A population-based cohort study defines prognoses in severe chronic kidney disease

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In older people with chronic kidney disease (CKD) and comorbidities, the risk of death or disability may overshadow the risk of kidney failure. To help refine this we did a retrospective population-based cohort study to evaluate the relative likelihood of adverse outcomes as functions of age and comorbidity burden among 47,228 adults with severe non–dialysis dependent CKD. We identified comorbidities using 29 validated algorithms applied to administrative data and assessed death, end-stage renal disease (ESRD), cardiovascular disease (CVD) events, and long-term care. Over five years of follow-up, 53.4% of participants died, 24.1% had a CVD event, 14.3% were placed into long-term care and 5.3% developed ESRD. Death was 145 times more likely and 11 times more likely than ESRD for participants aged 80 years or more and 60-79 years, respectively; long-term care was 30 times more likely and 1.7 times as likely as ESRD for participants aged 80 years or more and 60-79 years, respectively. Increasing comorbidity burden was similarly associated with increased risk of death and long-term care placement but reduced the likelihood of ESRD, and the risks of increasing age were similarly incremental. Thus, among patients with severe CKD, older age and/or higher comorbidity burden, death and long-term care placement are markedly more likely than ESRD. Hence, clinicians, patients and families should all consider the relative magnitude of these risks when making decisions about renal replacement.

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Chronic kidney disease (CKD) is common and associated with a high burden of comorbidity as well as an excess risk of adverse outcomes such as premature death, cardiovascular events, and progression to kidney failure.[1,2] CKD is commonly classified into stages based primarily on the estimated glomerular filtration rate (eGFR); eGFR <60 ml/min per 1.73 m^2 is commonly used to identify participants with CKD in epidemiologic studies.[3] However, this definition includes people with moderately reduced eGFR (30–59.9 ml/min per 1.73 m^2) as well as severely reduced eGFR (15–29.9 ml/min per 1.73 m^2) or kidney failure (eGFR <15 ml/min per 1.73 m^2). End-stage renal disease (ESRD) refers to people with kidney failure who are treated with dialysis or kidney transplantation.

As a group, non–dialysis dependent people with severe CKD have important clinical differences compared with those with eGFR of 30 to 59.9 ml/min per 1.73 m^2: they are more likely to be older, have more comorbid conditions, experience more adverse outcomes, and incur higher health care costs.[4,5] However, because eGFR of 30–59.9 ml/min per 1.73 m^2 is ~200 times more common than severe CKD,[6] most published data from unselected CKD cohorts better reflect findings from the former, and there are relatively few data on how to estimate prognosis in patients with severe CKD specifically. In addition, because mortality is a competing risk for kidney failure, it is unclear how the presence of age and comorbidity influence the absolute risk of death compared with the initiation of dialysis. Also, the burden of comorbidity also increases with age[7] (and might plausibly influence decisions to initiate renal replacement therapy). Finally, other outcomes such as cardiovascular events and loss of the capacity to live independently are common in CKD populations,[8,9] but have not frequently been studied despite their importance to patients and families. Therefore, better information on how age and comorbidity burden interact to influence the risk of death, initiation of renal replacement, and other patient-relevant outcomes in severe non–dialysis dependent CKD would be useful to clinicians and policymakers.

We designed this study to examine how the risks of death and ESRD change with increasing age and comorbidity burden among those with severe non–dialysis dependent CKD. Because of their relevance to patients and families, we also considered 2 other outcomes: cardiovascular events and a

proxy for loss of independent living (placement in a long-term care [LTC] facility).

RESULTS

Characteristics of study participants

Participant flow is shown in Supplementary Figure S1; 425 participants (0.9%) were excluded because they moved out of the province before the 5 years of follow-up were acquired, and 1543 participants (3.1%) were excluded because they started dialysis without previously identified severe CKD. There were 47,228 participants with severe non–dialysis dependent CKD, of whom 6391 (13.5%) were in LTC at baseline. Over 5 years of follow-up (interquartile range, 15–60 months), 25,211 of the 47,228 participants (53.4%) died, and 11,318 (24.1%) had at least 1 cardiovascular event; 6769 (14.3%) were placed in LTC; and 2509 (5.3%) reached ESRD. Participants were 56.3% female; the median age was 78 years at baseline (range, 18–108); 2.3% were indigenous; and 3.3% were receiving social assistance (Table 1). The median number of comorbidities was 5 (range, 0–8). The characteristics of patients who reached ESRD were strikingly different than those who died or experienced the other 2 clinical outcomes (cardiovascular event or placement into LTC): they were younger, were more likely to be male and indigenous, received social assistance, and had a lower burden of serious comorbidity.

Risk of clinical outcomes by number of comorbidities

The proportion of participants who died was higher among those with more comorbidities: 31.1, 45.3, and 67.2% for those with 0 to 2, 3 to 5, and ≥6 comorbidities, respectively. Figure 1 and Supplementary Table S1 show the proportion of participants who experienced each clinical outcome as a function of the number of comorbidities. The proportion of participants who experienced cardiovascular events (15.0%, 22.6%, and 27.5%) or were placed into LTC (9.0%, 13.5%, and 16.5%) both increased with an increasing number of comorbidities (0–2, 3–5 and ≥6 comorbidities, respectively). However, the proportion of participants who reached ESRD during follow-up was significantly lower in those with more comorbidities at baseline: 8.7%, 6.3%, and 3.4% for those with 0 to 2, 3 to 5, and ≥6 comorbidities, respectively.

Risk of the clinical outcomes by age

The proportion of participants who died was higher and the proportion reaching ESRD was lower among older participants (Figure 2, Supplementary Table S1): the percentage of patients dying during follow-up was 26.6%, 44.8%, and 69.3% for those 18 to 59, 60 to 79, and ≥80 years of age, respectively, whereas the corresponding percentages of those who reached ESRD were 17.4%, 6.1%, and 1.0%. The percentage of participants who were placed into LTC increased sharply with age (3.5%, 9.9%, and 21.6% for the same age categories, respectively), whereas the percentages experiencing a cardiovascular disease event were lower for participants 18 to 59 years of age and similar for those 60 to 79 years of age and 80 years of age and older (15.3%, 24.4%, and 26.2%, respectively). Overall, death was ∼145 times more likely (95% confidence interval [CI] 119–176) than ESRD for participants 80 years of age and older, whereas death was 11 times more likely (95% CI 10–12) for those 60–79 years of age and 1.6 times more likely for those 18 to 59 years of age (Supplementary Table S2). Results were very similar in a sensitivity analysis in which participants who were lost to follow-up (0.9%) were assumed to have died (Supplementary Table S2). Similarly, LTC placement was ∼30 times more likely (95% CI 25–35) than ESRD for participants aged 80 years and older, whereas LTC placement was 1.7 times more likely (95% CI 1.6–1.9) than ESRD for those aged 60–79 years of age, and ESRD was 7 times more likely (95% CI 6–8) than LTC placement for those aged 18–59 years of age.

Joint contribution of age and comorbidities to the risk of the clinical outcomes

Although the absolute proportion of those experiencing death, ESRD, LTC placement, or a CVD event all varied by age, age did not qualitatively modify the relationship between comorbidity and these outcomes (Figure 3, Supplementary Table S1). Specifically, death, LTC placement, and a CVD event were all more common among participants with more comorbidity (regardless of age), whereas the reverse was true for ESRD. However, the lower risk of ESRD associated with increasing comorbidity was further reduced at an older age: death and ESRD were equally likely for participants 18 to 59 years of age with 0 to 2 morbidities, but death was 81-fold (95% CI 43–150), 97-fold (95% CI 74–125), and 245-fold more likely (95% CI 175–343) than ESRD for participants 80 years of age and older with 0 to 2, 3 to 5, and ≥6 morbidities, respectively. The higher risks of LTC placement associated with age and increasing comorbidity were similarly incremental: LTC placement was 25 times less likely (95% CI 14–50) than ESRD for participants 18 to 59 years of age with 0 to 2 morbidities, but 18- (95% CI 11–30), 23- (95% CI 18–28), and 45-fold more likely (95% CI 34–59) than ESRD for participants 80 years of age and older with 0 to 2, 3 to 5, and ≥6 morbidities, respectively.

Participants with multiple outcomes during follow-up

Overall, 63.8% of participants remained free of CVD events, ESRD, and LTC placement during follow-up, of whom 51.1% (32.6% of the total) died during follow-up (Figure 4). The proportion of participants who experienced one of these outcomes followed by death (compared with those experiencing ≥1 of CVD events, ESRD, and LTC placement and surviving to the end of follow-up) was higher among those with more baseline comorbidity. Overall, death was the most common second outcome (70.2%), but other patterns also occurred: among patients surviving to the end of follow-up, 66.9%, 26.9%, 5.8%, and 0.4% experienced 0, 1, 2, and 3 of the 3 other outcomes. Only 79 participants (0.2%) experienced ESRD after LTC placement. Figure 4 shows only the 15 most frequent patterns.