### Clinical DIGEST 3

### **Diabetes journals**



#### GLP-1 protection in myocardial infarction?

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he article by Lønborg et al (summarised alongside) reports an exciting study that may have a large impact on clinical practice. It is well recognised that a significant number of people with ST-segment elevation myocardial infarction will develop hyperglycaemia, which may increase acute and chronic adverse events. The

study confirms that hyperglycaemia

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agonists. ""

is associated with a larger risk of myocardial infarction and increased infarct size compared to

people with normoglycaemia. Clinically, however, treatment with exenatide (a glucagon-like

peptide-1 [GLP-1] receptor agonist) on admission to hospital, prior to percutaneous coronary intervention, resulted in increased salvage both for people with hyperglycaemia and normoglycaemia. Thus, this study extends the putative pleiotropic effects of GLP-1 receptor agonists,

which may also be corroborated by large clinical trials currently ongoing.

#### **Diabetic Medicine**

## Ethnicity and long-term vascular outcomes

Readability	<b>////</b>
Applicability to practice	<b>////</b>
WOW! Factor	<b>////</b>

- In a sub-study from the UKPDS (United Kingdom Prospective Diabetes Study), data were analysed to investigate the association between ethnicity and long-term vascular outcomes among people with T2D.
- In total, there were 4273 participants: 83% were white Caucasian, 7% were Afro-Caribbean and 10% were Asian Indian.
- Accelerated failure time models were used to determine the relative risks of predefined outcomes.
- 4 During follow-up, 56% of participants had any defined diabetes-related end-point (24% had a myocardial infarction, 9% stroke

and 42% died).

- Asian Indians were at greater risk for any diabetes-related endpoint (relative risk [RR] 1.18, 95% confidence interval [CI], 1.07–1.29), but at lower risk of all-cause mortality (RR 0.89; 95% CI, 0.80–0.97) and peripheral vascular disease (RR 0.43; 95% CI, 0.33–0.93) compared to white Caucasians.
- Afro-Carribean participants were at lower risk for all-cause mortality, diabetes-related death, myocardial infarction and peripheral vascular disease compared to white Caucasians. There were no ethnicity-related associations found for stroke or microangiopathy.
- Asian Indian ethnicity is associated with the greatest overall risk for diabetes-related end-point burden of disease, but is not associated with an increased risk of major vascular complications or death.

Davis TM, Coleman RL, Holman RR, UKPDS Group (2014) Ethnicity and long-term vascular outcomes in type 2 diabetes: a prospective observational study (UKPDS 83). *Diabet Med* **31**: 200–7

#### **Diabetes**

## Hyperglycaemia, exenatide and myocardial infarction

Readability	<b>////</b>
Applicability to practice	<i>\\\\</i>
WOW! Factor	////

- Hyperglycaemia upon hospital admission of people with ST-segment elevation myocardial infarction (STEMI) occurs frequently and is associated with adverse outcomes. However, it is unclear whether hyperglycaemia is the cause or consequence of the myocardial infarction.
- This sub-study aimed to evaluate the association between hyperglycaemia and infarct size, myocardial salvage and area-at-risk, and to assess the interaction between hyperglycaemia and exenatide (a glucose-lowering drug with potential cardioprotective effect).
- In total, 210 people with STEMI were randomised to receive intravenous exenatide or placebo 15 minutes before percutaneous coronary intervention. Blood glucose was measured upon admission at the centre before the first angiogram as part of standard evaluation.
- Hyperglycaemia was associated with larger area-at-risk and infarct size compared to people with normoglycaemia, but the salvage index and infarct size adjusted for area-at-risk did not differ between the groups.
- 5 Treatment with exenatide resulted in an increased salvage index both among people with hyperglycaemia and normoglycaemia.
- 6 Hyperglycaemia does not influence the effect of the reperfusion treatment but rather represents a surrogate marker for the severity of the myocardium infarction.

Lønborg J, Vejlstrup N, Kelbæk H et al (2014) Impact of acute hyperglycemia on myocardial infarct size, area at risk and salvage in patients with ST elevation myocardial infarction and the association with exenatide treatment - results from a randomized study. *Diabetes* 28 Feb [Epub ahead of print]

#### **Diabetes Care**

### HbA<sub>1c</sub> and CHD risk in people with T2D

Readability	1111
Applicability to practice	////
WOW! Factor	<i>////</i>

This study aimed to provide definite evidence for the effects of HbA<sub>1c</sub> level on the risk of coronary heart

disease (CHD) in people with T2D.

- The study population comprised of Americans with low socioeconomic status: 17 510 African Americans and 12 592 white Caucasians with T2D.
- During a mean follow-up of 6 years, 7258 incident CHD cases were identified.
- The multivariable-adjusted hazard ratios for different levels of HbA<sub>1c</sub> were calculated for each population.
- With increasing HbA<sub>1c</sub>, hazard ratios for CHD increased for

Caucasian (P trend <0.001) and African American people (P=0.002). Each 1% (10.929 mmol/mol) increase in HbA<sub>1c</sub> was associated with a greater increase in CHD risk in Caucasian versus African American people with T2D.

There is a positive association between HbA<sub>1c</sub> increase from baseline and CHD risk over time in a low-income population.

Zhao W, Katzmarzyk PT, Horswell R et al (2014) Hb $A_{\rm tc}$  and coronary heart disease risk among diabetic patients. *Diabetes Care* **37**: 428–35

Asian Indian ethnicity is associated with the greatest overall risk for diabetes-related end-point burden of disease, but not with an increased risk of major vascular complications or death.

#### **Diabetes Care**

## Heart rate-corrected QT: An indicator for mortality

Readability	<b>////</b>
Applicability to practice	////
WOW! Factor	////

- Heart rate-corrected QT (QTc) interval is associated with mortality in the general population, but this association is less clear in individuals with T2D. The authors investigated the association between QTc interval with all-cause and cardiovascular disease (CVD) mortality.
- As part of a sub-study of the Diabetes Heart Study, 1020 people with T2D who were free from cardiac rhythm defects were included in the analysis.
- At baseline, the mean QTc duration was 414.9 ms and 3% of participants had prolonged QTc. After a median of 8.5 years follow-up, 204 participants had died.
- In adjusted multivariate models, a 1-standard deviation increase in QTc interval was associated with an 18% higher risk for all-cause mortality and 29% increased risk for CVD mortality.
- Heart rate QTc interval is an independent predictor of all-cause and CVD mortality in this population of people with T2D (mainly European Americans), suggesting that QTc interval could be an additional prognostic tool.

Cox AJ, Azeem A, Yeboah J et al (2014) Heart ratecorrected QT interval is an independent predictor of all-cause and cardiovascular mortality in individuals with type 2 diabetes. *Diabetes Care* **37**: 1454–61

#### **Diabetes Care**

# Cardiovascular outcomes at 30 years of the DCCT/EDIC study

Readability	////
Applicability to practice	////
WOW! Factor	1111

- Data from the DCCT (Diabetes Control and Complications Trial) and EDIC (Epidemiology of Diabetes Interventions and Complications) study were used to see if there were longterm benefits of an intensive diabetes therapy (INT) among people with T1D.
- In total, 1441 people were randomised to receive INT or conventional therapy (CON) as part of the DCCT study, and 90% were followed up as part of the observational EDIC study.
- 3 After a median 6.5 year followup, INT during the DCCT study was associated with thinner carotid intima-media thickness, less coronary calcification and a lower incidence of clinical cardiovascular events.
- There were no significant differences in cardiac structure and function between the former INT and CON groups during follow-up. However, overall, INT did provide long-term cardiac benefits.

Lachin JM, Orchard TJ, Nathan DM, DCCT/EDIC Research Group (2014) Update on cardiovascular outcomes at 30 years of the diabetes control and complications trial/epidemiology of diabetes interventions and complications study. *Diabetes Care* 37: 30–43

#### **Diabetes Res Clin Pract**

#### Proteinuria: Associated with mortality and morbidity?

Readability	///
Applicability to practice	<b>////</b>
WOW! Factor	JJJJ

- The authors aimed to investigate the effectiveness of currently recommended treatments on remission of proteinuria and its effects on morbidity and mortality.
- In total, 78 people took part in this observational study: all were receiving agents to block the renin–angiotensin system and were followed for a median 6 years after recognition of albumin:creatinine ratio (ACR) ≥50 mg/mmol until death or March 2011. Remission of proteinuria was defined as ≥70% reduction in peak ACR.
- Only 22% of participants achieved remission of proteinuria, which was significantly associated with lower incidence of end-stage renal disease (ESRD) or death, but not a reduction in cardiovascular events.
- There was a significant interaction between the severity of diabetic retinopathy and remission of proteinuria on the risk of ESRD and death (*P*=0.0003).

Tan J, Jaung R, Gamble G, Cundy T (2014) Proteinuric renal disease in type 2 diabetes — Is remission of proteinuria associated with improved mortality and morbidity? *Diabetes Res Clin Pract* **103**: 63–70