Clinical DIGEST 1

Major journals

LANCET

MI: A prediabetes risk equivalent?

The authors investigated the incidence of newly diagnosed diabetes and IFG in 8 291 Italian individuals with a history of MI in the previous 3 months.

New-onset diabetes was defined as the prescription of a hypoglycaemic agent or a fasting glucose level of ≥7 mmol/l. IFG was classified as >6.1 mmol/l and <7 mmol/l.

Also recorded at baseline were BMI, dietary habits, medications and data for other risk factors. A Mediterranean diet score was assigned each individual based on their consumption of raw vegetables, fruit, fish and olive oil.

The mean duration of follow up was 3.2 years. Over the course of the study, 12 % of participants developed diabetes and, among those without either condition at baseline, 33 % developed either diabetes or IFG.

When compared with results from population-based cohorts, rates of developing IFG were 15-times greater among people with a recent MI (1.8 % versus 27.5 %) and they were at least twice as likely to develop diabetes (0.8–1.6 % versus 3.7 %).

In this population of people who have had a recent MI, age and hypertension were independent risk factors for new-onset diabetes or IFG. Additionally, those who were also taking ß blockers, lipid-lowering medications or diuretics showed that each of these pharmacological interventions were independent risk factors.

The authors state that this study raises the possibility of MI being a prediabetes risk equivalent. They emphasise the importance of diet and lifestyle advice following an MI.

Mozaffarian D, Marfisi R, Levantesi G et al (2007) Incidence of new-onset diabetes and impaired fasting glucose in patients with recent myocardial infarction and the effect of clinical and lifestyle risk factors.

Elevated incidence of diabetes supports use of more OGTT in post-myocardial infarction assessments



Marc Evans, Consultant Physician, Llandough Hospital, Cardiff ype 2 diabetes is well recognised as a coronary heart disease risk factor. However, much less is known about the risk factors for and the development of diabetes and glucose intolerance in people

who have suffered a myocardial infarction.

This prospective study by Mozaffarian and colleagues evaluated data from 8 291 Italian individuals with documented myocardial infarction within the previous 3 months who did not have diabetes. Development of type 2 diabetes or glucose intolerance was assessed over the subsequent 3.2-year period. Over a third of participants developed diabetes or impaired fasting glycaemia (where FPG ≥6 mmol/l and <7 mmol/l) over the follow-up period. This figure increased to over two thirds when a lower cutoff point for impaired fasting glucose (> 5.6 mmol/l) was used.

Independent risk factors for new-onset diabetes included greater age, presence of hypertension and use of ß blockers and diuretics. Independent lifestyle risk factors included higher BMI, a greater BMI increase during the follow-up period, current smoking, a lower Mediterranean dietary score and a wine

consumption of >1 I/day. Data for physical activity was not assessed in this study, although inability to participate in a post-infarct exercise test was associated with a higher incidence of diabetes.

Previous studies have shown that impaired glucose tolerance in essence represents the burden of undiagnosed disease at the time of myocardial infarction. This study demonstrates the prevalence of new-onset diabetes or impaired fasting glycaemia in the years following a myocardial infarction in individuals with no previous evidence of glucose intolerance. With an annual incidence rate of 12.3 % per year, this study clearly demonstrates that myocardial infarction represents a major risk factor for the future development of diabetes.

These observations have important potential clinical implications, indicating the importance of surveillance and the implementation of preventative strategies. Thus, regular screening might be appropriate for people with identified risk factors. As the earliest manifestations of diabetes occur in the form of perturbations in post-prandial insulin secretion and glucose homeostasis, oral glucose tolerance testing should be considered part of the regular assessment of people with a history of myocardial infarction.

ARCHIVES OF INTERNAL MEDICINE

Life expectancy and CVD-free time decrease with diabetes

Using data from the Framingham Heart Study, the authors set out to define the associations between diabetes, life expectancy and number of years lived with and without CVD in people over the age of 50 years.

Life tables stratified by presence of diabetes at baseline were constructed

using hazard ratios for three stages of disease transition: healthy to death; healthy to CVD; CVD to death.

The risk of CVD was significantly increased in both sexes when diabetes was present; HR: 2.5 for women and 2.4 for men. This risk increase was also seen for death in the presence of CVD; HR: 2.2 for women and 1.7 for men.

The women involved in this study who had diabetes lived, on average, 8.2 (95 % CI: 6.1–10.4) years less than women who did not have the condition. In men, this decrease in life expectancy was 7.5 (95 % CI: 5.5–9.5) years.

Franco OH, Steyerberg EW, Hu FB et al (2007) Associations of diabetes mellitus with total life expectancy and life expectancy with and without cardiovascular disease. *Archives of Internal Medicine* **167**: 1145–51

Cardiovascular disease Clinical DIGEST

Measurement of an individual's apo B: apo A-I ratio predicted CHD as well as but not better than other lipid ratios,⁹

JOURNAL OF THE AMERICAN MEDICAL **ASSOCIATION**

Apo B: apo A-I ratio a predictor for CHD

Readability **Applicability to practice** 11111 **WOW!** factor 1111

The utility of apolipoproteins as an indicator for CHD was assessed and compared with that of traditionally-used lipid ratios.

This was a population-based, prospective cohort study using data from the Framingham Offspring Study.

Involved were 3 322 middle-aged Caucasians without CVD, 53% of whom were female. After a median follow up of 15 years 291 participants (8.8 %) developed CHD.

Measurement of an individual's apo B: apo A-I ratio predicted CHD as well as, but not better than, other lipid ratios

The conclusion of the study states that measuring apo B:apo A-I ratio is not appropriate where total cholesterol and HDL-c levels are available.

Ingelsson F. Schaefer F.J. Contois J.H et al. (2007) Clinical utility of different lipid measures for prediction of coronary heart disease in men and women. Journal of the American Medical Association 298: 776–85

syndrome was identified in 47 % of people who participated.

Individuals were randomly assigned to receive either aliskiren 150 mg (n=437), valsartan 160 mg (n=455), aliskiren 150 mg plus valsartan 160 mg (n=446) or placebo (n=459) for 4 weeks followed by titration to the maximum recommended dose for 4 weeks.

At week 8, combination therapy had lowered diastolic BP by a mean of 12.2 mmHg from baseline; valsartan by 9.7 mmHg; aliskiren by 9.0 mmHg and placebo by 4.1 mmHg (P<0.001 for combination versus all other regimens).

The tolerability profile of valsartan plus aliskiren was similar to

monotherapy. Oparil S, Yarows SA, Patel S et al (2007) Efficacy and safety of combined use of aliskiren and valsartan in patients with hypertension: a randomised, doubleblind trial. Lancet 370: 221-9

In individuals with UA/NSTEMI, diabetes was independently associated with higher 30-day mortality (OR: 1.78, 95 % CI: 1.24-2.56) and 1-year mortality (HR: 1.65, 95 % CI: 1.30 - 2.10).

Where STEMI was diagnosed, diabetes was also associated with higher 30 day mortality (OR: 1.40, 95 % CI: 1.24-1.57) and 1-year mortality (HR: 1.22, 95 % CI: 1.08-1.38).

The persistent elevation in mortality post ACS in people with diabetes should therefore be addressed using aggressive strategies.

Donahoe SM, Stewart GC, McCabe CH et al (2007) Diabetes and mortality following acute coronary syndromes. *Journal of the American Medical* Association **298**: 765–75

AMERICAN JOURNAL OF **MEDICINE**

Data suggest reducing diagnostic thresholds for diabetes in women

1111 Readability Applicability to practice //// **WOW!** factor 111

The aim of this study was to investigate whether or not small elevations in HbA_{1c} are predictive of type 2 diabetes and CVD in women without diabetes.

 A prospective cohort study design was used, examining data from 26 563 female healthcare professionals in the US aged >45 vears without diagnosed diabetes or CVD

Baseline characteristics were as follows. Mean age: 54.6 ± 7.1 years; mean BMI: $25.8 \pm 4.9 \text{ kg/m}^2$; mean HbA_{1c}: 5.03 ± 0.37 %. Participants were predominantly Caucasian (94.8 %).

The median duration of follow up was 10.1 years. During this time, 1238 cases of diabetes were diagnosed (4.7%) and 684 CVD events were recorded (2.6 %).

An association between HbA₁₀ and risk of diabetes or CVD events was seen in the raw data. However. when modelled as a continuous linear variable, a 1 % increase in HbA_{1c} was not associated with risk of CVD (P=0.28).

Incidence of diabetes was found to be significantly associated with baseline HbA_{1c} (P < 0.001).

In conclusion, in light of the elevated HbA_{1c} levels in advance of a diagnosis of diabetes, the authors recommend that diagnostic thresholds for diabetes should be reduced.

Pradhan AD, Rifai N, Buring JE, Ridker PM (2007) Hemoglobin A1c predicts diabetes but not cardiovascular disease in nondiabetic women. American Journal of Medicine 120: 720-7

LANCET

Aliskiren plus valsartan gives greater BP reduction than monotherapy

Readability Applicability to practice 1111 **WOW!** factor

This study set out to compare the efficacy of the combination of the ARB valsartan plus aliskiren, an orally active renin inhibitor, in controlling hypertension versus monotherapy and placebo.

Involved were 1 797 predominantly white individuals with a sitting diastolic BP of 95-109 mmHg and ambulatory BP ≥90 mmHg. Metabolic

JOURNAL OF THE AMERICAN MEDICAL ASSOCIATION

Diabetes still increases mortality **following ACS**

Readability 1111 Applicability to practice 11111 **WOW!** factor 1111

This study evaluated the impact of diabetes on mortality following acute coronary syndroms (ACS).

Participants were taken from 11 TIMI study group clinical trials (1997-2006; n=62036). Of these, 17.1 % had diabetes.

The tolerability profile of valsartan plus aliskiren was similar to monotherapy.⁵

Cardiovascular disease Clinical DIGEST

NEW ENGLAND JOURNAL OF MEDICINE

Gastric bypass surgery reduces long-term CAD mortality

Readability 1111 Applicability to practice 1111 **WOW!** factor /////

- The long-term mortality of individuals who had undergone Roux-en-Y gastric bypass surgery was compared with that of severely obese controls in this retrospective cohort study.
- For data collected between 1984 and 2002, death rates were calculated for 7925 consecutive gastric bypass patients and 7925 individuals with a self-reported BMI \geq 35 kg/m².
- The mean duration of follow up was 7.1 years. Over the follow-up period, long-term mortality from any cause was 40 % lower among the individuals who underwent surgery compared with obese controls: 37.6 versus 57.1 deaths per 10 000 person-years, respectively (P < 0.001).
- The mortality rate due to coronary artery disease (CAD) was significantly reduced by 56 % in the bariatric surgery group compared with controls: 2.6 versus 5.9 deaths per 10 000 person-years, respectively (P=0.006).
- In addition, deaths from diabetesrelated causes were calculated to be 92 % less frequent after bariatric surgery than controls who had not undergone the procedure: 0.4 versus 3.4 deaths per 10 000 person-years (P=0.005).
- While this kind of gastric bypass surgery significantly reduced both overall mortality and mortality from diabetes and heart disease over 7 years, the rates of death from non-diseaserelated causes was significantly higher in the surgery group: 11.1 versus 6.4 deaths per person—years (P=0.04).

Adams TD, Gress RE, Smith SC et al (2007) Longterm mortality after gastric bypass surgery. *New England Journal of Medicine* **357**: 753–61

AMERICAN JOURNAL OF **MEDICINE**

Elevated blood qlucose at admission for STEMI increases in-hospital mortality

Readability Applicability to practice 1111 WOW! factor 1111

- Data for this study on the relationship between admission blood glucose levels and in-hospital mortality among people with STEMI treated with primary angioplasty were collected between 2002 and 2004.
- Participants were separated into quartiles dependent on admission blood glucose levels: <6.6 mmol/l (n=258); 6.7–7.8 mmol/l (n=244); 7.9– 10.0 mmol/l (n=246); and >10.1 mmol/l (n=232).
 - At baseline, mean age was 62 years, 27 % of participants were

IAMA

THE PLEASE

female, mean blood glucose was 9.1 ± 4.4 mmol/l and 16 % were known to have diabetes. All participants were treated with primary angioplasty.

- Overall, in-hospital mortality was 3.8 %. Mortality was significantly positively correlated with admission blood glucose levels (P<0.001). For each quartile, the in-hospital mortality was as follows: 0.4 % for the <6.6 mmol/l group; 2 % for the 6.7-7.8 mmol/l group; 2 % for the 7.9-10.0 mmol/l group; and 10 % for the >10.1 mmol/l group.
- However, while in-hospital mortality was higher in STEMI patients with diabetes compared with those without (5.2 % versus 3.5 %), this difference was not significant.
- The authors highlight that the impact on mortality from admission blood glucose levels is independent of cardiogenic shock and restoration of coronary flow.

Worthley MI, Shrive FM, Anderson TJ, Traboulsi M (2007) Prognostic implication of hyperglycemia in myocardial infarction and primary angioplasty. American Journal of Medicine 120: 643.e1-7

Systematic review supports aggressive targeting of **HDL-c** levels to

Readability //// Applicability to practice 111 WOW! factor

reduce CV risk

This study's objective was to provide a systematic review of the current and emerging clinical strategies for increasing HDL-c levels.

Data were collected using keywords from MEDLINE and the Cochrane database for studies conducted between 1965 and May 2007. Additionally, presentations made at major CV meetings held between 2003 and 2007 were reviewed, as well as the current guidelines from major CV societies and any ongoing trials reported on ClinicalTrials.gov.

- The 31 randomised trials included in this review suggested that optimised pharmacological and nonpharmacological strategies could increase HDL-c levels by 20-30%.
- Among the lifestyle modifications, moderate alcohol consumption was shown to increase HDL-c levels by 5-15%, aerobic exercise by 5-10% and tobacco cessation by 5-10 %. Weight loss was shown to increase HDL-c by 0.35 mg/dl per kilogram of weight lost.
- The most effective available medications to improve HDL-c were nicotinic acid (vitamin B₂), the combination pill (in women) and fibric acid derivatives.
- Data are still needed to prove that increasing HDL-c results in CV benefits independent of changes in LDL-c.
- It is suggested that ongoing clinical trials may elucidate specific pathways in HDL-c metabolism that may help expand our current treatment armamentarium.

Singh IM, Shishehbor MH, Ansell BJ et al (2007) High-density lipoprotein as a therapeutic target: a systematic review. *JAMA* **298**: 786–98

While in-hospital mortality was higher in STEMI patients with diabetes compared with those without (5.2% versus 3.5%), this difference was not significant.⁹

The mortality rate due to coronary artery disease (CAD) was significantly reduced by 56% in the bariatric surgery group compared with controls."