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Original Investigation

A Clinical Risk Prediction Tool for 6-Month Mortality After Dialysis Initiation Among Older Adults

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Background: Information on an individual's risk for death following dialysis therapy initiation may inform the decision to initiate maintenance dialysis for older adults. We derived and validated a clinical risk prediction tool for all-cause mortality among older adults during the first 6 months of maintenance dialysis treatment.

Study Design: Prediction model using retrospective administrative and clinical data.

Setting & Participants: We linked administrative and clinical data to define a cohort of 2,199 older adults (age ≥ 65 years) in Alberta, Canada, who initiated maintenance dialysis therapy (excluding acute kidney injury) in May 2003 to March 2012.

Candidate Predictors: Demographics, laboratory data, comorbid conditions, and measures of health system use.

Outcomes: All-cause mortality within 6 months of dialysis therapy initiation.

Analytical Approach: Predicted mortality by logistic regression with 10-fold cross-validation.

Results: 375 (17.1%) older adults died within 6 months. We developed a 19-point risk score for 6-month mortality that included age 80 years or older (2 points), glomerular filtration rate of 10 to 14.9 mL/min/1.73 m^2 (1 point) or ≥15 mL/min/1.73 m^2 (3 points), atrial fibrillation (2 points), lymphoma (5 points), congestive heart failure (2 points), hospitalization in the prior 6 months (2 points), and metastatic cancer (3 points). Model discrimination (C statistic = 0.72) and calibration (Hosmer-Lemeshow $\chi^2 = 10.36$; $P = 0.2$) were reasonable. As examples, a score < 5 equated to <25% of individuals dying in 6 months, whereas a score > 12 predicted that more than half the individuals would die in the first 6 months.

Limitations: The tool has not been externally validated; thus, generalizability cannot be assessed.

Conclusions: We used readily available clinical information to derive and internally validate a 7-variable tool to predict early mortality among older adults after dialysis therapy initiation. Following successful external validation, the tool may be useful as a clinical decision tool to aid decision making for older adults with kidney failure.

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Editorial, p. 555

The majority of older adults with chronic kidney failure who want to receive renal replacement therapy are treated with maintenance hemodialysis.[1] In Canada, the proportion of incident dialysis patients who are 65 years or older has increased from 41.8% in 1994 to 53.5% in 2013.[1] Older adults undergoing dialysis are at an increased risk for poor outcomes, including death, with a mortality rate of up to 37.0 deaths/100 person-years within the first 6 months of dialysis therapy initiation.[2] Because older adults with kidney failure may also have multiple comorbid conditions and poor outcomes, decisions regarding dialysis therapy initiation are often complicated. Clinical risk prediction tools may help patients and providers in this decision-making process by comparing their risk for mortality to that of other similar patients.

Although a number of clinical risk prediction tools have been developed for early mortality in the dialysis population, few have focused specifically on older adults.[3-8] Previous studies suggest differences in outcomes and their predictors for older adults, including initiating dialysis therapy at higher estimated glomerular filtration rates (eGFRs), increased comorbid conditions, and greater risk for hospitalization.[9] Thus, there is a need for tools developed specifically for this population, providing information relevant to

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the older adult context. Of tools developed for the elderly population for 6-month mortality, one was developed in the French Renal Epidemiology and Information Network (REIN) database and one in the US Renal Data System (USRDS).[10,11] One study compared discrimination of tools developed for various purposes in various populations to attempt to predict 6-month mortality with an older adult dialysis population, finding often poor performance.[12] To date, no tools have been developed for early mortality in the Canadian older adult population.

Of the tools developed to date in older adults, the study populations commonly consist of those 75 years and older. However, there are equal numbers of adults aged 65 to 74 years who initiate maintenance dialysis therapy as those 75 years and older.[1] Therefore, a tool derived in those 65 years and older would add to the limited literature in the older adult population. We sought to derive and internally validate a clinical risk prediction tool based on clinical and comorbid predictors from laboratory and administrative data sources that could be used to predict all-cause mortality among older adults during their first 6 months of maintenance dialysis treatment.

METHODS

Study Cohort

We identified a cohort of all adults 65 years or older initiating maintenance hemodialysis or peritoneal dialysis therapy in Alberta, Canada, from May 1, 2003, through March 31, 2012, as recorded in the Northern and Southern Alberta Renal Program (NARP/SARP) registries.[13] The registries include all individuals initiating maintenance dialysis therapy in Alberta. Periods of dialysis lasting less than 90 days followed by recovery of kidney function were excluded, whereas patients were included if they died within 90 days and the intent of the treatment (established by case review of electronic medical records) was maintenance dialysis. The index date was the first date of a maintenance dialysis session recorded within the study period. Patients with maintenance dialysis or transplantation prior to May 1, 2003, were excluded. Outcome status and potential candidate variables for the prediction tool were established from the administrative and clinical data holdings of the Alberta Kidney Disease Network, which include demographic, laboratory, and comorbid information and records of health system use.[14] We obtained ethics approval from the University of Calgary Conjoint Health Research Ethics Board, which granted a waiver of patient consent.

Data and Predictors

Available data included hospital files, physician claims, and ambulatory care records, as well as population health registry files, date of death data from Alberta Vital Statistics, provincial laboratory data, and aggregated data from the Canadian census. Demographic information included the participant's age, sex, First Nations status, median neighborhood income quintile, and rural/urban residence. We used the most recent outpatient serum creatinine measurement prior to the index date to estimate GFR using the CKD-EPI (Chronic Kidney Disease Epidemiology Collaboration) creatinine equation.[15] Age and eGFR were categorized a priori as in prior studies for simplicity in clinical use, and allowing for assignment of integer points. We defined health care resource use as emergency department use (without subsequent hospitalization) in the 6 months prior to the index date, hospitalization in the 6 months prior to the index date, and late referral to a nephrologist (within 90 days prior to dialysis therapy initiation). We used hospitalization and physician claims data to define 28 chronic conditions using validated algorithms (Table S1, available as online supplementary material).[16] Only comorbid conditions present prior to the index date were included.

Study Outcome

The study outcome was all-cause mortality within 6 months of dialysis therapy initiation. Patients were censored if they outmigrated from Alberta or received a kidney transplant prior to the date of death.

Model Development

We used the full cohort for model derivation and for internal validation, using the 10-fold cross-validation sample use-reuse method.[17] We used logistic regression to determine potential predictors of the outcome. The order of predictor variables entering the prediction model was done via forward selection based on a strategy using the Akaike information criterion (AIC), which balances goodness of fit with parsimony of predictors.[18] Potential predictors were added sequentially to the model to minimize the AIC. To enter the model, a potential predictor had to have a Wald test $P \leq 0.1$, but was subsequently omitted if the P value increased beyond $P = 0.025$. The model with the lowest AIC in which all predictors met these criteria was considered the final model.

For model validation, the full cohort was used. The cohort was divided randomly into tenths such that validation could be approximated using 10-fold cross-validation, a method producing results similar to bootstrapping and preferable to the commonly used split-sample method.[19] In this way, we estimated the performance of the model in the data, quantified the estimation of overfitting, and shrunk the regression coefficients to account for potential error in a new data set.[20]

We used the C statistic (also referred to as area under the curve) to assess model discrimination, a common method in studies such as this, useful for its ease of interpretability. Model calibration was assessed using a comparison of deciles of risk, the number and proportion of individuals assigned to each point score, and the Hosmer-Lemeshow statistic to determine how well the observed number of events for each risk level matched the number of events that would be expected for that level based on the model. The calibration curve was defined as a logistic function of predicted mortality across point scores.

Generation of a Point System

We created a point system based on the method described for the Framingham Score.[21] To assign point scores, a defined "constant risk equivalent" was chosen, equivalent to a 10-year increase in age, the relative amount of risk to which every other predictor and level was compared. The regression unit difference of each category was then divided by the constant risk equivalent to generate an integer value that was proportional to the level of risk and also proportional between predictors. This integer was rounded to the nearest whole number.

Summation of the points assigned to categories of each predictor within the model present or relevant to the patient allowed for calculation of a point score. All described analyses were completed using STATA, version 11.2 (StataCorp LP).[22]

RESULTS

Patient Characteristics

Our study cohort included 2,199 individuals 65 years or older for whom maintenance dialysis therapy