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Newer Biomarkers Slightly Improve Prediction of Progression to Renal Replacement Therapy in CKD Patients – CanPREDDICT Study Outcomes

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BACKGROUND: Patients with chronic kidney disease (CKD) experience variable progression of kidney disease (KD). Better prediction models are needed. To assess if newer biomarkers (NBM), alone or as a panel, improve risk prediction of renal replacement therapy (RRT), over and above conventional clinical, demographic and laboratory predictors.

METHODS: Pan-Canadian prospective cohort study of 2544 referred CKD patients, from 25 centres. NBM tests at baseline included asymmetric dimethylarginine (ADMA), high sensitivity C-reactive protein (hsCRP), interleukin 6, pro-brain natriuretic peptide (NTproBNP), troponin I, transforming growth factor β1, cystatin C and fibroblast growth factor (FGF23). Outcome: dialysis or transplantation (RRT) within 3 years. We compared discrimination (C statistic) and classification (net reclassification index (NRI)) of proportional hazards models based on conventional vs. combination of conventional and NBM predictors.

RESULTS: Mean age of the cohort is 68yrs; median eGFR was 28ml/min/1.73m2 (20% <20ml/min, 38% 20-29ml/min and 41% 30-45ml/min); 62% were male. 14.4% patients initiated RRT during the 3-year follow-up. Models based on base, base+NBM and 'best' predictors are presented in the following figure:

Variables	Base Model	Base + NBM	'Best' Model
Age (per 5 yrs.)	0.97 (0.93-1.01)	0.91 (0.87-0.95)	0.91 (0.87-0.95)
Male Sex	1.88 (1.46-2.40)	1.77 (1.38-2.27)	1.68 (1.31-2.15)
eGFR (per 1 mL/min/1.73m^2)	0.89 (0.87-0.91)	0.92 (0.90-0.94)	0.92 (0.90-0.94)
Hemoglobin (per 5 g/L)	0.94 (0.91-0.98)	0.97 (0.93-1.01)	
Phosphate (per 0.1 mmol/L)	1.06 (1.02-1.11)	1.05 (1.01-1.09)	
Albumin (per 1 g/L)	0.96 (0.94-0.98)	0.97 (0.95-0.99)	0.97 (0.94-0.99)
Bicarbonate (per 1g/L)	1.06 (1.03-1.10)	1.06 (1.02-1.09)	1.05 (1.02-1.09)
log ACR (per 1SD)	2.07 (1.78-2.41)	1.87 (1.61-2.17)	1.87 (1.61-2.17)
Cystatin C (per 1SD)		1.33 (1.15-1.53)	1.33 (1.15-1.54)
log NT-ProBNP (per 1SD)		1.36 (1.20-1.55)	1.36 (1.20-1.55)
log TGF-β1 (per 1SD)		0.87 (0.78-0.97)	0.86 (0.77-0.96)
log FGF-23 (per 1SD)			1.12 (1.02-1.24)
C statistic	85.6 (83.9-87.3)	86.3 (85.2-87.9)	86.4 (85.1 - 88.0)
NRI Categorical, %		6.6 (-1.6 - 10.9)	2.9 (-6.9 - 10.6)

CONCLUSIONS: This is the first analysis of CKD cohort progression that includes NBM as a panel. Although NBMs are independent predictors of RRT progression, addition of the panel of NBMs to models based on conventional clinical, demographic and laboratory predictors results in only modest improvement of RRT risk prediction.