

Canadian Study of Prediction of Death, Dialysis and Interim Cardiovascular Events: CANPREDDICT: Biomarkers improve prediction of one year outcomes in Chronic Kidney Cohort

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BACKGROUND: Patients with chronic kidney disease (CKD) experience variable progression of kidney disease and heart disease. Better prediction models are needed.

OBJECTIVE: To determine if measurement of selected novel biomarkers improves prediction of renal replacement therapy (RRT), cardiovascular (CV) events, or death at one year.

METHODS: Design, Setting, and Patients: Pan-Canadian prospective cohort study of 2546 referred CKD patients. Patients from 25 rural, urban, academic and non-academic nephrology centres were enrolled in 2008-2009 with a planned follow up of 3 years. Entry criteria included estimated glomerular filtration rate (eGFR) 15-45 ml/min/1.73m². Clinical, demographic and laboratory data (including urine albumin-to-creatinine ratios [uACR]), were collected at 6 month intervals. Blood was tested at baseline for asymmetric dimethylarginine (ADMA), high sensitivity C-reactive Protein (CRP), Interleukin 6 (IL6), pro-brain natriuretic peptide (proBNP), troponin I, transforming growth factor beta-1 (TGβ1), cystatin C and 25-hydroxyvitamin D ('novel biomarkers').

Main Outcome Measures: Dialysis or transplantation (RRT), CV events or death, within one year. We used multivariate logistic analysis to evaluate the association traditional and novel biomarkers and outcomes at one year.

RESULTS: The mean age of the cohort is 68yrs; the median eGFR of the cohort was 28 ml/min/1.73m² (20% < 20ml/min, 38% 20-29ml/min and 41% 30-45ml/min); 62% were male; 68% had diabetes, ischemic heart disease or congestive heart failure on history at the time of enrolment. The relationship between uACR, GFR and biomarkers differed for each novel biomarker. Logistic regression models were created for the outcomes of RRT, death and CV events at one year. Improvement in the C statistic was demonstrable with the addition of novel biomarkers for the outcomes of CV events and death (0.72 to 0.76, p<.001, and 0.76 to 0.79, p=.005, respectively); net reclassification index using novel biomarkers in addition to conventional parameters were 8% and 3% for CV events and death respectively

CONCLUSION: Variability of biomarkers between individuals at similar levels of eGFR and uACR was seen, which when added to conventional demographic and laboratory tests improved the prediction of important 1-year outcomes. Stability of those biomarkers over time and their utility in prediction models requires further study.