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Proteomic marker and IL-6 predicts 5 year mortality and major cardiovascular events in hemodialysis patients

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Objectives : Frailty is common in hemodialysis paitents. We reported low skeletal muscle fraction is an independent risk factor of intradialytic hypotension. Biomarker study of long-term mortality among frail populations is essential for patient risk classification and as a prognosticator marker.
Methods : Total 146 adult patients undergoing maintenance hemodialysis were analyzed in this study. Blood collection, clinical/laboratory data, and bioimpedance measurements were conducted simultaneously. As an ad-hoc study of previous observational cohort, mortality and major cardiovascular events (MACE) were collected retrospectively. Proteomes were measured in unsupervised way by liquid chromatography-tandem mass spectrometry, and selected by least absolute shrinkage and selection operator method. Literature based four biomarkers (IL-6, P3NP, TNF-alpha, myostatin) were additionally measured.
Results : Average follow-up period was 4.8 ± 2.4 years. Mortality occurred in 35 cases (24%). MACE occurred in 37 patients (25%). In multivariable analysis, several clinical risk factors were statistically significant (reported as variable name; hazard ratio (95% confidence interval): age (1 yr); 1.082 (1.040–1.123), female sex; 0.234 (0.083–0.659), height adjusted muscle mass (1 kg/m^2); 0.324 (0.192-0.548), stroke history; 0.122 (0.025 – 0.592), nt-proBNP (1000 ng/mL); 1.047 (1.008-1.087), intact PTH (100 pg/mL); 1.215 (1.017-1.451). In the multivariable competing risk model, IL-6 was shown subdistribution hazard ratio to MACE as 6.425 (1.508 – 27.382). C-statistics of clinical prediction model to patient mortality was modest as 0.758 (0.671 – 0.845) (Table 1). When selected three peripheral blood biomarker were added to clinical variables to predict patient mortality, c-statistics was 0.781 (0.697 – 0.865) and net reclassification index was increased by 0.880 (0.127 – 1.257)
Conclusions : In among prevalent hemodialysis patients, age, male sex, low muscle mass, high nt-proBNP, and high PTH are significant risk factors. In addition to clinical parameters, IL-6 was significant risk factor for MACE in competing risk model. Three biomarker panel added net reclassification index when added to clinical prediction model.

Table 1.jpg

Table 1. Predictability of peripheral blood proteomic markers panel to patient mortality

Models	C-statistics (95% CI)	Delta C-statistics (95% CI)	P-value	NRI (95% CI)	P-value
Clinical model	0.758 (0.671 – 0.845)	NA		NA	
Proteomics 3 panel model	0.713 (0.621 – 0.806)	-0.045 (-0.143 – 0.054)	0.377	-0.171 (-1.142 – 0.791)	0.785
Clinical + 3 panel model	0.781 (0.697 – 0.865)	0.023 (-0.022 – 0.069)	0.229	0.880 (0.127 – 1.257)	0.010