Management & prevention of type 2 diabetes

Does hypoglycaemia increase the risk of arrhythmias?

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The precise relationship between intensive glycaemic control and a reduction in cardiovascular disease (CVD) risk in people with type 2 diabetes remains unclear.

In recent trials, namely the VADT (Veterans Affairs Diabetes Trial; Duckworth et al, 2009) and ADVANCE (Action in Diabetes and Vascular Disease; Patel et al, 2008) trial, intensive glycaemic control of an HbA_{1c} of 48 mmol/mol (6.5%) for between 3 and 5 years did not reduce cardiovascular mortality. Also, in the intensively controlled arm of the ACCORD (Action to Control Cardiovascular Risk in Diabetes; Gernstein et al, 2011) trial, there were more hypoglycaemic events that required assistance and a higher death rate compared to the standard control group, which ultimately led to the trial being terminated early.

From these trials, hypoglycaemia has been strongly associated with an increased risk of vascular events and death, but there is as yet no conclusive proof of a direct causal link or precise mechanistic explanation.

Case reports have suggested that hypoglycaemia may be associated with supraventricular and ventricular arrhythmias and bradycardia. However, reports of ventricular arrhythmias are rare, perhaps because such events are generally fatal if uncorrected. The aim of the recently published study by Chow et al, summarised alongside, was to examine the frequency of arrhythmias during spontaneous hypoglycaemia versus euglycaemia in people with increased CVD risk and type 2 diabetes.

In total, 25 insulin-treated people with type 2 diabetes participated in the study; all had a history of CVD and/or two additional CVD risk factors. They had a mean age of 64 years (range, 60–74 years) and a mean duration of diabetes of 17 years (range, 15–21 years). During the study, each person underwent 5 days of continuous electrocardiogram (ECG) monitoring and continuous interstitial glucose monitoring using a time-synchronised continuous glucose monitor.

The authors defined an episode of hypoglycaemia as an interstitial glucose level of ≤3.5 mmol/L for 20 minutes or longer, and an episode of hyperglycaemia as an interstitial glucose level of ≥15 mmol/L for 20 minutes or longer.

The authors obtained 2323 hours of valid simultaneous ECG and interstitial glucose recordings. Among the 25 participants, 14 people experienced at least one episode of hypoglycaemia and 11 experienced none. The baseline characteristics of those who did and did not experience at least one hypoglycaemic event were similar.

When the authors considered the effect of hypoglycaemia on CVD risk, they found that bradycardia and atrial and ventricular ectopic activity were significantly higher during nocturnal hypoglycaemia compared with euglycaemia, and that arrhythmias were more frequent during nighttime hypoglycaemia than daytime hypoglycaemia. Longer QT intervals and abnormal T-wave morphology were also observed during hypoglycaemia in some participants.

This study confirms that hypoglycaemia is common, frequently asymptomatic and prolonged in people with high CVD risk and long-standing type 2 diabetes. The authors also suggest that hypoglycaemia is associated with an increased susceptibility to significant cardiac arrhythmias; this could be a mechanism of action that could contribute to increased CVD mortality during intensive glycaemic control.

These findings may also be relevant for "dead-in-bed" syndrome in type 1 diabetes, which occurs at night, typically in individuals with recurrent asymptomatic hypoglycaemia. ■

Duckworth W, Abraira C, Moritz T et al (2009) Glucose control and vascular complications in veterans with type 2 diabetes. *N Engl J Med* **360**: 129–39
Gerstein HC, Miller ME, Genuth S et al (2011) Long term effects of intensive glucose lowering on cardiovascular outcomes. *N Engl J Med* **364**: 818–28
Patel A, MacMahon S, Chalmers J et al (2008) Intensive blood glucose control and vascular outcomes in patients with type 2 diabetes. *N Engl J Med* **358**: 2560–72

Diabetes

Risk of cardiac arrhythmias during hypoglycaemia

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! Factor	✓✓✓✓✓

1 The aim of this study was to measure the risk and frequency of arrhythmias during spontaneous hypoglycaemia compared to hyperglycaemia and euglycaemia in people with T2D.

2 Twenty-five people with T2D, a history of cardiovascular disease and/or two additional cardiovascular risk factors from Sheffield Teaching Hospitals diabetes outpatient clinics were included in the analysis.

3 All participants underwent 5 days of simultaneous ambulatory electrocardiogram monitoring and continuous interstitial glucose monitoring.

4 There were 134 hours of participant recordings at hypoglycaemia, 65 hours at hyperglycaemia and 1258 hours at euglycaemia.

5 Bradycardia and atrial and ventricular ectopic counts were eight times higher during nocturnal hypoglycaemia compared with euglycaemia (incidence risk ratio, 8.42; 95% confidence interval, 1.40–51.0).

6 Arrhythmias were more frequent during nocturnal versus daytime hypoglycaemia.

7 QT intervals of >500 ms (corrected for heart rate) and abnormal T-wave morphology were observed during hypoglycaemia in some participants.

8 Hypoglycaemia may increase the risk of arrhythmias in people with T2D and high cardiovascular risk. This is a potential mechanism that could contribute to increased cardiovascular mortality during intensive glycaemic therapy.

Chow E, Bernjak A, Williams S et al (2014) Risk of cardiac arrhythmias during hypoglycemia in patients with type 2 diabetes and cardiovascular risk. *Diabetes* **63**: 1738–47

Diabetes Care

Weight gain after insulin initiation

Readability	✓✓✓
Applicability to practice	✓✓✓
WOW! Factor	✓✓✓

1 The authors aimed to identify the factors associated with weight gain among people with T2D after starting insulin therapy.

2 Body weight change data at 1 year from baseline of 2179 people were used to investigate the predictive factors and the mean weight gain was 1.78 kg.

3 Weight gain at 1 year was associated with higher baseline HbA_{1c}, higher baseline insulin dose and at 1 year, and lower baseline BMI.

Balkau B, Home PD, Vincent M et al (2014) Factors associated with weight gain in people with type 2 diabetes starting on insulin. *Diabetes Care* **37**: 2108–13

Diabetes Metab Res Rev

Safety of DPP-4 and SGLT2 inhibitors

Readability	✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! Factor	✓✓✓

1 This meta-analysis aimed to assess the safety profiles of dipeptidyl peptidase-4 (DPP-4) inhibitors and sodium–glucose cotransporter 2 (SGLT2) inhibitors in comparison to placebo as add-ons to metformin therapy in people with T2D.

2 Twenty eligible studies published before July 2013 were found using Cochrane, PubMed and Embase.

3 There was no significantly increased risk of any serious adverse events associated with DPP-4 or SGLT2 inhibitors. However, there was an increased risk of genital infections when using SGLT2 inhibitors.

Kawalec P, Mikrut A, Łopuch S (2014) The safety of dipeptidyl peptidase-4 (DPP-4) inhibitors or sodium-glucose cotransporter 2 (SGLT-2) inhibitors added to metformin background therapy in patients with type 2 diabetes mellitus. *Diabetes Metab Res Rev* **30**: 269–83

Diabetologia

Changes in HbA_{1c} over 10 years

Readability	✓✓✓✓✓
Applicability to practice	✓✓✓✓✓
WOW! Factor	✓✓✓✓✓

1 The authors studied the changes in HbA_{1c} and glucose-lowering drug treatments over a 10-year period after T2D diagnosis in 4529 individuals from the UK.

2 From 6 months to 10 years after diagnosis, HbA_{1c} increased from 53.4 mmol/mol (7.04%) to 58.3 mmol/mol ([7.49%]; average annual change, 0.51 mmol/mol [0.047%]). The greatest annual change occurred in the first 2 years after diagnosis, with no significant increase in HbA_{1c} occurring between 5 and 10 years.

3 HbA_{1c} increased by approximately 5 mmol/mol (0.5%) over 10 years after diagnosis.

4 More frequent monitoring of HbA_{1c} and adjustments to glucose-lowering drugs may prevent an increase in HbA_{1c}.

Lind M, Pivodic A, Cea-Soriano L et al (2014) Changes in HbA_{1c} and frequency of measuring HbA_{1c} and adjusting glucose-lowering medications in the 10 years following diagnosis of type 2 diabetes: a population-based study in the UK. *Diabetologia* **57**: 1586–94

Diabetic Medicine

Activity level and cardiovascular risk

Readability	✓✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓

1 Anonymised data of 65 666 people with T2D were used to investigate the association between activity level and cardiovascular risk in a gender- and age-specific way.

2 The population was categorised as physically inactive (PA0), active 1–2 times per week (PA1) or active >2 times per week (PA2), and then stratified by age (20–59 or 60–80 years).

3 In total, 90% of participants were PA0. In both age groups, BMI, HbA_{1c} (both $P<0.0001$) and triglycerides ($P<0.002$) were lower in the PA2 group compared to the PA0 group.

4 Glycaemic control and cardiovascular risk in T2D are positively related to physical activity, which underlines the need to promote physical activity to people with T2D.

Hermann G, Herbst A, Schütt M et al (2014) Association of physical activity with glycaemic control and cardiovascular risk profile in 65 666 people with type 2 diabetes from Germany and Austria. *Diabet Med* **31**: 905–12

Diabetic Medicine

Polypharmacy in T1D and T2D: In line with current guidelines?

Readability	✓✓✓
Applicability to practice	✓✓✓✓
WOW! Factor	✓✓✓✓

1 The study aim was to assess the number of medications prescribed to people with T1D (n=155) and T2D (n=154) and to compare these to guideline recommendations.

2 People with T2D were prescribed 8.4±3.0 different drug compounds per day, 8.6±3.9 tablets per day and 2.6±1.6 injections per day. In total, 11.6±4.5 doses of any medication were prescribed to a person with T2D per day. The total medication prescribed for a person with T1D was 8.5±5.1 doses of any medication per day.

3 Over 97% of the prescriptions corresponded to recommendations by guidelines.

4 Although the number of prescribed drugs was higher for people with T2D than T1D, prescriptions were in line with guidelines suggesting polypharmacy provides a clinical benefit.

Bauer S, Nauck MA (2014) Polypharmacy in people with type 1 and type 2 diabetes is justified by current guidelines. *Diabet Med* **31**: 1078–85

"Hypoglycaemia may increase the risk of arrhythmias among people with T2D and high cardiovascular risk."