Cardiovascular journals

Intensive lipid lowering is beneficial. PROVE IT-TIMI!

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Diabetes represents a major global health burden and is associated with an excess cardiovascular event rate and as such people with diabetes are over represented in the patient population presenting with acute coronary syndrome.

The impact of intensive lipid lowering in people with diabetes and acute coronary syndrome is not well characterised despite the fact that dyslipidaemia is a major determinant of cardiovascular complications in diabetes. This 2x2 factorial design study (summarised on right) examined the effects of pravastatin 40 mg daily versus intensive atorvastatin therapy 80 mg daily on outcomes in people with and without diabetes presenting with acute coronary syndrome.

Intensive therapy resulted in improved clinical outcomes in both groups, but since those with diabetes were at higher risk, more acute cardiac events were prevented in the diabetic patient group (55 versus 40 per 1000 patients treated without diabetes). Intensive therapy resulted in a 44% reduction in LDL cholesterol, equating with an absolute risk reduction in the primary endpoint (death, myocardial infarction or unstable angina) of 5.5% in people with diabetes versus 4% in those without diabetes, which was proportional to the order of magnitude of cholesterol reduction. Furthermore those subjects with diabetes who did not achieve the dual LDL cholesterol targets of <1.8 mmol/l and high-sensitivity CRP <2 mg/l had an event rate double that of those subjects who did not have diabetes (24.7% versus 12.8%).

These data are of importance to current clinical practice. The most recent treatment targets (British Cardiac Society et al, 2005) advocate an LDL cholesterol goal of <2 mmol/l in high risk patients such as those represented in this study, there is however debate relating to the cost effectiveness of such an approach with national treatment guidelines still advocating a target LDL cholesterol <3 mmol/l. Data such as those presented in this study demonstrate the utility of intensive lipid lowering in those subjects at the highest risk of cardiovascular disease such as patients with type 2 diabetes with acute coronary syndromes. Thus while there may be significant cost implications to treating all subjects at risk of cardiovascular disease to lower cholesterol targets, the observations from this study support both the clinical utility and cost effectiveness of intensive lipid reduction in those individuals at the highest risk of cardiovascular disease.

British Cardiac Society et al (2005) JBS 2: Joint British Societies' guidelines on prevention of cardiovascular disease in clinical practice. *Heart* **91** (Suppl 5): vi–52

AMERICAN HEART JOURNAL

Long-term risk is lower in diabetes controlled by diet

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

1 The authors of this study compared coronary artery bypass graft patients with and without diabetes to assess the long-term risks of death or acute myocardial infarction (AMI).

2 Of 6727 patients who were admitted to the Karolinska Hospital in Stockholm between 1980 and 1995 for coronary artery bypass grafting, 13% had a diagnosis of diabetes on admittance.

3 Risk of death within 30 days of the operation was increased in those patients with diabetes who managed the condition with insulin or oral drugs, but not in those who were controlled using diet. Ten-year survival rate without AMI was 40% in insulin dependent patients, 48% for those on oral drugs, 59% in diet managed patients and 66% in those without diabetes.

4 Those patients with diabetes who control the condition with drugs are at increased risk of early death than those who use diet to control diabetes.

Alserius T, Hammar N, Nordqvist T, Ivert T (2006) Risk of death or acute myocardial infarction 10 years after coronary bypass surgery in relation to type of diabetes. *American Heart Journal* **152**: 599–605

EUROPEAN HEART JOURNAL

Lipid lowering in acute coronary syndromes and diabetes

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

1 This study tested standard versus intensive statin therapy outcomes between people with and without diabetes.

2 The study involved 4162 people with acute coronary syndrome. They were followed for clinical events for a mean of 24 months.

3 Participants were randomised in an equal ratio to receive pravastatin or atorvastatin and to gatifloxacin (every 10 days) or placebo.

4 Over the 2 years there were more acute cardiac events in those with diabetes than without. The acute endpoints were death, myocardial infarction or unstable angina requiring re-hospitalisation.

5 The biochemical parameters to achieve were a decrease in LDL cholesterol and a reduction in C-reactive protein levels. Only 38% of participants with diabetes managed to reach this endpoint, despite intensive therapy.

6 It was seen that there were no significant differences in participants with diabetes between the cardiac stimulant gatifloxacin and placebo.

7 From these data the authors conclude that in people with diabetes and acute coronary syndromes, intensive statin therapy does indeed reduce acute cardiac events. This reduction is also seen in patients without diabetes.

Ahmed S, Cannon CP, Murphy SA, Braunwald E (2006) Acute coronary syndrome and diabetes: is intensive lipid lowering beneficial? Results of the PROVE IT-TIMI 22 trial. *European Heart Journal* **27**: 2323–29

AMERICAN HEART JOURNAL

Aggressive lowering of LDL cholesterol will help provide guidance

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

1 This 3-year trial will examine the aggressive reduction of LDL-cholesterol and blood pressure against the normal standards of these two parameters.

2 The subjects in the study will be American Indians. Randomisation and recruitment lasted from May 2003 to September 2004 when the number of participants reached 549.

3 To be eligible for the study, participants had to be 40 years of age or older, be of American Indian origin and have type 2 diabetes.

4 The study is a two arm, open label, multicentre randomised trial. Participants were seen every three months of the follow-up period and had a carotid ultrasound and echocardiography at baseline, 18 months and 36 months.

5 The Stop Atherosclerosis in Native Diabetics Study will be the first CVD prevention trial that will aggressively target blood pressure and LDL cholesterol.

6 SANDS will help to provide guidance on blood pressure goals and lipid levels for all populations with diabetes, not just for American Indians, and will hopefully advance the understanding of atherosclerosis and enable guidelines to be drawn up to prevent it.

Russell M, Fleg JL, Galloway J et al (2006) Examination of lower targets for low density lipoprotein cholesterol and blood pressure in diabetes - the Stop Atherosclerosis in Native Diabetics Study (SANDS). *American Heart Journal* **152**: 867–75

AMERICAN HEART JOURNAL

Evidence-based treatments are under-used in management of ACS

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

1 This study was undertaken to examine the differences between acute coronary syndrome patients with and without diabetes in terms of clinical outcome, management and patient characteristics.

2 This was a prospective, multicentre, observational study. Recruitment took place over 51 hospitals in 9 Canadian provinces and enrolled 4578 patients.

3 The authors examined the impact of diabetes on the use of coronary revascularisation and thrombolytic therapy.

4 The authors found that patients who had both acute coronary syndromes and diabetes had more CV risk factors and presented with higher clinical risk.

5 Patients with diabetes and acute coronary syndromes received less evidence-based treatments than those without the condition, despite a higher predicted 1-year mortality.

6 The authors acknowledge that patients with ACS and diabetes represent a high-risk group and that novel therapies should be explored to deal with ACS as the percentage of the population with diabetes increases.

Yan RT, Yan AT, Tan M et al (2006) Underuse of evidence-based treatment partly explains the worse clinical outcome in diabetic patients with acute coronary syndromes. *American Heart Journal* **152**: 676–83

AMERICAN JOURNAL OF CARDIOLOGY

Apolipoprotein may explain CV risk in people with the metabolic syndrome

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

1 The idea behind this study was to investigate whether the metabolic syndrome and apolipoprotein-B: apolipoprotein-AI ratio are related.

2 There were 2964 people analysed in this study. The investigators compared the mean values for apo-B: apo-AI ratio in those with and without the metabolic syndrome.

3 The authors found that the ratio had a significant association with each of the defined components of the metabolic syndrome.

4 The components and their respective odds ratios were; low HDL cholesterol (5.7), high triglycerides (4.7), high waist circumference (2.6), high fasting glucose (1.9) and high blood pressure (1.5). The mean apo-B: apo-AI ratio significantly increased as the number of components of the metabolic syndrome in an individual increased ($P=0.0001$).

5 This study is supported by several others reporting that individuals with increased levels of apolipoprotein-B had a greater number of metabolic syndrome components than those with low apo-B levels.

6 Even when excluding HDL cholesterol and triglycerides as a component, elevated apo-B:apo-AI ratio is strongly associated with the metabolic syndrome and insulin resistance and thus may help explain increased CV risk in these populations.

Sierra-Johnson J, Somers VK, Kuniyoshi FHS et al (2006) Comparison of Apolipoprotein-B/Apolipoprotein-AI in subjects with versus without the metabolic syndrome. *American Journal of Cardiology* **98**: 1369–73

'Even when excluding HDL cholesterol and triglycerides as a component, elevated apo-B:apo-AI ratio is strongly associated with the metabolic syndrome and insulin resistance...'

'Patients who had both acute coronary syndromes and diabetes had more CV risk factors.'

'A strong association was seen between long-term mortality and body mass index.'

'Stronger hazard ratio associations were seen in those <60 years old and alcohol drinkers.'

EUROPEAN HEART JOURNAL

Serum gamma-glutamyltransferase predicts future risk of CHD

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

1 This study looked at whether serum gamma-glutamyltransferase could predict coronary heart disease or not, and if it could distinguish fatal and non fatal cardiac events.

2 The authors carried out baseline risk surveys in Finland in 1982, 1987, 1992 and 1997.

3 In each year and study area at least 500 people with type 2 diabetes were selected between the ages of 25 and 64 years.

4 The study population was selected randomly. Of the 29890 people selected, 971 were excluded due to having had a previous myocardial infarction. Another 81 were excluded and the final study population was made up of 13811 men and 15027 women.

5 The cut-off points for serum gamma-glutamyltransferase were the 25th, 50th, 75th and 90th sex-specific percentiles. Stronger hazard ratio associations were seen in those <60 years old and alcohol drinkers. Associations were similar for those with non-fatal myocardial infarction and fatal coronary heart disease.

6 The authors conclude that there is an independent mechanism linking coronary heart disease with serum gamma-glutamyltransferase. Measuring this in people with diabetes could be useful as an aide to predicting future risk of coronary heart disease.

Lee DH, Silventoinen K, Hu G et al (2006) Serum gamma-glutamyltransferase predicts non-fatal myocardial infarction and fatal coronary heart disease among 28838 middle-aged men and women. *European Heart Journal* **27**: 2170–76

AMERICAN JOURNAL OF CARDIOLOGY

Low BMI increases mortality risk after coronary artery bypass grafting

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

1 The authors of this study focused on the effect of obesity on the risk of long-term mortality in patients who had undergone coronary artery bypass grafting.

2 There were 1209 patients involved in this study. All had undergone coronary artery bypass grafting at a centre in Texas between January 1998 and August 1999.

3 Coronary artery bypass grafting was carried out through median sternotomy using an aortic cross clamp and a cardiopulmonary bypass pump.

4 Thirty-five patients were excluded from the study group as they died in the hospital or within 1 day of discharge, bringing the total group for analysis to 1174.

5 The mean survival rate for the study group was 1906 days. The minimum follow-up was 52 months and the maximum was 6 years.

6 A strong association was seen between long-term mortality and body mass index. There appeared to be a decrease in risk of mortality as BMI increased. Once this was adjusted for various factors, such as age, diabetes and renal failure, the benefit became non-significant.

7 More research needs to be done to understand the factors associated with BMI and long-term mortality and whether obesity increases mortality risk.

Hamman BL, Filardo G, Hamilton C, Grayburn PA (2006) Effect of body mass index on risk of long-term mortality following coronary artery bypass grafting. *American Journal of Cardiology* **98**: 734–38

EUROPEAN HEART JOURNAL

OGTT for people without diabetes

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

1 This investigation looked at admission hypoglycaemia in patients without diabetes who presented with acute myocardial infarction and whether it is a surrogate for undiagnosed abnormal glucose tolerance.

2 The study involved 200 patients with acute myocardial infarction who had no previous history of diabetes.

3 An oral glucose tolerance test was performed by each patient to split them into three groups depending on admission glucose level. Group 1 <7.8 mmol/l; group 2 7.8–11.1 mmol/l; group 3 >11.1 mmol/l.

4 The test identified impaired glucose tolerance in 78 people and diabetes in 53. Only 14 were diagnosed with diabetes after fasting glucose criteria were applied.

5 The relationship between fasting glucose ($r^2=0.50$, $P<0.001$) and HbA_{1c} ($r^2=0.34$, $P<0.001$) to post-load was significant; however, the relationship with admission glucose was not significant ($r^2=0.02$, $P=0.08$).

6 Analysis of results showed that both HbA_{1c} and fasting glucose levels could independently predict abnormal glucose tolerance; however, admission glucose could not be used to do this.

7 The authors conclude that any patient presenting with acute myocardial infarction and hyperglycaemia should receive an oral glucose tolerance test.

Ishihara M, Inoue I, Kawagoe T et al (2006) Is admission hyperglycaemia in non-diabetic patients with acute myocardial infarction a surrogate for previously undiagnosed abnormal glucose tolerance. *European Heart Journal* **27**: 2413–19