Cardiovascular risk profiles and outcomes in patients with type 2 diabetes - Implications for choice of new diabetes therapies

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Topic(s):
Risk Factors and Prevention – Epidemiology

Citation:

Funding Acknowledgements:
Mariam Elmegaard Malik was funded by a research grant from Department of Cardiology, Herlev and Gentofte Hospital.

Background: Reflecting recent clinical trial findings, updated type 2 diabetes (T2D) guidelines recommend targeting SGLT2 inhibitors at patients at risk of heart failure (HF)-related events and GLP-1 receptor agonists at those at greater risk of atherosclerotic events. However, which cardiovascular disease phenotype in patients with T2D is more predictive of one or other type of these events is unclear.

Purpose: To estimate the risk of HF-related events and atherosclerotic events, according to background cardiovascular phenotype, in patients with T2D.

Methods: Patients with T2D and new-onset cardiovascular disease were identified using Danish health care registers (period 1995 to 2015). Patients were divided in four groups based on the primary type of cardiovascular disease: 1) HF, 2) ischemic heart disease (IHD), 3) ischemic stroke, and 4) peripheral artery disease (PAD). The absolute 5-year risks of the subsequent event, either a HF-related event or an atherosclerotic event (IHD, ischemic stroke and PAD), and the associated risk of death, were compared across the four groups. The Aalen-Johansen estimator was used to account for censoring, the competing risk of HF and atherosclerotic events, respectively, and death.

Results: We included 37,850 patients with T2D and new-onset cardiovascular disease. Median age was 70 years and 40% were female. Patients with HF were at higher risk of readmission for HF (18.1%; 95% confidence interval (CI): 17.2-19.0) than of an atherosclerotic event (14.2%; 13.4-15.0) (Figure). Patients with IHD were at higher risk of a new atherosclerotic event (23.5%; 22.8.-24.2) than of developing HF (9.3%; 8.9-9.8), although the risk of HF was still substantial. Conversely, patients with ischemic stroke were at low risk of HF (3.3%; 2.9-3.8) and higher risk of an atherosclerotic event (16.9%; 95% CI: 16.0-17.7). Patients with PAD had the lowest risk of HF (3.1%; 95% CI: 2.8-3.4) and the highest risk of an atherosclerotic event (35.0%; 95% CI: 33.4-36.7). Compared to a new atherosclerotic event, developing HF was associated with a higher 1-year risk of death (16.0%; 95% CI: 14.7-17.3 versus 33.0%; 95% CI: 31.8-34.2) amongst all patients.

Conclusions: In T2D, a patient’s history of cardiovascular disease was predictive of type of subsequent cardiovascular event. While history of ischemic stroke and PAD were associated with a high risk of future atherosclerotic events, and low risk of HF, patients with IHD were at substantial risk of both types of event.
Conversely, while history of HF was most predictive of future HF events, the risk of atherosclerotic events in patients with HF was also high. Our findings may help determine which type of therapy T2D patients with a particular cardiovascular disease history might benefit from – SGLT2 inhibitors, GLP-1 receptor agonists or potentially both.