

MULTIMODAL INSTRUMENTAL PHENOTYPING FOR INDIVIDUAL CARDIOVASCULAR RISK PREDICTION IN METABOLIC SYNDROME AND ATHEROSCLEROSIS

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Background. The coexistence of metabolic syndrome and atherosclerosis promotes parallel remodeling of the myocardium and arterial tree through insulin resistance, low-grade inflammation, endothelial dysfunction, increased arterial load, and neurohormonal activation. Conventional scores are essential for prevention, but they may not capture early target-organ damage or the heterogeneous phenotype of Central Asian populations. Multimodal assessment is therefore relevant when estimated clinical risk and the actual burden of vascular or myocardial injury do not coincide.

Objective. To define a clinically feasible multimodal instrumental panel and a methodological framework for individualized cardiovascular risk prediction in adults with combined metabolic syndrome and atherosclerosis in Uzbekistan.

Methods. Guidelines, consensus statements, meta-analyses, and cohort studies published from 2016 to 2026 were narratively synthesized. Candidate domains included 24-hour ambulatory blood pressure monitoring, carotid ultrasonography, carotid-femoral pulse wave velocity, ankle-brachial index, conventional and speckle-tracking echocardiography, and coronary artery calcium scoring. Sample size, event count, discrimination, hazard ratios, confidence intervals, accessibility, and reproducibility were considered.

Results. SCORE2 was derived in 677,684 participants with 30,121 cardiovascular events and externally validated in 1,133,181 individuals with 43,492 events; C-indices across validation cohorts ranged from 0.67 to 0.81. This variability demonstrates why local recalibration is necessary. Vascular markers provide complementary information: a carotid-femoral pulse wave velocity around or above 10 m/s indicates advanced arterial stiffening, whereas carotid plaque directly documents structural atherosclerosis. In a secondary SPRINT analysis, patients whose estimated pulse wave velocity decreased over 12 months had a 42% lower risk of all-cause death in the standard-treatment group (HR 0.58, 95% CI 0.36-0.94; $p=0.03$). In a contemporary cohort of 206 patients with type 2 diabetes, 19.6% had an absolute global longitudinal strain below 18%, illustrating that subtle systolic dysfunction may be present despite preserved ejection fraction.

A pragmatic Uzbek risk model should combine routinely available clinical variables with a parsimonious instrumental signature. A candidate set may include carotid plaque burden, pulse wave velocity, nocturnal systolic pressure, left ventricular mass index, and global longitudinal strain. Predictor selection should be prespecified and limited according to the number of outcome events. Penalized regression and bootstrap validation can reduce optimism. Model performance should be reported using discrimination, calibration slope and intercept, and clinical net benefit. External validation across geographically distinct regions is necessary before clinical implementation, because direct transfer of foreign risk equations may produce systematic miscalibration.

A practical Uzbek model should combine routinely available clinical predictors with a parsimonious instrumental signature. Candidate variables include carotid plaque burden, pulse wave velocity, nocturnal systolic pressure, left ventricular mass index, and global longitudinal strain. Penalized regression and bootstrap validation should be used to limit overfitting. Performance should be reported not only by AUC or C-index, but also by calibration slope, calibration intercept, and decision-curve net benefit. External validation in geographically distinct regions is required before clinical use.

Conclusion. Multimodal phenotyping can identify vascular and myocardial injury before overt cardiovascular events and can refine risk stratification beyond conventional factors. A staged pathway beginning with carotid ultrasound, echocardiography, ankle-brachial index, and ambulatory blood

pressure monitoring, followed by pulse wave velocity, strain imaging, or coronary calcium in selected patients, is both clinically coherent and resource-conscious. Prospective multicenter validation is required to convert this framework into a reliable prediction tool for the Uzbek population.