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.

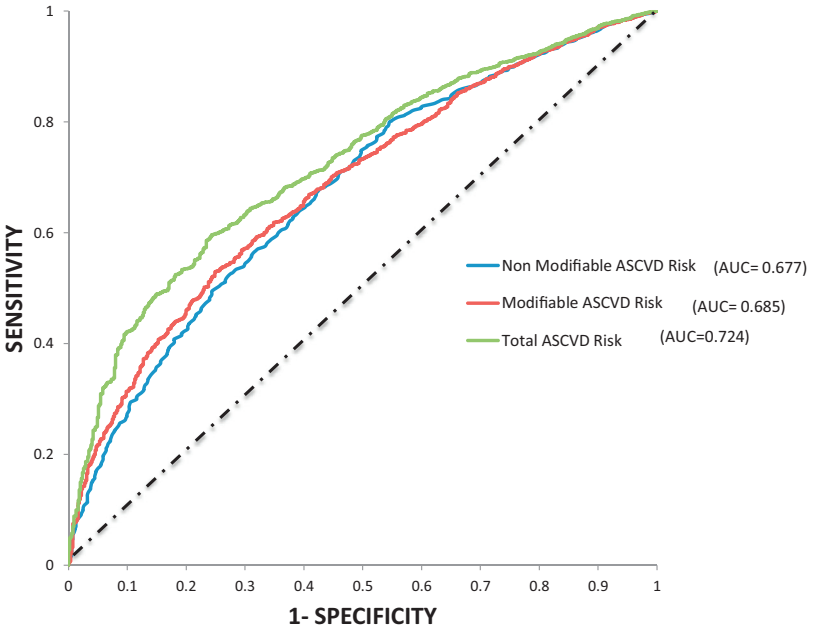

Figure 1. Area under the curve analysis showing the discriminative ability of nonmodifiable atherosclerotic cardiovascular disease (ASCVD) risk factors, modifiable ASCVD risk factors and total ASCVD risk factors for future ASCVD events in MESA. MESA = Multi Ethnic Study of Atherosclerosis.

Disclosures

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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

Caucasian patients.[3] Black patients experience a higher prevalence of other classic cardiovascular risk factors, which inevitably lead to significant disparities in the incidence of major adverse cardiovascular events (MACEs),[4] with T2DM representing a strong and independent risk factor both for cardiovascular morbidity and mortality.[5] Therefore, appropriate treatment strategies are urgently required.

Sodium-glucose co-transporter 2 (SGLT-2) inhibitors and glucagon-like peptide-1 receptor agonists (GLP-1RAs) are 2 relatively novel classes of antidiabetic drugs that have brought a significant landscape change in the therapeutic management of patients with T2DM and cardiovascular disease during the last years. We have welcomed the publication of the hallmark cardiovascular outcome trials (CVOTs) with SGLT-2 inhibitors, namely the Empagliflozin Cardiovascular Outcome Event Trial in Type 2 Diabetes Mellitus Patients−Removing Excess Glucose,[6] the Canagliflozin Cardiovascular Assessment Study,[7] the Dapagliflozin Effect on Cardiovascular Events −Thrombolysis in Myocardial Infarction 58 trial[8] and the recently published VERTIS CV, utilizing ertugliflozin,[9] and with GLP-1RAs, namely the Evaluation of Lixisenatide in Acute Coronary Syndrome trial,[10] the Exenatide Study of Cardiovascular Event Lowering,[11] the Liraglutide Effect and Action in Diabetes: Evaluation of Cardiovascular Outcome Results (trial,[12] the preapproval Trial to Evaluate Cardiovascular and Other Long-term Outcomes with Semaglutide in Subjects with type 2 Diabetes (SUSTAIN-6),[13] the Harmony Outcomes trial utilizing albiglutide,[14] the Researching Cardiovascular Events with a Weekly Incretin in Diabetes trial,[15] and the most recent Peptide Innovation for Early Diabetes Treatment 6 trial.[16]

We sought to determine the cardiovascular efficacy of SGLT-2 inhibitors and GLP-1RAs in black patients, extracting corresponding data from subgroup analyses of the aforementioned CVOTs.

Two independent reviewers (D.P. and C.P.) extracted the data from the eligible reports, by using a pilot tested, data extraction form. We assessed the surrogate composite end point of death from cardiovascular causes, nonfatal myocardial infarction, or nonfatal stroke, as defined across the selected trials. We did not assess safety outcomes.

As we assessed only dichotomous variables, differences were calculated with the use of risk ratio (RR), with 95% confidence interval (CI), after implementation of the Mantel-Haenszel (M-H) random effects formula. Statistical heterogeneity among studies was assessed by using I^2 statistics. Heterogeneity was considered to be low if I^2 was from 0% to 25%, moderate if I^2 was from 25% to 50%, or high if I^2 was greater than 75%.[17] All analyses were performed at the 0.05 significance level, whereas they were undertaken with RevMan 5.3 software.[18]

Two independent reviewers (D.P. and K.S.) assessed the quality of the included RCTs, by using the Revised Cochrane risk of bias tool for randomized trials (RoB 2.0) for the primary efficacy outcome.[19] Discrepancies between reviewers were solved by discussion, consensus or arbitration by a third senior reviewer (M.D.).

Concerning the CVOTs with SGLT-2 inhibitors, only trialists of the Dapagliflozin Effect on Cardiovascular Events−Thrombolysis in Myocardial Infarction 58 trial did not perform a subgroup analysis specifically for black patients, whereas, all CVOTs with GLP-1RAs provided corresponding subgroup analyses. Therefore, we pooled data from 3 CVOTs with SGLT-2 inhibitors in a total of 928 black patients and from 7 CVOTs with GLP-1RAs in a total of 3,091 black patients. Risk of bias is low across all selected CVOTs.

SGLT-2 inhibitor treatment resulted in a non-significant decrease in the risk for MACEs, equal to 3% (RR 0.97, 95% CI 0.61 to 1.53, $I^2 = 30\%$), as shown in Figure 1. Sim-

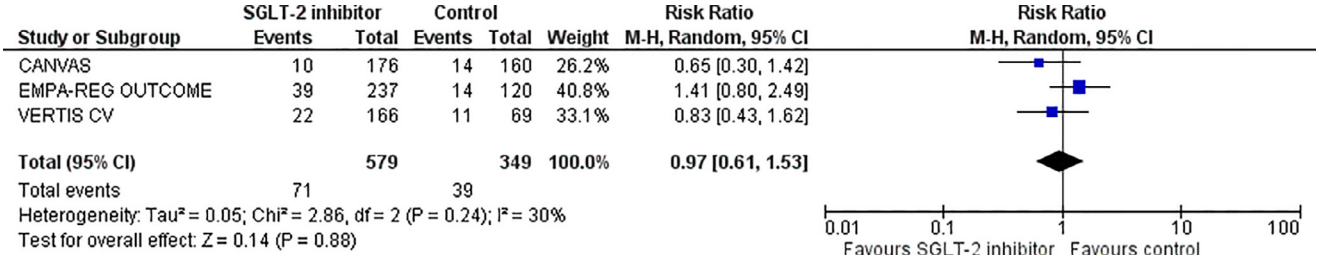

Figure 1. Effect of SGLT-2 inhibitors compared with placebo on the composite cardiovascular end point.

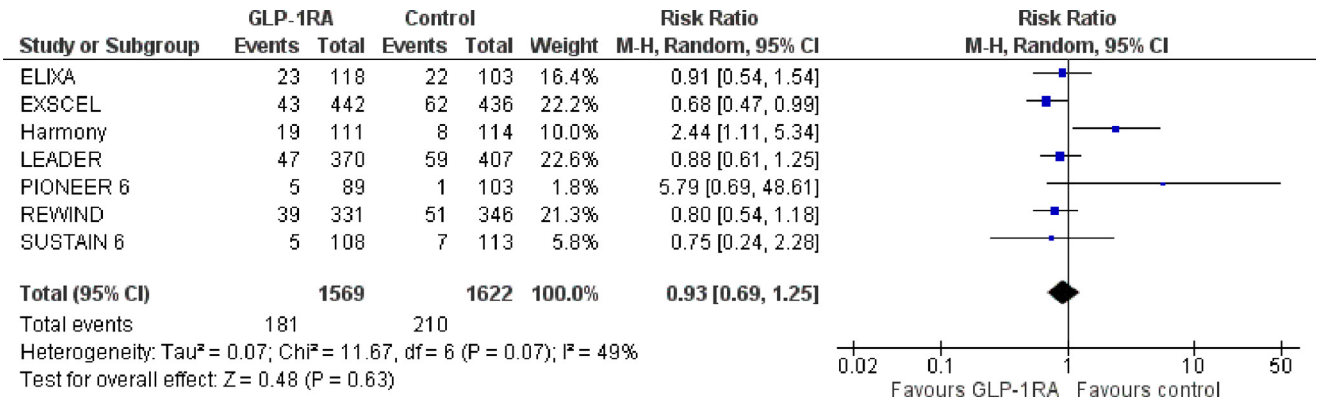

Figure 2. Effect of GLP-1RAs compared with placebo on the composite cardiovascular end point.

ilarly, GLP-1RA treatment produced a nonsignificant decrease in the risk for MACE, equal to 7% (RR 0.93, 95% CI 0.69 to 1.25, $I^2 = 49\%$), as shown in Figure 2.

Our meta-analysis updates the results of a previous meta-analysis performed by Mishriky et al,[20] incorporating data from the recently published CVOTs.

In conclusion, neither SGLT-2 inhibitors nor GLP-1RAs provide significant cardiovascular benefit in black patients, in terms of MACEs incidence. Future trials enrolling a larger proportion of black patients will clarify whether these observations are due to inadequate power of present CVOTs, or due to true racial disparities with the use of novel antidiabetics.

Disclosures

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Handgrip Strength and Risk of Atrial Fibrillation

Consistent evidence suggests inverse and independent associations between