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Association of novel biomarkers with long-term outcomes in atherosclerotic renovascular disease.

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OBJECTIVES

- Novel biomarkers have been shown to be associated with important end-points in chronic kidney disease, but their value in atherosclerotic renovascular disease (ARVD) has not yet been investigated[1,2]. Our aims were:
  - To investigate whether the addition of novel biomarkers to a model based on traditional risk factors improves risk prediction.
  - To explore whether any novel biomarker can help identify patients who may benefit from revascularization.

METHODS

- Patients recruited to the Salford Renovascular Study who had the following biomarkers analyzed on a stored baseline sample were included in this study: fibroblast growth factor-23 (FGF-23), cystatin C, kidney injury molecule-1 (KIM-1), myeloperoxidase, neutrophil gelatinase-associated lipocalin (NGAL), N-terminal prohormone of brain natriuretic peptide (NT-proBNP), high-sensitivity troponin T and anti-apolipoprotein A1 IgG. The date of sampling was considered as time zero.
- Multivariable analyses, receiver-operating characteristics (ROC) curves and net reclassification index (NRI) were used to evaluate the incremental predictive value of these biomarkers in predicting the following adverse outcomes: death, progression to end-stage kidney disease (ESKD) (start of renal replacement therapy or reaching eGFR <10ml/min/1.73m^2), cardiovascular events (CVE) and a composite outcome of all these events. Kaplan-Meier curves were used to analyze the effect of revascularization on patients with different levels of the 'best biomarker'.

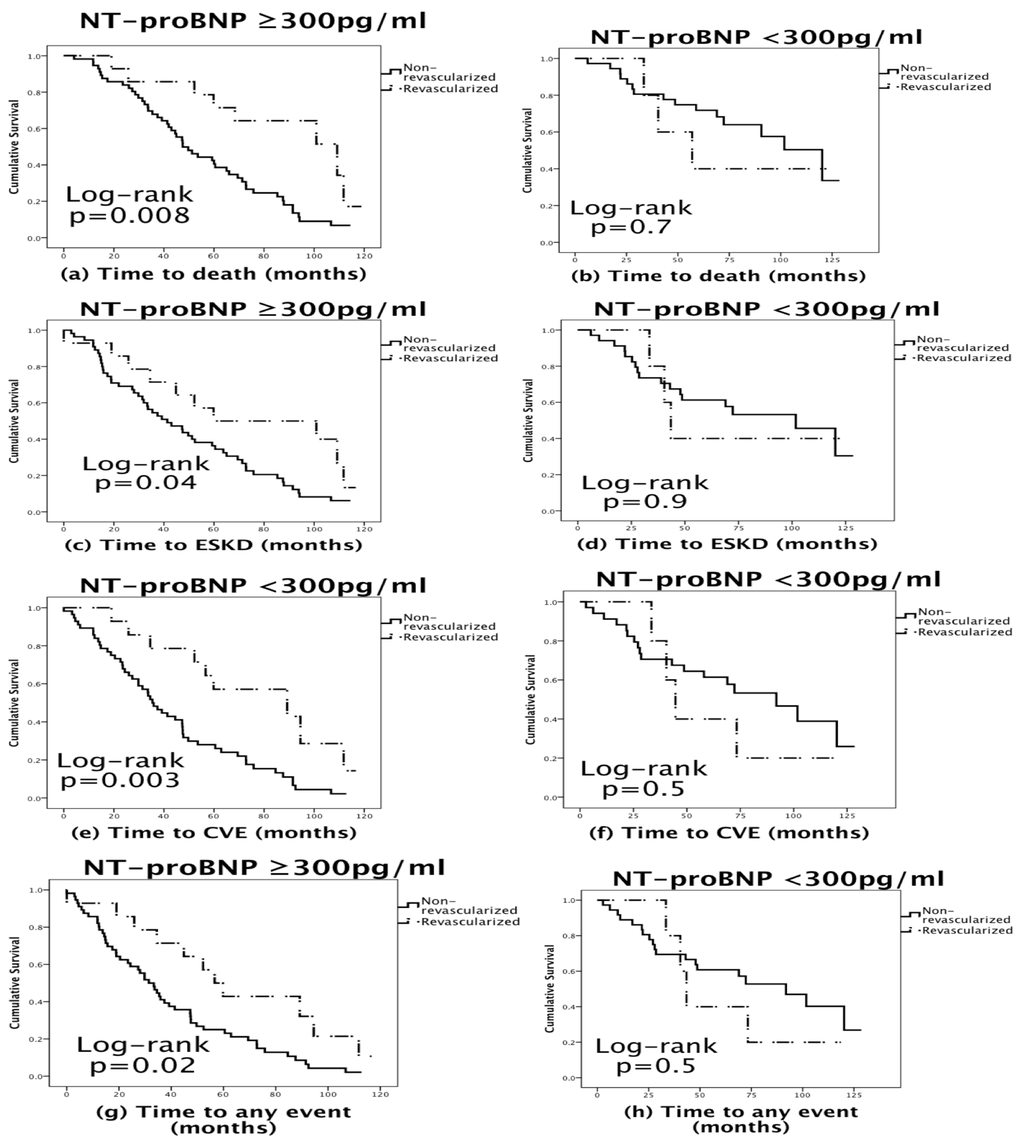
RESULTS

- n=112, median follow-up = 59.9 months (IQR 33.6-86.9)
- On multivariable analyses adjusted for a base model consisting of traditional risk factors (age, MVD, CHF, FPE, baseline proteinuria, eGFR, PTH, serum calcium, serum phosphate), **NT-proBNP** was the only biomarker independently associated with all end-points:
  - Death: HR 1.62 (95% CI 1.26-2.10), p<0.0005
  - ESKD: HR 1.51 (95% CI 1.19-1.91), p=0.001
  - CVE: HR 1.56 (95% CI 1.23-1.97), p<0.0005
  - Any: HR 1.48 (1.19-1.84, p<0.0005

Risk Prediction for base model, the base model in combination with all biomarkers, and base model with NT-proBNP:

		Base model only	Base model + all biomarkers[b]	Base model + NT-proBNP only[b]
Death	AUC	0.90 (0.84-0.96)	0.95 (0.92-0.99)	0.91 (0.85-0.96)
	NRI continuous	-	**1.06 (0.72-1.40)**	**0.42 (0.03-0.81)**
ESKD[a]	AUC	0.87 (0.80-0.94)	0.94 (0.91-0.98)	0.88 (0.81-0.94)
	NRI continuous	-	**0.99 (0.62-1.37)**	0.21 (-0.21-0.62)
CVE[a]	AUC	0.87 (0.79-0.94)	0.93 (0.88-0.98)	0.87 (0.80-0.94)
	NRI continuous	-	**0.96 (0.58-1.34)**	0.21 (-0.22-0.63)
Any	AUC	0.84 (0.77-0.92)	0.91 (0.86-0.97)	0.84 (0.77-0.92)
	NRI continuous	-	**0.64 (0.20-1.07)**	0.18 (-0.27-0.63)

Kaplan-Meier curves showing the effect of revascularization on all four clinical end-points in patients with serum NT-proBNP levels above and below standard cut-off of 300pg/ml:



CONCLUSIONS

- Although these results require validation in larger studies, our results suggest that novel biomarkers may have a strong incremental value in risk prediction when used as a panel in combination with traditional risk factors
- Patients with higher NT-proBNP values appear to benefit from revascularization.

References:
1. Tangri N, Stevens L, Griffith J, et al. A predictive model for progression of chronic kidney disease to kidney failure. *JAMA*. 2011;305(15):1553-1559.
2. Levin A, Rigatto C, Barrett B, et al. Biomarkers of inflammation, fibrosis, cardiac stretch and injury predict death but not renal replacement therapy at 1 year in a Canadian chronic kidney disease cohort. *Nephrol Dial Transplant*. 2014;29(5):1037-47.

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