# Diabetes journals

DIABETES CARE

## Postprandial blood glucose predicts CV events and mortality

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓ |

1 The objective of this study was to determine the predictive power of postprandial blood glucose on cardiovascular (CV) events and all-cause mortality in 505 people with T2D, taking into account $HbA_{1c}$ level and common CV risk factors.

2 Baseline parameters included a history of CV events, CV risk factors and five glycaemic control parameters determined by fasting blood glucose, blood glucose 2 hours after breakfast and after lunch, blood glucose before dinner, and $HbA_{1c}$ level; outcome measures were first CV event and all-cause mortality during the 14-year follow-up.

3 In total, 34.1% of the cohort ($n$=172) had a first CV event and 29.1% ($n$=147) died during the study.

4 When the five glycemic control parameters were combined, the predictors for CV events were: blood glucose 2 hours after lunch (hazard ratio [HR], 1.507; $P$=0.010) and $HbA_{1c}$ (1.792; $P$=0.002); and for mortality were: blood glucose 2 hours after lunch (HR, 1.885; $P$<0.0001) and $HbA_{1c}$ (1.907; $P$=0.002).

5 When combining blood glucose 2 hours after lunch and $HbA_{1c}$ with the common CV risk factors, the following glycaemic control parameters were predictors for: (a) CV events – blood glucose 2 hours after lunch (HR, 1.452; $P$=0.021) and $HbA_{1c}$ (1.732; $P$=0.004); and for mortality – blood glucose 2 hours after lunch (HR, 1.846; $P$=0.001) and $HbA_{1c}$ (1.896; $P$=0.004).

6 The authors concluded that both parameters – blood glucose 2 hours after lunch and $HbA_{1c}$ – predicted CV events and all-cause mortality.

Cavalot F, Pagliarino A, Valle M et al (2011) Postprandial blood glucose predicts cardiovascular events and all-cause mortality in type 2 diabetes in a 14-year follow-up. *Diabetes Care* **34**: 2237–43

## *Lessons from the San Luigi Gonzaga Diabetes Study*

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Considerable debate has reigned as to the significance of the 2-hour post-prandial or post-oral glucose tolerance test (OGTT) glucose value in relation to all-cause mortality and cardiovascular (CV) events.

The DECODE (Diabetes Epidemiology Collaborative Analysis of Diagnostic Criteria in Europe) study has suggested that blood glucose concentration at 2 hours post-OGTT is a better predictor of CV events in all-cause mortality than fasting blood glucose (DECODE Study Group and the European Diabetes Epidemiology Group, 2001).

Similar results were suggested by the Framingham Offspring Study (Meigs et al, 2002). Indeed, meta-analyses have also suggested that 2-hour post-challenge glucose values predict fatal and non-fatal CV events (Levitan et al, 2004) and that there is a linear relationship between the 2-hour glucose value and CV deaths (Ceriello et al, 2004). However, these studies have examined the effect of 2-hour glucose values after an OGTT and not subsequent to a mixed meal.

Only two studies have previously investigated the relationship between post-prandial glucose values and CV events: the Diabetes Intervention Study (Hanefeld et al, 1996), and the San Luigi Gonzaga Diabetes Study (Cavalot et al, 2006).

The article summarised alongside by Cavalot et al (2011) examines the long-term effect of the 2-hour post-prandial glucose value on mortality and CV events in participants from the San Luigi Gonzaga Diabetes Study. It demonstrates a clear relationship between post-prandial glucose values and CV events in all-cause mortality, but also a similar effect with $HbA_{1c}$. Consequently, post-prandial glucose, and indeed $HbA_{1c}$ (as a measure of overall glycaemia including fasting glucose and post-prandial glucose values), appear to predict CV events and all-cause mortality.

Cavalot F, Petrelli A, Traversa M et al (2006) *J Clin Endocrinol Metab* **91**: 813–19
Ceriello A, Hanefeld M, Leiter L et al (2004) *Arch Intern Med* **164**: 2090–5
DECODE Study Group, the European Diabetes Epidemiology Group (2001) *Arch Intern Med* **161**: 397–405
Hanefeld M, Fischer S, Julius U et al (1996) *Diabetologia* **39**:1577–83
Levitan EB, Song Y, Ford ES, Liu S (2004) *Arch Intern Med* **164**: 2147–55
Meigs JB, Nathan DM, D'Agostino RB Sr et al (2002) *Diabetes Care* **25**: 1845–50

DIABETES

## HDL function is impaired in people with T2D

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓ |
| WOW! factor | ✓✓✓ |

1 People with T2D are at high risk of cardiovascular events despite achieving recommended serum cholesterol, blood pressure and $HbA_{1c}$ targets.

2 Differences in lipoproteins may be responsible for this residual risk, as they are associated with inflammation and oxidative stress that are considered important steps in atherosclerosis development.

3 The antioxidant and anti-inflammatory properties of HDL-cholesterol was examined in 93 people with T2D and 31 controls.

4 Measures included the HDL and LDL inflammatory indices, the plasma inflammatory index, cell-free assay and determination of oxidised fatty acids in HDL-cholesterol.

5 The HDL inflammatory index was 1.42±0.29 in the T2D group compared with 0.70±0.19 in the control group ($P$<0.001); the cell-free assay was impaired in the T2D group (2.03±1.35) compared with the control group (1.60±0.80; $P$<0.05), and HDL-intrinsic oxidisation was higher in the T2D group compared with the control group ($P$<0.001).

6 All oxidised fatty acids were significantly increased in the HDLs of the T2D group. The authors concluded that the anti-inflammatory and anti-oxidant properties of HDL-cholesterol were impaired in the T2D group.

Morgantini C, Natali A, Boldrini B et al (2011) Anti-inflammatory and antioxidant properties of HDLs are impaired in type 2 diabetes. *Diabetes* **60**: 2617–23

*"A high prevalence of lipid abnormalities persisted in people with diabetes despite statin treatment, increasing their risk of cardiovascular disease."*

DIABETIC MEDICINE

## Some ECG signs are predictive for adverse outcomes

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| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓✓ |

1 This study assessed the prognostic value of electrocardiograph (ECG) signs in 5231 people with T2D.

2 Participants underwent ECGs at baseline, yearly and at last follow-up.

3 In total, 223 (4.3%) people had atrial fibrillation/flutter (AFF), 213 (4.1%) had right branch block (BB), 111 (2.1%) had left BB and 706 (13.5%) had left axis deviation (LAD).

4 Heart rate and cQT-interval were associated with increased mortality risk, the composite secondary endpoint and heart failure; right and left BB were significantly associated with heart failure; LAD was associated with heart failure; and AFF was associated with mortality and heart failure.

5 ECG signs were concluded to be predictive for adverse outcomes in this high-risk group.

Pfister R, Cairns R, Erdmann E, Schneider CA (2011) Prognostic impact of electrocardiographic signs in patients with type 2 diabetes and cardiovascular disease. *Diabet Med* **28**: 1206–12

DIABETIC MEDICINE

## Insulin reduces infarct size in people with ACS and hyperglycaemia

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓✓ |
| WOW! factor | ✓✓✓ |

1 As part of the BIOMarker study to identify the acute risk of a coronary syndrome, the BIOMArCS 2 glucose component aims to investigate the efficacy of intensive compared with conventional blood glucose therapy in people presenting with acute coronary syndrome (ACS) and hyperglycaemia.

2 In total, 300 people admitted with ACS and an elevated plasma glucose of 7.8–16 mmol/L not treated on insulin will be randomised to either intensive or conventional blood glucose therapy in addition to standard care.

3 The main outcome measure is infarct size expressed by the cardiac troponin T level 72 hours after admission.

4 Hyperglycaemia in people presenting with ACS has a detrimental effect on infarct size and left ventricular function; it is hoped that this study will clarify mechanisms and generate hypotheses regarding limiting myocardial infarct size by glucose management.

de Mulder M, Umans VA, Stam F et al (2011) Intensive management of hyperglycaemia in acute coronary syndromes. Study design and rationale of the BIOMArCS 2 glucose trial. *Diabet Med* **28**: 1168–75

DIABETIC MEDICINE

## Lipid abnormalities persist in people treated with statins

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| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓✓ |

1 This study aimed to determine whether lipid abnormalities persist in statin-treated people with diabetes with and without metabolic syndrome (MetS).

2 Data were collected from 22 063 people regarding diabetes and MetS status, lipid measures, cardiovascular (CV) risk factors and statin therapy.

3 Nearly half of the people with diabetes did not meet their cholesterol target and were not at optimal triglyceride level.

4 A high prevalence of lipid abnormalities persisted in people with diabetes despite statin treatment, increasing their CV risk.

5 The authors concluded that statin-treated people with diabetes had a high prevalence of lipid abnormalities and improved statin therapy is warranted.

Leiter LA, Lundman P, da Silva PM et al (2011) Persistent lipid abnormalities in statin-treated patients with diabetes mellitus in Europe and Canada. *Diabet Med* **28**: 1343–51

DIABETOLOGIA

## Optimal $HbA_{1c}$ and TC:HDL values reduce CVD risk

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| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓✓ |

1 The authors sought to determine the relative importance of $HbA_{1c}$ control and total cholesterol:HDL-cholesterol ratio (TC:HDL) as risk factors for cardiovascular disease (CVD) in 22 135 people with T2D.

2 $HbA_{1c}$ and TC:HDL were measured at baseline and every year for a mean follow-up of 4.8 years; outcome measures included fatal and non-fatal coronary heart disease (CHD), CVD and stroke, as well as total mortality.

3 Adjusted hazard ratios (HRs) per 1 standard deviation increase in updated mean $HbA_{1c}$ and TC:HDL values, respectively, were 1.13 (95% confidence interval [CI], 1.07–1.19) and 1.31 (1.25–1.37) for CHD, 1.15 (1.06–1.24) and 1.25 (1.17–1.34) for stroke, 1.13 (1.08–1.18) and 1.29 (1.24–1.34) for CVD and 1.07 (1.02–1.13) and 1.18 (1.12–1.24) for total mortality (all $P<0.001$).

4 Mean 5-year event rates of outcome were calculated for four category combinations of the lowest and highest quartiles of updated mean $HbA_{1c}$ and TC:HDL; mean 5-year event rates increased from 4.8%, 7.0% and 9.1% to 14.5% for CHD and from 7.1%, 9.9% and 12.8% to 19.4% for CVD.

5 Adjusted HRs for highest- versus lowest-category combinations were 2.24 (1.58–3.18) for CHD and 2.43 (1.79–3.29) for CVD ($P<0.001$).

6 CVD and total mortality risk increased with increased levels of $HbA_{1c}$ and TC:HDL; the lowest combination of both variables conferred the lowest CVD and total mortality risk.

7 It was concluded that optimal $HbA_{1c}$ and TC:HDL values reduce the risk of CVD in people with T2D.

Gudbjörnsdottir S, Eliasson B, Eeg-Olofsson K et al (2011) Additive effects of glycaemia and dyslipidaemia on risk of cardiovascular diseases in type 2 diabetes: an observational study from the Swedish National Diabetes Register. *Diabetologia* **54**: 2544–51

DIABETIC MEDICINE

## Soluble E-selectin and factor XIIa relate to CVD risk

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| Readability | ✓✓✓ |
| Applicability to practice | ✓✓✓ |
| WOW! factor | ✓✓ |

1 People with T2D are at high risk of cardiovascular disease (CVD), although this risk is more than that conferred by traditional risk factors.

2 The authors sought to determine the 10-year risk for incident coronary heart disease (CHD) and CVD associated with the novel biomarkers soluble E-selectin, activated factor XII (factor XIIa), thrombin-antithrombin III complex and plasminogen activator inhibitor-1 (PAI-1).

3 The novel biomarkers were measured at baseline in 86 people with T2D without known CHD.

4 Cox proportional hazards regression was performed to determine multivariable-adjusted hazard ratios (HRs) associated with the baseline biomarker levels for 10-year CHD risk ($n$=33 events) or total CVD risk ($n$=45 events).

5 Mean age at baseline was 62 years and 62 (72%) were men; medication prescribed in the year before first CVD event was 55% aspirin, 43% statin and 40% angiotensin-converting enzyme inhibitor.

6 Log soluble E-selectin at baseline was significantly related to CHD and CVD; HRs (95% confidence interval [CI]) associated with a 1-unit increase in log soluble E-selectin were 4.6 (1.9–11.3) for CHD and 3.6 (1.7–7.4) for CVD (both $P$=0.001).

7 Factor XIIa was significantly related to CVD; the HR (95% CI) associated with a 1-unit increase in factor XIIa was 1.5 (1.1–1.9; $P$=0.003).

8 The authors concluded that soluble E-selectin and factor XIIa were significantly related to 10-year incident macrovascular disease in T2D.

Natarajan A, Marshall SM, Kesteven PJ et al (2011) Impact of biomarkers for endothelial dysfunction and procoagulant state on 10-year cardiovascular risk in type 2 diabetes. *Diabet Med* **28**: 1201–5

DIABETIC MEDICINE

## Intensive treatment reduces CVD in T2D

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| Readability | ✓✓ |
| Applicability to practice | ✓✓✓ |
| WOW! factor | ✓✓ |

1 This study aimed to determine whether intensive management of blood glucose, blood pressure, lipid profiles and lifestyle behaviour can reduce the incidence of cardiovascular (CV) events in 2984 people with T2D from the Japan Diabetes Clinical Data Management (JDDM) study group.

2 There were 90 CV events over 10 827 person-years' follow-up; incidences (per 1000 person-years; 95% confidence interval) of composite, coronary heart disease, ischaemic stroke and peripheral artery disease in the JDDM group were 8.3 (6.6–10.0), 4.4 (3.2–5.6), 3.1 (2.1–4.2) and 0.7 (0.2–1.2), respectively.

3 The authors concluded that a reduced incidence of CV disease can be achieved through multifactorial therapy in primary care.

Yokoyama H, Matsushima M, Kawait K et al (2011) Low incidence of cardiovascular events in Japanese patients with type 2 diabetes in primary care settings. *Diabet Med* **28**: 1221–8

DIABETOLOGIA

## Long-term survival after a first MI is still lower in people with diabetes

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| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓✓ |

1 The authors of this study sought to determine if the difference in long-term mortality rate after a first myocardial infarction (MI) in people with and without diabetes has diminished.

2 The study comprised 6776 people from the Northern Sweden MONICA Myocardial Infarction Registry who had suffered a first MI; 1054 had diabetes.

3 The median follow-up was 6.8 years (total follow-up, 50 667 patient-years); during this time 34.7% of the people without diabetes and 50.6% of those with diabetes died.

4 Median survival was 123 months and 227 months for men with and without diabetes, respectively; for women, the figures were 81 months and 222 months, respectively.

5 People with diabetes had an age-adjusted hazard ratio for all-cause mortality of 1.65 (1.50–1.82) compared with those without diabetes.

6 It was concluded that long-term survival after a first MI is still lower in people with diabetes.

Eliasson M, Jansson J-H, Lundblad D, Näslund U (2011) The disparity between long-term survival in patients with and without diabetes following a first myocardial infarction did not change between 1989 and 2006. *Diabetologia* **54**: 2538–43

DIABETES CARE

## Neither $HbA_{1c}$ nor FPG predict CVD in high-risk people

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| Readability | ✓✓✓✓ |
| Applicability to practice | ✓✓✓✓ |
| WOW! factor | ✓✓✓✓ |

1 This study compared $HbA_{1c}$ and fasting plasma glucose (FPG) in predicting cardiovascular disease (CVD) in 3850 adults with a high prevalence of diabetes and obesity.

2 Participants ($n$=1386) with no CVD at baseline underwent baseline and follow-up examinations including FPG, $HbA_{1c}$, lipids, creatinine and blood pressure; CVD events were determined over a median 15-year follow-up.

3 $HbA_{1c}$ was more useful to detect diabetes than FPG. However, adjusted models showed that neither $HbA_{1c}$ nor FPG predicted CVD risk in people without diabetes.

4 It was concluded that neither $HbA_{1c}$ nor FPG adds to conventional CVD risk factors in predicting coronary heart disease or total CVD.

Wang H, Shara NM, Lee ET et al (2011) Haemoglobin $A_{1c}$, fasting glucose and cardiovascular risk in a population with high prevalence of diabetes. *Diabetes Care* **34**: 1952–8

***"Neither $HbA_{1c}$ nor fasting plasma glucose adds to conventional cardiovascular disease (CVD) risk factors in predicting coronary heart disease or total CVD."***