

Selected Biomarkers have Differential Prognostic Value in Specific Primary Kidney Diseases

Adeera Levin, MD^{*1}, Ognjenka Djurdjev², Claudio Rigatto, MD³, Francois Madore, MD⁴, Brendan J. Barrett, MD⁵ and Norman Muirhead, MD⁶

¹University of British Columbia, Vancouver, BC, Canada, ²BC Provincial Renal Agency, Vancouver, BC, Canada, ³University of Manitoba, Winnipeg, MB, Canada, ⁴University of Montreal, Montreal, QC, Canada, ⁵Memorial University of Newfoundland, St. John's, NL, Canada, ⁶University of Western Ontario, Hamilton, ON, Canada

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

OBJECTIVE: To determine if inclusion of selected novel biomarkers (NBM) improves prediction of renal replacement therapy (RRT) at one year in specific primary KD.

METHODS: Pan-Canadian prospective cohort study of 2546 referred CKD patients, from 25 rural, urban, academic and non-academic nephrology centres. NBM tests at baseline included asymmetric dimethylarginine (ADMA), high sensitivity C-reactive protein (CRP), interleukin 6 (IL6), pro-brain natriuretic peptide (proBNP), troponin I, transforming growth factor beta-1 (TG β 1) and cystatin C.

Main Outcome: Dialysis or transplantation (RRT) within one year. We used proportional hazards modeling to evaluate impact of NBM to base models for specific KD.

RESULTS: Mean age of the cohort is 68yrs; median eGFR was 28 ml/min/1.73m² (20% < 20ml/min, 38% 20-29ml/min and 41% 30-45ml/min); 62% were male. Base models for each KD included age, sex, eGFR and uACR. Base models, extended (base + NBM) models and improvement in prediction with the extended models are presented in the following table.

| | Diabetic Nephropathy | Hypertensive Nephropathy | Glomerular Nephritis | Other |
|-----------------------|-----------------------------|---------------------------------|-----------------------------|------------------|
| | HR (95% CI) | HR (95% CI) | HR (95% CI) | HR (95% CI) |
| Age (5 years) | 0.91 (0.80-1.03) | 0.99 (0.86-1.14) | 0.99 (0.86-1.15) | 0.94 (0.77-1.15) |
| Sex (Male vs. Female) | 2.75 (1.39-5.43) | 2.06 (0.89-4.77) | 2.53 (0.85-7.52) | 0.78 (0.22-2.73) |
| GFR mL/min | 0.88 (0.83-0.93) | 0.85 (0.79-0.91) | 0.78 (0.70-0.88) | 0.88 (0.79-0.98) |
| Log uACR | 1.33 (1.10-1.62) | 1.34 (1.07-1.69) | 1.56 (1.07-2.29) | 1.48 (1.07- |

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|------------------------|--------------------|-------------------|--------------------|----------------------|
| | | | | 2.06) |
| Log ProBNP | 1.43 (1.14-1.78) | 1.37 (1.02-1.85) | n.s. | n.s. |
| Log IL6 | n.s. | 0.65 (0.45-0.94) | n.s. | n.s. |
| Log CRP | n.s. | n.s. | n.s. | 1.67 (1.03-1.70) |
| C Statistic Difference | 0.01 (-0.00-0.03) | 0.02 (0.01-0.05) | -0.00 (-0.00-0.02) | 0.02 (-0.00-0.08) |
| NRI | 0.4% (-8.4%-19.5%) | 3.0% (0.8%-33.2%) | | -4.0% (-12.1%-27.6%) |

CONCLUSIONS: Different NBM's are independently associated with RRT progression in specific KD's after adjustment for age, sex and kidney markers (eGFR and uACR). Addition of NBM's to base models results in differential and modest improvement of RRT risk prediction.