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Newer biomarkers improve prediction of death in CKD patients - CanPreddict study outcomes

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BACKGROUND: Chronic kidney disease (CKD) patients have variable risk of death. General population risk prediction tools perform poorly in this patient group. Better prediction models are needed.

OBJECTIVE: To assess if the inclusion of newer biomarkers (NBM) improves risk prediction of death in the CKD cohort, 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: all-cause mortality 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; 62% were male. 15.5% patients died during 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.)	1.31 (1.23 - 1.38)	1.25 (1.18 - 1.33)	1.30 (1.22 - 1.38)
Male Sex	1.22 (0.97 - 1.53)	1.29 (1.03 - 1.61)	
eGFR (per 1 mL/min/1.73m^2)	0.97 (0.95 - 0.98)	0.98 (0.96 - 0.99)	0.98 (0.97 - 0.99)
History of CVD			
Ischemic HD	1.85 (1.37 - 2.48)	1.37 (1.01 - 1.86)	1.46 (1.09 - 1.98)
Congestive HF	2.18 (1.57 - 3.02)	1.40 (0.99 - 1.97)	1.48 (1.06 - 2.08)
Both IHD & CHF	2.76 (2.11 - 3.63)	1.60 (1.20 - 2.15)	1.67 (1.25 - 2.24)
Diabetes	1.30 (1.05 - 1.62)	1.27 (1.02 - 1.58)	1.32 (1.06 - 1.65)
Hemoglobin (per 5 g/L)	0.94 (0.90 - 0.97)	0.96 (0.92 - 0.99)	
Albumin (per 1 g/L)	0.93 (0.91 - 0.95)	0.95 (0.92 - 0.97)	0.95 (0.93 - 0.98)
Bicarbonate (per 1g/L)	1.04 (1.01 - 1.07)	1.02 (0.99 - 1.06)	
log PTH (per 1SD)	1.19 (1.06 - 1.34)	1.09 (0.97 - 1.21)	
ADMA (per 1SD)		1.20 (1.11 - 1.29)	1.21 (1.12 - 1.31)
log NT-ProBNP (per 1SD)		1.64 (1.44 - 1.88)	1.59 (1.39 - 1.81)
log hsCRP (per 1SD)		1.24 (1.11 - 1.39)	1.25 (1.12 - 1.40)
log FGF-23 (per 1SD)		1.23 (1.11 - 1.37)	1.25 (1.12 - 1.39)
C statistic	79.1 (77.7 - 80.8)	82.4 (81.0 - 84.5)	82.1 (80.4 - 84.3)
NRI, Categorical, %		13.8 (8.2 - 26.5)	13.7 (8.8 - 23.1)

After adjusting for base predictors, NTproBNP yields the highest improvement in mortality prediction (NRI=8.9;95%CI:3.3-17.4), followed by hsCRP (NRI=4.5;95%CI:1.3-9.6) and FGF23 (NRI=3.1;95%CI:0.4-11.4).

CONCLUSIONS: Inclusion of NBMs in risk prediction models significantly improves precision of death prediction in the cohort of CKD patients but needs to be validated in similar cohorts.