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Next-Generation Primary Atherosclerotic Cardiovascular Risk Prediction Tool. Are Nonmodifiable Risk Factors Relevant in the Equation?

Atherosclerotic cardiovascular disease (ASCVD) continues to be a major cause of morbidity and mortality especially in developed countries. Most of these ASCVD events occur in individuals without prior history of the disease. As documented by Dr Geoffrey Rose, a large number of individuals exposed to low risk will generate more cases than a small number of individuals exposed to high risk. Thus a focus on primary ASCVD prevention, which contributes mostly to our annual ASCVD events, has been emphasized in societal documents and guidelines. Current guidelines recommend behavioral and lifestyle changes and medications to minimize ASCVD risk.[1]

The targeting and treatment of traditional ASCVD risk factors including age, male gender, race/ethnicity, blood pressure, lipids levels, diabetes mellitus, and cigarette smoking forms the basis of primary ASCVD prevention and in recent times have been incorporated into risk prediction tools for assessing an individual's future risk of having a clinical ASCVD event.[2] Clinicians are advised to use these risk prediction tools to calculate the 10-year ASCVD risk, discuss this risk with their patients and then come up with a plan to minimize this risk. Current data show that these risk prediction tools have suboptimal discrimination for predicting future ASCVD events.[3] Hence other nontraditional risk factors have been suggested to help refine the calculated ASCVD risk using the risk prediction tools. Even though current data show that targeting some of the ASCVD risk factors results in a reduction in future ASCVD events. It is fair to say that till date the efficacy of an approach that employs these ASCVD risk prediction tools and other nontraditional risk factors to reduce primary ASCVD events has not been tested. In addition, the role and contribution of nonmodifiable ASCVD risk factors such as age, male gender, race/ethnicity, and their possible interactions with the known treatment effects of modifiable risk factors is less known.

In communicating ASCVD risk during the recommended clinician-patient discussion by current guidelines, clinicians often communicate the calculated 10-year risk to the patient without clearly articulating how much of the calculated risk is actually modifiable with interventions. This makes the clinician-patient discussion incomplete. Data from one of the well-

characterized, multiethnic primary ASCVD prevention studies, Multi Ethnic Study of Atherosclerosis, which enrolled about 6,714 participants, showed that after about 10 years of follow-up, 560 participants had an adjudicated ASCVD event. Figure 1 shows the discriminative ability of nonmodifiable ASCVD risk factors (age, race/ethnicity, and male gender), modifiable ASCVD risk factors (total cholesterol, low density lipoprotein, High density lipoprotein cholesterol, cigarette smoking status, diabetes mellitus, systolic and diastolic blood pressure and use of antihypertensive medication) and total ASCVD risk factors(all combined) for future ASCVD events in the Multi Ethnic Study of Atherosclerosis cohort. As shown, the area under the curve for nonmodifiable ASCVD risk factors is similar to that of the modifiable ASCVD risk factors (0.677 vs 0.685). Thus nonmodifiable ASCVD risk factors contributes equally if not more to the discriminative ability and therefore the 10-year calculated risk of the ASCVD risk calculator used in clinical practice. In addition, the issue of about 50% of the calculated ASCVD risk being nonmodifiable and the potential for overtreatment is often not brought up in the clinician-patient discussion. It's very possible that a patient will choose not to take statins or be treated with other medications if he or she knows that the modifiable portion of the 10-year risk of ASCVD is 5% instead of the 10% using the ASCVD risk calculator. The relevance of nonmodifiable ASCVD risk factors in ASCVD risk prediction tools is therefore questionable at best but it inflates the calculated 10-year risk, even though presently nothing can be done about that portion of the calculated risk.

It is acceptable for educational purposes to know that age, male gender, and race/ethnicity are traditional ASCVD risk factors but including them in risk prediction tools developed to calculate, communicate and possibly modify ASCVD risk, knowing very well that they cannot be modified is problematic. In other words older black males, for example, should know that their traits are associated with a higher risk for future ASCVD events than young white females but they (older black males) cannot be treated aggressively for that since this trait-associated risk is not modifiable. Next-generation ASCVD prediction tools should consist of modifiable traditional and nontraditional ASCVD risk factors. The discriminative abilities of these next-generation ASCVD risk prediction tools can be improved or refined using other biomarkers similar to what is available today. This will ensure that patients are accurately informed during the clinician-patient discussion about their modifiable ASCVD risk in order to make better decisions about their health.

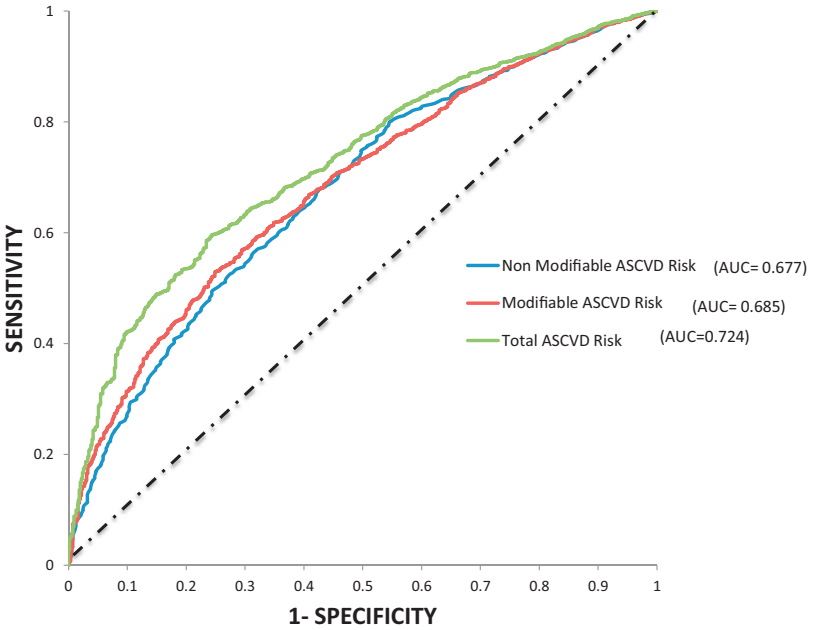

Figure 1. Area under the curve analysis showing the discriminative ability of nonmodifiable atherosclerotic cardiovascular disease (ASCVD) risk factors, modifiable ASCVD risk factors and total ASCVD risk factors for future ASCVD events in MESA. MESA = Multi Ethnic Study of Atherosclerosis.

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Updated Meta-Analysis of Trials Assessing the Cardiovascular Efficacy of Sodium-Glucose Co-Transporter-2 Inhibitors and Glucagon-Like Peptide-1 Receptor Agonists in Black Patients

Type 2 diabetes mellitus (T2DM) prevalence rates are increasing, whereas expectations are rather pessimistic.[1] Recent, large observational studies have demonstrated that black patients feature increased odds for suffering from T2DM,[2] whereas they experience an increased risk for the development of T2DM-related co-morbidities and all-cause mortality, compared with