Cardiovascular journals

AMERICAN JOURNAL OF CARDIOLOGY

Increased risk of acute MI following NPH insulin initiation

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

1 The present study compared incidence of acute myocardial infarction (AMI) following basal insulin initiation among people with type 2 diabetes receiving either neutral protamin Hagedorn (NPH) insulin or the long-acting synthetic insulin, glargine, for the management of hyperglycaemia.

2 In a cohort that had been initiated on either NPH insulin (n=5461) or insulin glargine (n=14 730), inpatient medical claims for AMI from more than 30 managed healthcare plans in the US were retrospectively examined.

3 Mean follow-up was 2 years. Unadjusted AMI incidence per 1000 person-years was 17.6 among those initiated on NPH insulin and 11.5 on insulin glargine (rate ratio, 1.53; 95% confidence interval [CI], 1.29–1.81).

4 Following Cox regression (hazard ratio [HR], 1.39; 95% CI, 1.14–1.69) and sensitivity analysis (HR range, 1.30–1.56) indicated a greater risk of AMI in the NPH insulin arm.

5 The incidence of AMI among those initiated on NPH insulin remained higher than that among the insulin glargine arm following 1:1 propensity matched analysis (odds ratio 1.55, 95% CI, 1.23–1.96 NPH vs. insulin glargine).

6 The authors suggest that AMI risk is greater among people with type 2 diabetes who have been initiated on an NPH basal insulin regimen than it is among those receiving insulin glargine. However, the NPH insulin group had greater rates of comorbidities at baseline.

Rhoads GG, Kosiborod M, Nesto RW et al (2009) Comparison of incidence of acute myocardial infarction in patients with type 2 diabetes mellitus following initiation of neutral protamine Hagedorn insulin versus insulin glargine. *Am J Cardiol* **104**: 910–16

Are different insulin formulations and regimens associated with different CV risk profiles?

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Recent public controversy has focused both on the cardiovascular safety of intensive blood glucose control and the cardiovascular profiles of different oral antidiabetes agents (Currie et al, 2010). There is, however, little evidence relating to the cardiovascular safety of different insulin preparations.

Hypoglycaemia has been suggested as a possible confounding factor with respect to the cardiovascular benefit of intensive blood glucose control. Insulin glargine is an alternative basal insulin to neutral protamine Hagedorn (NPH) insulin, with the primary benefit being a lower incidence of hypoglycaemia (Duckworth and Davis, 2007). Rhoads et al (2009; summarised alongside) retrospectively compared the acute myocardial infarction (AMI) rate among people newly initiated on either NPH insulin or insulin glargine.

Cox proportional hazard models and propensity score methods were used to compare the subsequent AMI rates in the two arms. After a mean follow-up period of 2 years, the unadjusted AMI rates were 17.6/1000 person years for NPH insulin, and 11.5/1000 person years for insulin glargine. This translated in the Cox model to a hazard ratio of 1.39 (95% confidence interval [CI], 1.14–1.69 for NPH insulin vs. insulin glargine). Propensity matched analysis (1:1) yielded similar results, with an odds ratio of 1.55 (95% CI, 1.23–1.96 for NPH insulin vs. insulin glargine).

This large retrospective cohort study raises the possibility that different insulin formulations or regimens might be associated with different cardiovascular risk profiles among people with type 2 diabetes. Rhoads et al's (2009) observations suggest that insulin glargine initiation is associated with a significantly lower AMI risk compared with NPH insulin.

A possible mechanism to account for this observation might be a lower incidence of hypoglycaemia and, thus, lower incidences of glucose variability, oxidant stress and myocardial strain in individuals receiving insulin glargine. Alternative mechanisms might be the differential effect of NPH insulin and insulin glargine on insulin-like growth factor-1, with the suggestion that the elimination of overnight periods of insulinopaenia associated with insulin glargine result in enhanced insulin-like growth factor-1 secretion, which has both anti-inflammatory and antioxidative effects.

"This study gives rise to an intriguing hypothesis relating to the potential cardiovascular benefits of insulin glargine compared with NPH insulin and requires further evaluation."

When interpreting the results of any retrospective cohort study, such as Rhoads et al (2009), issues relating to allocation bias and confounding by indication need to be considered. Notwithstanding such considerations, this study gives rise to an intriguing hypothesis relating to the potential cardiovascular benefits of insulin glargine compared with NPH insulin and requires further evaluation. Broadening the scope of the investigation to include insulin detemir would also be informative.

Currie CJ, Peters JR, Tynan A et al (2010) Survival as a function of HbA_{1c} in people with type 2 diabetes: a retrospective cohort study. *Lancet* **375**: 481–89

Duckworth W, Davis SN (2007) Comparison of insulin glargine and NPH insulin in the treatment of type 2 diabetes: a review of clinical studies. *J Diabetes Complications* **21**: 196–204

"The ability of single photon emission computed tomography to differentiate coronary risk among people with type 2 diabetes who had a degree of coronary artery disease and those with no coronary plaque was low."

AMERICAN JOURNAL OF CARDIOLOGY

SPECT poor at determining coronary risk in T2D

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

1 Coronary artery disease (CAD) was assessed among a group of asymptomatic people with T2D using two computed tomography (CT) techniques: single photon emission CT (SPECT) and coronary computed tomographic angiography (CCTA).

2 Participants (n=116, 59% men, age 62±7 years) with T2D and without clinical evidence of peripheral artery disease or abnormal electrocardiographic findings were included in the study.

3 Normal SPECT results were returned for 88 participants, 28 had abnormal perfusion defects. CCTA found that 92 participants had atherosclerotic plaques and 20 had significant stenosis.

4 Participants with normal and abnormal findings on SPECT has similar provenances of atherosclerotic plaque, significant and severe stenosis, and calcified, mixed and noncalcified plaques and a high (>100) coronary artery calcium score (all P>0.05).

5 At follow-up (24±4 months), five cardiac events had occurred in participants with normal SPECT findings, all of whom had occult CAD diagnosed by CCTA.

6 The ability of SPECT to differentiate coronary risk among people with T2D who had a degree of CAD and those with no coronary plaque was low, though these circumstances represent very different levels of risk.

Choi EK, Chun EJ, Choi SI et al (2009) Assessment of subclinical coronary atherosclerosis in asymptomatic patients with type 2 diabetes mellitus with single photon emission computed tomography and coronary computed tomography angiography. *Am J Cardiol* **104**: 890–6

CIRCULATION

Central obesity not an obligatory factor in metabolic syndrome diagnosis

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

1 A group of risk factors for CV disease and type 2 diabetes (including raised blood pressure, dyslipidemia, raised fasting glucose and central obesity) have become known as the metabolic syndrome (MetS).

2 Various diagnostic criteria for MetS have been proposed by different organisations over the past decade, most recently from the International Diabetes Federation and the American Heart Association/National Heart, Lung, and Blood Institute.

3 This article presents the interim statement on the MetS from the International Diabetes Federation Task Force on Epidemiology and Prevention.

4 The Task Forces' conclusion differs from previous statements by rejecting central obesity as an obligatory component in the diagnosis of MetS. Rather, it holds that abnormal findings in three out of five measures – one of which is central obesity – diagnoses MetS.

5 It was concluded that a single set of cut-off points would be used for all components except waist circumference, for which further work is required, and that in the interim, national or regional cut-off points for waist circumference can be used.

Alberti KG, Eckel RH, Grundy SM et al (2009) Harmonizing the metabolic syndrome: a joint interim statement of the International Diabetes Federation Task Force on Epidemiology and Prevention; National Heart, Lung, and Blood Institute; American Heart Association; World Heart Federation; International Atherosclerosis Society; and International Association for the Study of Obesity. *Circulation* **120**: 1640–5

AMERICAN JOURNAL OF CARDIOLOGY

Mild hyperglycaemia reduces risk of death following acute myocardial infarction

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

1 Previous research studies have reported that acute hyperglycaemia is associated with high mortality following acute myocardial infarction (AMI).

2 The authors of this study aimed to assess the relationship between admission blood glucose and in-hospital mortality following AMI in people with or without diabetes.

3 Plasma glucose levels were recorded in people (with diabetes, n=1190; no diabetes, n=2560) admitted to hospitals participating in the Japanese Acute coronary syndrome Study within 48 hours of an AMI.

4 A linear relationship between blood glucose levels and mortality was observed in people without diabetes (<6 mmol/L, mortality 2.5%).

5 Conversely, a U-shaped curve was found in people with diabetes. Both severe hyperglycaemia (≥11 mmol/L) and hypoglycaemia (<7 mmol/L) were associated with significantly higher mortality (9.1% [P<0.001] and 9.4% [P=0.009], respectively) than mild hyperglycaemia (9–11 mmol/L, 3.2%).

6 People with diabetes with admission glucose of 9–10 mmol/L had the lowest mortality, whereas lower blood glucose was better in people without diabetes.

7 The authors concluded that optimal glycaemia for positive outcome following AMI differs between people with and without DM.

Ishihara M, Kojima S, Sakamoto T et al (2009) Comparison of blood glucose values on admission for acute myocardial infarction in patients with versus without diabetes mellitus. *Am J Cardiol* **104**: 769–74

AMERICAN JOURNAL OF CARDIOLOGY

Bivalirudin monotherapy safe and effective in DM

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

1 Bivalirudin has been shown to demonstrate similar efficacy but a lower rate of bleeding compared with unfractionated heprin. The authors of the present study sought to evaluate whether this can also be applied to people with diabetes.

2 The authors randomised 335 people with diabetes (DM) referred for elective percutaneous coronary intervention in the Novel Approaches for Preventing or Limiting Events trial to receive bivalirudin monotherapy (BM) or unfractionated heprin plus tirofiban (UHT).

3 Primary composite end-point (30-day composite incidence of death, myocardial infarction, urgent repeat revascularisation, all bleeding) was significantly lower among those randomised to receive BM compared with the UHT group (18.0% vs. 31.5%; odds ratio, 0.47; 95% confidence interval, 0.28–0.79; P=0.004). No death, urgent revascularisation or Q-wave myocardial infarction occured.

4 Significantly fewer participants in the BM group experienced bleeding (8.4% vs. 20.8%, P=0.002).

5 BM was found to be safe, effective and associated with a significant reduction in in-hospital bleeding during percutaneous coronary interventions among people with DM.

Tavano D, Visconti G, D'Andrea D et al (2009) Comparison of bivalirudin monotherapy versus unfractionated heparin plus tirofiban in patients with diabetes mellitus undergoing elective percutaneous coronary intervention. *Am J Cardiol* **104**: 1222–8

AMERICAN HEART JOURNAL

HbA_{1c} and platelet reactivity in people with T2D and CVD

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

1 The authors sought to examine the relationship between platelet reactivity and glycaemic control in people with type 2 diabetes on aspirin and clopidogrel therapy.

2 Platelet aggregation (PA) in response to adenosine diphosphate (ADP; 5 and 20 µmol/L) was compared between participants (with type 2 diabetes, n=36; with no diabetes, n=25); all were undergoing stenting on aspirin and clopidogrel therapy.

3 The effect of HbA_{1c} levels <7 g/dL (n=16) and ≥7 g/dL (n=20) on PA were assessed.

4 The T2D group had higher 5 and 20 µmol/L ADP-induced PA than those without diabetes (45±17 vs. 33±12, P=0.009 and 52±19 vs. 40±12, P=0.004).

5 Those with HbA_{1c} levels ≥7 g/dL had higher 5 and 20 µmol/L ADP-induced PA than those with HbA_{1c} levels <7 g/dL (54±15 vs. 34±14, P<0.001 and 62±14 vs. 40±17, P<0.001, respectively).

6 As measured by 5 and 20 µmol/L ADP-induced PA, the prevalence of high platelet reactivity in the HbA_{1c} ≥7 g/dL group was 65% and 60%, respectively, and in the HbA_{1c} <7 g/dL group was 19% and 13%, respectively.

7 The results showed a significant correlation between 5 and 20 µmol/L ADP-induced PA and HbA_{1c} (P=0.0001).

8 The authors concluded that an important relationship exists between blood glucose control and platelet reactivity in people with T2D treated with dual antiplatelet therapy, but that further research is warranted.

Singla A, Antonino MJ, Bliden KP et al (2009) he relation between platelet reactivity and glycemic control in diabetic patients with cardiovascular disease on maintenance aspirin and clopidogrel therapy. *Am Heart J* **158**: 784.e1–6