A simple clinical tool to inform the decision-making process to refer elderly incident dialysis patients for kidney transplant evaluation

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Patients over the age of 70 constitute the fastest growing segment of the ESKD population worldwide, but most of them are not considered candidates for kidney transplantation (KT). We have developed a simple clinical screening score to identify incident elderly dialysis patients over 70 years with an acceptable long-term prognosis to identify those patients most suitable for KT evaluation. From the French national prospective registry, a logistic regression was used to develop a risk score of mortality within 3 years in a derivation cohort (years 2002–06) and validated in a separate cohort (years 2007–08). Of the 9305 patients in the derivation cohort, the points assigned for the score were: male (1pt); age (75–80); 2pts), (80–85; 5pts), 85 and over (9pts); diabetes (2pts); intermittent hemodialysis (2pt); peripheral vascular disease stage III–IV (5pts); congestive heart failure stages I–II (2pts), III–IV (4pts); dysrhythmia (2pts); chronic respiratory disease (2pts); active malignancy (5pts); severe behavioral disorder (6pts); cardiovascular disease (1pt); mobility (needs assistance for transfers (4pt), totally dependent (9pts)); BMI (21–25; 1pt), BMI (<21; 3pts); and temporary central vascular catheter (3pts). In the 7947 patient validation cohort, the probability of patients being alive within 3 years was around 70% for the lowest risk score quintile (0–6 pts) representing about 20% of incident patients. Thus, our tool identified a subgroup of patients to help nephrologists select individuals who, despite their age, could be suitable candidates for KT evaluation.

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Patients over the age of 70 years have higher incidence rates of end stage kidney disease (ESKD) than younger patients and constitute the fastest growing segment of the ESKD population worldwide.[1–5] This elderly population defined as older than 70 years usually presents complex comorbidity patterns with geriatric syndromes resulting in heterogeneity in life expectancy, functional status and health priorities.[6,7] The heterogeneity and the specificity of this elderly population have tended to favor an individualized patient-centered model of care over more traditional disease-based approaches.[8] An individualized approach for elderly patients with ESKD prioritizes patient preferences with shared decision-making for the different therapeutic options, defined as conservative care, especially if the prognosis for the first 6 months of dialysis is poor, and renal replacement therapy (RRT) such as dialysis or kidney transplantation (KT).[9–14]

Although the number of patients over 65 years awaiting KT continues to grow,[4,15,16] most patients over 70 years are not considered candidates for KT, as the process of placing an elderly patient on the waiting list remains a significant challenge.[16] In the United States only 3.4% of patients aged 70 years and older were reported to be listed for transplantation and in the French Registry only 1.5% of incident dialysis patients over 70 years were reported to be registered on the waiting list 5 years after dialysis.[2,4,17,18] However, several studies have shown that elderly patients have improved life expectancy[19,20] and quality of life after KT,[21] and that it is also cost effective.[22,23]

Most guidelines support transplantation for older patients with ESKD.[4,24–26] Old age is not usually a contraindication to transplantation but age-related comorbidity is a major limitation.[4,27] Although the guidelines also recommend that elderly patients with ESKD be screened more aggressively for cardiovascular disease and malignancy,[26] they do not give specific criteria to determine which patients may be suitable candidates. A kidney transplant is recommended in the European Guidelines if the patient's expected survival with

dialysis is more than 2 years,[25] and it is recommended in the Canadian Society of Transplantation guidelines if the patient has a reasonable probability of surviving beyond current waiting times for KT.[24] In this context and because of the survival advantage of KT after 2 years follow-up,[20,25,28] we considered patients with an expected survival time of at least 3 years with dialysis to be suitable candidates for KT evaluation.

The aim of this study was to develop a simple clinical screening score to identify, among elderly incident dialysis patients over 70 years, those with an acceptable long-term prognosis (i.e., a 3-year survival rate around 70%). This score could therefore be helpful for identifying which of these elderly patients might be referred for kidney transplant evaluation.

RESULTS

Patient characteristics

The numbers of patients included for analysis were 8,955 in the Derivation Cohort and 7,382 in the Validation Cohort. They are reported in the flow chart (Figure 1). Compared with the Derivation Cohort, the patients from the Validation Cohort were older and were mostly male (Table 1).

Risk factors for 3-year mortality

The 3-year mortality rate was 57% in the Derivation Cohort and 56% in the Validation Cohort. The crude analysis identified 14 factors significantly associated with increased 3-year mortality rate: male, age over 75 years, low body mass index (BMI), presence of diabetes, ischemic heart disease, peripheral vascular disease (PVD) stage III–IV, dysrhythmia, congestive heart failure (CHF) stage I–II and stage III–IV, cerebrovascular disease, chronic respiratory disease, active malignancy, severe behavioral disorder, total or partial dependence for transfers, and the use of a temporary central vascular catheter (CVC) (Supplementary Data S1 online).

Construction of the point scoring system

Based on the results of the multivariate analysis, we assigned points to each significant risk factor in the Derivation Cohort (Table 2) and a risk score was calculated for each patient by adding up these points in the second cohort. The distribution of the risk score quintiles was similar in the two cohorts (Table 3). The accuracy of the score in the Validation Cohort was acceptable with a mean *c*-statistic of 0.71 and a *p* for the Hosmer–Lemeshow goodness-of-fit test of 0.20. The calibration curve showed good concordance between observed and predicted mortality for each quintile score group (Supplementary Figure S1 online). The similarity of the mortality rates in the Derivation and Validation Cohort within each quintile score also reflected good score calibration (Table 3). In the Validation Cohort, the risk of mortality increased significantly with the quintile score, from 30% (0–6 points) to 83% (18 points and more; Table 3). The Kaplan–Meier survival curves depict a similar gradient: risk increases significantly with the quintile score in both the Derivation and the Validation Cohort (Figure 2).

Candidate population for KT evaluation

More precisely, in the quintile with the lowest risk (score $\leqslant 6$ points), the probability of being alive 3 years after initiating dialysis was 85% for 0–2 points, 75% for 3 points, 66% for 4 points, 65% for 5 points and 66% for 6 points (Table 4). The sensitivity/specificity of the score in predicting survival at 3 years after RRT initiation was 99%/6% for 0–2 points, 98%/11% for 3 points, 96%/17% for 4 points, 92%/24% for 5 points, and 89%/34% for 6 points.

This population (0–6 points) represented 1552 patients, i.e. 21% of the Validation Cohort. In this group, the characteristics of the patients aged <80 years ($n=1452$) are presented according to their score (Table 5). None of them had any of the most common contraindications for KT,

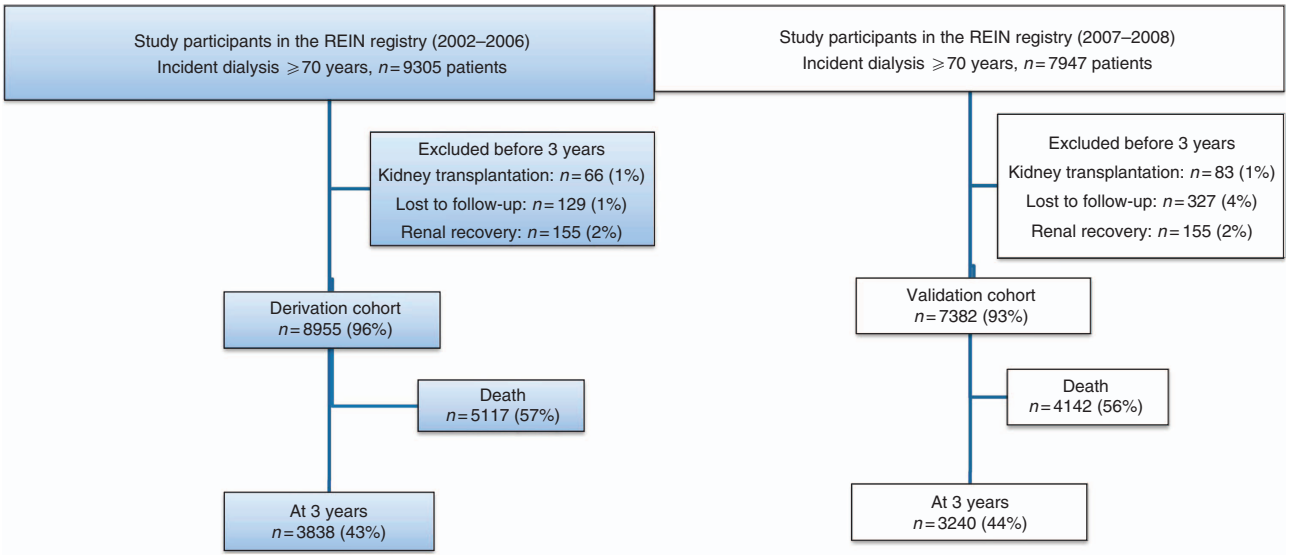

Figure 1 | Participant flow for the Derivation Cohort and the Validation Cohort.