Development of a Novel Atherosclerotic Heart Disease Biomarker Program

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Background: Atherosclerotic cardiovascular disease (ASCVD) is the leading cause of heart attack, stroke, and sudden death worldwide. Clinical risk scores help estimate the likelihood of adverse cardiac events to guide preventative strategies. Current risk scores for atherosclerotic events like heart attack and stroke use known cardiovascular risk factors including smoking, diabetes, lipid levels, and blood pressure. However, these scores underestimate risk in certain patient populations and do not predict the atherosclerotic disease in individual patients that leads to subsequent events. Our aim is to design a novel biomarker-enabled model to predict the presence and burden of coronary artery atherosclerosis in patients with diabetes, to ultimately help personalize preventive therapies that target disease burden, not just risk factors, for more effective prevention of ASCVD events.

Methods: Patients with diabetes have been prospectively enrolled in a health plans-based screening program with co-enrollment in the Indiana Biobank, which includes coronary CT angiography, an AI-based quantitation of atherosclerosis, and biobanking of DNA, plasma, and serum. We identified candidate biomarkers based on current literature and determined which could be impactful based on cost, efficacy, and feasibility of implementation guided by interviews with potential collaborating entities.

Results: We have identified polygenic risk scores, non-coding RNAs and candidate blood biomarkers with predictive potential for atherosclerotic heart disease. Subsequent work will entail i) direct assays of banked biospecimens for the selected minimally invasive biomarkers and ii) computational analysis to assess incremental predictive value for disease burden over clinically available risk scores.

Conclusions and Potential Impact: We are progressing towards the development of a novel mode to predict patient-specific burden of coronary atherosclerotic disease burden in patients with diabetes. We expect that a multidimensional approach including contemporary biomarkers will improve predictive value of atherosclerotic heart disease burden, affording more tailored treatment to prevent ASCVD events.

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