Impact of glycated hemoglobin A1c on cardiovascular risk in diabetes patients with and without coronary artery disease

K.K.W. Olesen¹, P.G. Thrane², M.K. Hansen², C. Gyldenkerne², M. Maeng²

¹Aarhus University Hospital, Aarhus, Denmark
²Aarhus University Hospital, Department of Cardiology, Aarhus, Denmark

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Background: Guidelines recommend a haemoglobin A1c (HbA1c) target <53 mmol/mol (7%) to achieve microvascular risk reduction. However, the impact of HbA1c target levels on macrovascular complications is less certain. Moreover, we have previously shown that the risk of macrovascular complications is dependent on presence of coronary artery disease (CAD).

Purpose: We tested the hypothesis that HbA1c ≥53 mmol/mol is associated with cardiovascular risk in diabetes patients with and without CAD.

Methods: We conducted a contemporary cohort study including diabetes patients examined by coronary angiography in Western Denmark from 2011-2021. The association between HbA1c and major adverse cardiovascular events (MACE, a composite outcome of myocardial infarction, ischemic stroke, and cardiovascular death) was modeled using restricted cubic splines. Patients were followed for up to 10 years. We estimated adjusted hazards ratios (aHR) using HbA1c of 52 mmol/mol as reference. We also performed stratified analyses by presence of CAD.

Results: We included 15,825 patients with diabetes, of whom 12,200 (77%) had CAD. Median HbA1c was 52 mmol/mol in patients with CAD and 51 mmol/mol in patients without CAD. Using restricted cubic splines, we observed significantly increased MACE rates with HbA1c ≥53 mmol in the entire cohort (Figure 1A). MACE rates plateaued with increasing HbA1c above 65 mmol/mol. When stratifying by presence of CAD, this association between HbA1c and MACE was sustained in patients with CAD (Figure 1B). In contrast, we did not observe any relation between HbA1c and MACE rates in patients without CAD (Figure 1C).

Conclusions: The current study suggests two novel findings. Firstly, a HbA1c <53 mmol/mol target is associated with a reduced risk of macrovascular complications in patients with diabetes. Thus, the impact of glucose control on macrovascular complications corresponds to the HbA1c levels recommended for avoidance of microvascular complications. Secondly, the association between HbA1c and MACE is restricted to diabetes patients with CAD while not observed in those without CAD.