Biomarkers

Cardiac biomarkers for cardiovascular risk prediction among women and men from the general population

Zhu F.; Arshi B.; Aribas E.; Ikram MA.; Ikram MK.; Kavousi M.

Erasmus University Medical Centre, Rotterdam, Netherlands (The)

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Purpose: To evaluate the sex-specific predictive value of two cardiac biomarkers; N-terminal pro B-type natriuretic peptide (NT-proBNP) and high sensitivity cardiac troponin T (hs-cTnT), alongside traditional cardiovascular risk factors, for 10-year cardiovascular risk prediction in general population.

Methods: A total of 5430 participants (mean age 68.1 years; 59.9% women) free of cardiovascular disease (CVD), with blood sample measurements between 1997 and 2001 were included. We developed a 'base' model using cardiovascular risk factors used in the Pooled Cohort Equation (includes age, sex, systolic blood pressure, treatment of hypertension, total and high-density lipoprotein cholesterol levels, smoking, and diabetes) and then extended the 'base' model with NT-proBNP or hs-cTnT. These models were developed for coronary heart disease (CHD), stroke, and heart failure (HF) and also for composite CVD outcomes. To evaluate biomarkers' added predictive value, c-statistic, and net reclassification improvement index (NRI) for events and non-events were calculated. NRI was calculated using cutoffs of 5%, 7.5% and 20% to categorize participants as low, borderline, intermediate, or high risk.

Results: Adding NT-proBNP to the 'base' model significantly improved c-statistic for all outcomes (increases ranged between 0.012-0.047), with the largest improvement in HF [0.026 (95% CI, 0.013, 0.040) for women and 0.047 (95% CI, 0.026, 0.069) for men]. Adding hs-TnT to 'base' model increased the c-statistic for CHD in women by 0.040 (95% CI, 0.013, 0.067) and for HF in men by 0.032 (95% CI, 0.005, 0.059). Improvments in reclassification by both biomarkers were mostly limited to modest improvemetns in reclassification of non-events [largest non-event NRI for global CVD in women (NT-proBNP: 11.8%; hs-cTnT: 10.5%) and for HF in men (NT-proBNP: 9.6%; hs-cTnT: 8.4%)].

Conclusion: NT-proBNP improved model performance for prediction of all cardiovascular outcomes, in particular for HF, beyond traditional risk factors for both women and men. Hs-cTnT showed modest added predictive value beyond traditional risk factors for CHD among women and for HF among men. Imropovements in reclassification by both biomarkers were modest and not clinically relevant.

Improvements of 10-year risk predictions

Events	Adding NT-proBNP			Adding troponin T		
	Delta c-statistic*	Event NRI, %	Non-event NRI, %	Delta c-statistic*	Event NRI, %	Non-event NRI, %
Women ASCVD Global CVD	0.012 (0.004, 0.020) 0.018 (0.010, 0.026)	-1.7 (-5.0, 1.5) -0.8 (-3.8, 2.2)	5.4 (3.5, 7.2) 11.8 (9.6, 14.1)	0.028 (0.009, 0.048) 0.025 (0.009, 0.040)	-0.4 (-7.1, 6.2) 2.9 (-2.4, 8.3)	6.9 (3.9, 9.9) 10.5 (7.3, 13.8)
Men ASCVD Global CVD	0.016 (0.005, 0.027) 0.023 (0.012, 0.033)	0.7 (-2.3, 3.7) -0.3 (-3.0, 2.4)	5.2 (3.2, 7.2) 7.2 (4.9, 9.4)	0.007 (-0.002, 0.016) 0.011 (0.000, 0.021)	-1.1 (-5.0, 2.7) -1.6 (-6.0, 2.8)	4.0 (1.2, 6.9) 6.4 (3.1, 9.7)

ASCVD comprises coronary heart disease and stroke; Global CVD comprises coronary heart disease, stroke and heart failure.