Associations of SCORE2, circulating cardiovascular biomarkers and carotid intima-media-thickness in a population-based cohort

B. Toprak¹, J. Lehmacher¹, Y. Hu², C. Waldeyer¹, G. Thomalla³, D.L. Rimele³, A. Ziegler², T. Zeller¹, S. Blankenberg¹, J.T. Neumann¹, R. Twenerbold¹

¹University Heart & Vascular Center Hamburg, University Medical Center Hamburg-Eppendorf, Department of Cardiology, Hamburg, Germany; ²Cardio-CARE, Medizincampus Davos, Davos, Switzerland; ³The University Medical Center Hamburg-Eppendorf, Department of Neurology, Hamburg, Germany

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Background: The updated SCORE2 model to estimate the 10-year risk of fatal and non-fatal cardiovascular disease (CVD) was recently introduced, which is based solely on traditional cardiovascular risk factors.

Purpose: We aimed to investigate the associations of SCORE2-predicted risk with four circulating cardiovascular biomarkers (high-sensitivity troponin I [hs-cTnI], N-terminal pro B-type natriuretic peptide [NT-proBNP], cystatin C-derived estimated glomerular filtration rate [eGFR] and high-sensitivity C-reactive protein [hs-CRP]) as well as mean carotid intima-media-thickness (cIMT) in a prospective, population-based German cohort.

Methods: In the first set of 10,000 participants, who were aged 45–74 years and recruited between 2016 and 2019, the SCORE2 model was applied in a cross-sectional manner. Individuals with prevalent CVD were excluded for this purpose. Eligible individuals were then categorized into five risk groups (<2.5%, 2–<5%, 5–<10%, 10–<15%, and ≥15%) according to SCORE2. To test for the associations of circulating biomarkers and cIMT with SCORE2, we created box plots and computed Pearson’s correlation coefficients (R). Considering cIMT as a biological surrogate for incident CVD, we explored the incremental utility of circulating biomarkers to predict cIMT beyond SCORE2 by multivariable logistic regression analysis with stepwise selection of variables, quantified by Beta-coefficients per one standard deviation (SD) increase with respective 95% confidence intervals (CI). Discrimination (C-index) and category-free net reclassification improvement (NRI) for predicting mean cIMT >1mm were calculated for this extended model in comparison to SCORE2 alone as the reference.

Results: In 8,518 individuals free of CVD, median estimated 10-year risk of CVD based on SCORE2 was 6.1 (interquartile range [IQR] 3.2, 9.9)%.

All four investigated biomarkers (hs-cTnI, R=0.41; NT-proBNP, R=0.21; hs-CRP, R=0.22; eGFR, R=−0.44; all P<0.001), and mean cIMT (R=0.42, P<0.001) correlated strongly with the continuous SCORE2 risk and the respective SCORE2 risk categories (Figure 1). In multivariable regression analysis, all four circulating biomarkers remained significant independent predictors of mean cIMT when added to SCORE2 (Figure 2). When compared to SCORE2 as the reference model (C-index 0.763, 95% CI 0.742–0.784) to predict mean cIMT >1mm, the joint addition of all four stepwise-selected investigated biomarkers led to a small but significant improvement of discrimination (C-index 0.770, 95% CI 0.749–0.791, P<0.001) and reclassification yield (NRI 0.154, 95% CI 0.059–0.250, P=0.002).

Conclusions: All four investigated circulating biomarkers depicting different pathophysiological pathways and mean cIMT correlate strongly with the cardiovascular risk estimated by SCORE2. Circulating biomarkers may further improve CVD-risk prediction when added to the traditional cardiovascular risk factors currently considered by SCORE2.