderly is more limited concerning kidney disease progression than for CVD risk estimation. Table 3 shows that low eGFR and increased ACR are important independent risk factors in several populations, and a sub analysis of the HUNT 2 study indicates that this also proves true for the elderly.

However, the current CKD definition has a low specificity. Only a minor portion of those classified as CKD patients progress to kidney failure [44, 45]. There has recently been some important progress on risk stratification; combining eGFR and albuminuria at all levels are now considered as the way forward [46]. This is based on previous reports with certain shortcomings [47–50] and a recent comprehensive analysis on the improved classification of CKD using these principles [51]. Previous reports have shown that the relative risk for ESRD increases strongly with decreasing eGFR and increasing albuminuria, independently of each other. However, some of the studies were based on men with high CVD risk or African-Americans with hypertensive nephrosclerosis [48, 50], some did not adjust for relevant confounders [47, 50], and some only tested for macroalbuminuria [47]. Furthermore, all previous studies have only reported relative risk estimates for ESRD exclusively, although this is regarded as a less suitable/relevant measure for risk prediction and classification [52].

Based on 65,000 subjects from the population-based HUNT 2 study with 10.3 years of follow-up, we found that eGFR and ACR were the major risk predictors after adjusting for other known risk factors [51]. They were also synergistic implying increased discrimination when used together. Age, sex, hypertension, diabetes, and other cardiovascular risk factors did not increase predictive value. We also performed receiver operating characteristics analysis, which describes how well a model discriminates those CKD cases progressing to ESRD from those cases not progressing. This confirmed that eGFR discriminates better than ACR when equal importance is given to sensitivity and specificity. However, for screening related situations a very low false-positive rate is needed, and in this case eGFR and ACR had equal diagnostic accuracy. Both strongly outperformed a model including all other known risk factors, and combining eGFR and ACR significantly

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**Table 3.** Data from the literature on the association between eGFR and albuminuria and kidney failure risk in elderly subjects

<table>
<thead>
<tr>
<th>Study</th>
<th>Age group</th>
<th>Variable</th>
<th>Relative risk</th>
<th>Study conclusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Japan (Okinawa study) [47] (general population)</td>
<td>≥71 years</td>
<td>proteinuria (0, trace, 1 to 4+) eGFR (&gt;79, 64–79, 50–64, &lt;50)</td>
<td>1.0, 4.7, 9.4, 14.1, 18.8, 23.5, 28.3 1.0, 9.8, 19.6, 29.4</td>
<td>dipstick screening useful, especially in the elderly</td>
</tr>
<tr>
<td>Norway (HUNT study) [51] (general population)</td>
<td>≥70 years*</td>
<td>albuminuria (normo, micro, macro) eGFR (&gt;60, 45–59, 30–44, &lt;30)</td>
<td>1.0, 8.2, 26.3 1.0, 3.3, 10.4, 30.3</td>
<td>major independent risk factors for kidney failure</td>
</tr>
</tbody>
</table>

Relative risk given for albuminuria and GFR are adjusted for each other and age, sex, diabetes, hypertension, and other relevant risk factors.

* Unpublished data [from 51], i.e. a subanalysis of the elderly.
improved diagnostic accuracy. We therefore recently proposed a new classification system for CKD based on four eGFR categories (≥60, 45–59, 30–44, <30 ml/min/1.73 m²) that are further subdivided by three ACR categories (normal, microalbuminuria, macroalbuminuria) [51]. Importantly, we showed that this classification system could reduce the number of CKD patients referred to specialists by 70% without losing CKD cases that would progress to ESRD in the future. These results need to be confirmed in other cohorts, and a joint effort to do so is on its way within the KDIGO organization [6]. Fifty CKD cohorts including more than a million subjects worldwide will be analyzed following the same analytical approach as in the previous 2009 HUNT 2 study, with the first results expected during 2010. The new CKD classification system that we present here also provides clear information about kidney failure risk in the elderly. Importantly, we have also recently been able to show that this CKD classification system provides strong predictive information on CVD risk in the elderly as well [39].

**Should Normoalbuminuric Elderly Subjects with eGFR 30–59 ml/min/1.73 m² Be Classified as CKD Patients?**

CKD stage 3 in the elderly has been one of the main problems fuelling the debate on the current CKD classification. Including information on albuminuria in all CKD patients substantially improves risk prediction [51]. However, subjects with eGFR 30–59 ml/min/1.73 m² without micro- or macroalbuminuria remain problematic as far as classification is concerned. The question is whether these subjects really have CKD? This question is indeed of major clinical importance, because this group comprises a large number of subjects. Prevalence and relative risk estimates for serious outcomes in this group of subjects are given in table 5 (based on data of the HUNT 2 study). We have provided evidence above that eGFR <60 ml/min/1.73 m² is not normal even in the elderly, as long as unbiased estimation formulas are used. Furthermore, the relative risk for ESRD is substantially increased (more than 10 times) in this group, although the absolute risk is still very low. The absolute risk for cardiovascular morbidity and mortality is high in this age group, and we see that a slight reduction in eGFR is associated with a strong increased risk even in the absence of microalbuminuria. The same is found for total mortality. Therefore, we conclude that eGFR in the range of 45–59 ml/min/1.73 m² should be classified as CKD.

**Summary and Clinical Implications for the Handling of Elderly CKD Patients**

Based on the above discussed data, the following considerations are of major importance in the diagnostic and therapeutic decision making when dealing with suspected CKD cases:

(1) Estimation of GFR should be based on the recalibrated MDRD formula or, even better, on the CKD-EPI equation. This notion does not only hold true for the el-
derly, but also the young. However, eGFR still has a clinically significant inaccuracy necessitating the use of other markers of kidney damage to enable an accurate diagnosis of CKD.

(2) Studies in healthy subjects show that there is a natural loss of GFR with increasing age, but this decrease is only minor and 95% of octogenarians have eGFR >60 ml/min/1.73 m². An eGFR of 45–59 ml/min/1.73 m² is a significant and independent renal risk factor in elderly subjects from the general population. Therefore, even in very old subjects GFR levels below 60 ml/min/1.73 m² have to be regarded as pathological and should be defined as CKD (despite the fact that the absolute risk to progress to kidney failure is low in this subgroup).

(3) Estimation of GFR should be complemented by measurement of urinary ACR in all subjects with an eGFR >60 ml/min/1.73 m². For renal (but not cardiovascular) risk prediction, a dipstick test for the detection of macroalbuminuria is sufficient in those with eGFR >60 ml/min/1.73 m². The new CKD classification that we have recently proposed is given in table 4 and is based on eGFR and urinary albumin excretion. The advantage of this classification compared to the current KDOQI classification system is a substantially improved prediction of the future ESRD risk. We also find that renal risk stratification based on the combined eGFR-ACR approach is efficient in the elderly, which is of major clinical importance since the prevalence of CKD is very high in this subgroup.

(4) In patients recognized to be at moderate or high renal risk the search for a primary or secondary renal disease and/or underlying vascular risk factors is mandatory. The treatment of the underlying cause should follow current state-of-the-art therapies/guidelines, irrespective of the age of the patient. Specific and unspecific therapeutic and prophylactic interventions with the aim to prevent or retard progression to ESRD are certainly poorly studied areas among the highest age groups, but diagnosing and treating CKD even in the oldest is more than justified based on the current knowledge.

Acknowledgements

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We also thank Prof. K. Amann, Head of the Nephropathology Department of the University of Erlangen-Nürnberg, Germany, for providing figure 1.

References


Table 5. Risk for serious outcomes in elderly subjects with stage 3 CKD by presence or absence of microalbuminuria

<table>
<thead>
<tr>
<th></th>
<th>eGFR ≥60 ml/min/1.73 m²</th>
<th>eGFR 45–59 ml/min/1.73 m²</th>
<th>eGFR 30–44 ml/min/1.73 m²</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prevalence</td>
<td>66% 15%</td>
<td>11% 4%</td>
<td>3% 1%</td>
</tr>
<tr>
<td>ESRD risk</td>
<td>1.0 20.0c</td>
<td>11.4c 55.0c</td>
<td>19.5c 221.4c</td>
</tr>
<tr>
<td>CV mortality risk</td>
<td>1.0 1.1</td>
<td>1.2b 1.5c</td>
<td>1.6c 2.2c</td>
</tr>
<tr>
<td>Total mortality risk</td>
<td>1.0 1.1a</td>
<td>1.1a 1.3c</td>
<td>1.4c 1.7c</td>
</tr>
</tbody>
</table>

Data are based on subjects aged ≥70 years from the HUNT 2 study. NA = Normoalbuminuria; MA = microalbuminuria. Hazard ratios are adjusted for age and sex. a p < 0.05, b p < 0.01, c p < 0.001.


The minireview by Hallan and Orth is timely as it discusses the controversial issue of CKD definition and prognosis in the elderly. Most CKD surveys reporting a significant prevalence (~10%) of CKD within the population merely reflect the fact that a large percentage (40–60%) of elderly individuals have decreased GFR. I recently argued that such a decrease in age-related kidney function, which is not universal, may be a manifestation of diffuse vascular damage, with the kidney being one of many end organs affected; I called it cardio-kidney damage [1]. Hallan and Orth suggest that in order to identify elderly individuals at increased risk of ESRD or death, the KDOQI CKD classification should be revised by subdividing CKD stage 3 into CKD3a and CKD3b and qualifying the severity of proteinuria. This goes along with the recommendations made by the UK National Institute for Health and Clinical Excellence (NICE) for the revised CKD classification issued in 2008 (http://www.nice.org.uk/Guidance/CY73). They also support the recommendations made by the KDIGO Consensus Conference held in London in 2009. These recommendations are supported by recently published data from the Chronic Kidney Disease Prognosis Consortium showing an association between decreased GFR and raised albuminuria with increased mortality in the general population [2]. Clearly, a growing body of data is suggesting that elderly individuals with underlying, overt or covert, cardiovascular pathology have microalbuminuria (a sign of atherosclerosis and endothelial dysfunction) and a reduced GFR (a sign of renal underperfusion and ischemia). It is therefore not too surprising that these markers of CVD predict mortality. Whether they add much to current CVD risk stratification and scoring is debatable, but there is no doubt that the recommendations of Hallan and Orth, UK NICE and KDIGO will help nephrologists to identify elderly patients at higher risk and direct healthcare resources to address their underlying risk factors: most likely progressive cardiovascular in nature.

References


Editorial Comment

M. El Nahas, Sheffield