Biochemical profiles and risk of cardiovascular events in patients with Type 2 Diabetes: implications for choice of novel antihyperglycemic therapy

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Background: Guidelines on type 2 diabetes (T2D) recommend targeting patients at greater risk of heart failure with sodium-glucose cotransporter-2 inhibitors (SGLT2-i) and patients at greater risk of cardiovascular ischemic events with glucagon-like peptide-1 receptor agonists (GLP1-RA) or SGLT2-i. It is currently unclear whether distinct biochemical profiles are more or less associated with the occurrence of heart failure or a cardiovascular ischemic event.

Purpose: To investigate the risk of the first occurring event of either heart failure or a cardiovascular ischemic event associated with different biochemical profiles in newly diagnosed T2D patients without cardiovascular disease.

Methods: From Danish nationwide registers, we identified all patients newly diagnosed with T2D who were free of cardiovascular disease (heart failure, ischemic heart disease, peripheral artery disease, and previous stroke), from 2013-2021. Patients <40 years, and patients without a registered blood test within three months prior to the T2D diagnosis, were excluded. The absolute 5-year risk of the first occurring event of either heart failure or a cardiovascular ischemic event, was calculated for patients with different levels of three biochemical markers that are known to be associated with cardiovascular disease: 1) HbA1c 2) low-density lipoprotein (LDL); and 3) estimated glomerular filtration rate (eGFR) calculated from serum creatinine.

Results: Of the 81,095 patients included in the study, 53% were male and the median age was 60 years [interquartile range 52-69]. For all pre-defined biochemical profiles—HbA1c below or above 8%, LDL below or above 4 mmol/L, and eGFR below or above 60 ml/min/1.73 m2—the absolute 5-year risk of a cardiovascular ischemic event was greater than the risk of heart failure (risk ratio ranging from 2.3–4.2), as the first occurring event following the diagnosis of T2D. The highest risk of heart failure was observed in those with moderately to severely reduced eGFR (<60 ml/min/1.73 m2).

Conclusions: Among patients newly diagnosed with T2D and free of cardiovascular disease, different biochemical profiles of HbA1c, LDL, and eGFR, were all associated with a higher risk of an ischemic cardiovascular event as the first occurring event following T2D diagnosis, as opposed to heart failure.

Flowchart of patient selection
Cumulative incidence of CIE Vs. HF

- **HbA1c**
  - <8%

- **LDL**
  - <4 mmol/L

- **eGFR**
  - >60 ml/min/1.73m²

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Cumulative incidence of CIE Vs. HF

- **Cardiovascular ischemic event**
- **Heart failure**