Clinical DIGEST 3

Cardiovascular journals

AMERICAN HEART JOURNAL



Comprehensive data on diabetes in patients at high risk of CAD

Early recognition and treatment of diabetes has potential benefit in reducing the incidence of vascular complications of type 2 diabetes.

This study investigated the prevalence, predictors and consequences of unrecognised diabetes in 3266 consecutive patients scheduled for coronary angiography.

The results revealed that 556 (17%) had known diabetes and 486 (18%) of those presumed not to have diabetes were diagnosed with diabetes, giving a total of 1042 (32%) with diabetes.

Almost half of those with diabetes were previously undiagnosed.

In half of the newly diagnosed patients, diabetes was only detectable by glucose challenge.

Independent predictors of unrecognised type 2 diabetes were C-reactive protein > 5 mg/l, arterial hypertension, BMI > 30, age ≥ 65 years old, and a family history of diabetes.

Patients with unrecognised type 2 diabetes had a significantly higher risk of CAD, and multivessel disease, and a borderline association with MI, compared with those without diabetes.

Oral glucose challenge was not superior to fasting glucose in predicting higher risk.

Findings indicate that in patients at high risk of CAD, scheduled for coronary angiography, screening for diabetes should be performed routinely to initiate preventive efforts.

Taubert G, Winkelmann BR, Schleiffer T et al (2003) Prevalence, predictors, and consequences of unrecognised diabetes mellitus in 3266 patients scheduled for coronary angiography. *American Heart Journal* **145**: 285–91

Coronary angiography: an opportunity for diabetes screening?



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he very simple study by Taubert and colleagues is an excellent illustration of the scale of the effect that diabetes has on patients treated by cardiologists. It is a shame, but a fact of life at the moment, that this sort of study is not published

in higher impact journals.

The authors evaluated 3266 consecutive patients referred for diagnostic coronary arteriography. The aim of the study was to: assess the prevalence of unrecognised diabetes mellitus in this cohort of patients; evaluate predictors of unrecognised type 2 diabetes in this population; and explore the impact of unrecognised diabetes on the incidence and severity of coronary artery disease (CAD).

After patients with known diabetes had been excluded, participants had a standard oral glucose tolerance test (OGTT) after an overnight fast. Diabetes was diagnosed when fasting plasma glucose was > 7.0 mmol/l or 2-hour glucose was > 11.1 mmol/l. CAD was defined as > 20% narrowing of any epicardial artery and multivessel disease as > 50% stenosis in two or all three coronary arteries or the left main stem artery.

The key findings of this study were as follows. Of 2710 patients previously undiagnosed with diabetes, almost 18% presented with newly diagnosed diabetes. Half were diagnosed by fasting glucose and the other half by OGTT. Of the whole cohort, 556 had diabetes already diagnosed, resulting in a total of almost 32% of the cohort having diabetes. There was a stepwise increase in the risk for CAD and multivessel disease and severity of CAD from people without diabetes to those with new diabetes to those with recognised diabetes. Body mass index, hypertension, C-reactive protein, age, and a positive family history of diabetes were independent predictors of unrecognised diabetes, but did not as an integrated index, perform well in discriminating between groups (C statistic 0.62).

The authors of the study and an accompanying editorial advocate the use of fasting glucose rather than the OGTT. This recommendation is debatable from the data presented. Clearly, patients with any suspicion of CAD should be screened for diabetes; in the study discussed it is surprising that so many reached the point of diagnostic coronary angiography without a fasting sugar being performed — a simple yet potentially invaluable test.

ARTERIOSCLEROSIS, THROMBOSIS AND VASCULAR BIOLOGY



Rosiglitazone lowers MMP levels in CAD patients with diabetes

Readability /
Applicability to practice /
WOW! factor / /

Matrix metalloproteinases (MMPs) are critically involved in the development of unstable plaques.

Recent research suggests that, in addition to their metabolic effects, thiazolidinediones (TZDs) might have anti-inflammatory effects in the vessel wall.

This study determined MMP levels in patients with coronary artery disease (CAD), with and without type 2 diabetes.

MMP-1, -8 and -9 serum levels were significantly higher in CAD patients with type 2 diabetes than in age-, sex, and BMI-matched CAD patients without diabetes.

Thirty-nine patients with diabetes and CAD were randomly allocated to rosiglitazone 4mg (twice daily) or placebo for 12 weeks.

Rosiglitazone, but not placebo, significantly reduced MMP-9 levels. Serum amyloid A and tumour necrosis factor-a (other biomarkers of arteriosclerosis) were also significantly reduced.

The findings suggest that rosiglitazone reduces inflammatory serum biomarkers in CAD patients with diabetes, and support the hypothesis that TDZs might be protective in the vessel wall.

Marx N, Froehlich J, Siam et al (2003) Antidiabetic PPARg-activator rosiglitazone reduces MMP-9 serum levels in type 2 diabetic patients with coronary heart disease. Arteriosclerosis, Thrombosis and Vascular Biology 23: 283–88

Cardiovascular disease Clinical DIGEST

4 Young people with diabetes have a calcified plaque burden similar to that of older people with diabetes. ⁹

AMERICAN HEART IOURNAL

Diabetes doubles the risk of early death after PCI

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

Patients with diabetes are known to have higher rates of restenosis, late MI, and late death after percutaneous coronary interventions (PCIs).

This study aimed to determine whether they were at greater risk of early death after PCI than those without diabetes, and whether inhospital survival for patients with diabetes was improving over time.

Rates of early death (defined as inhospital death) were determined in 25223 patients undergoing either elective or urgent PCI over a 20-year period (1980-99).

Elective PCI was performed on 17 341 and 4308 patients with and without diabetes, respectively, and urgent PCI on 2946 and 628 patients with and without diabetes.

There were twice as many inhospital deaths in patients with diabetes compared with those without diabetes (mortality rates 1.4% vs 0.8% after elective PCI, and 12.7% vs 6.9% after urgent PCI, respectively).

Inhospital deaths in patients with diabetes appeared to decrease over time in the elective cohort (P=0.007) but not in the urgent cohort (P=0.68).

Patients with diabetes thus have an increased risk of early death after PCI (elective and urgent) compared with patients without diabetes.

Improved inhospital survival after elective PCI was evident, but has yet to be realised in the urgent cohort.

Marso SP, Giorgi LV, Johnson WL et al (2003) Diabetes mellitus is associated with a shift in the temporal risk profile of inhospital death after percutaneous coronary intervention: an analysis of 25,223 patients over 20 years. American Heart Journal 145: 270-77

CIRCULATION V ple

Anti-inflammatory effect of TZDs

Readability /
Applicability to practice / WOW! factor

This randomised placebo-controlled trial examined the effect of rosiglitazone treatment on sCD40L serum levels in people with type 2 diabetes and coronary artery disease (CAD).

A total of 39 people with diabetes and CAD received rosiglitazone (4 mg BID) or placebo for 12 weeks.

Rosiglitazone treatment (but not placebo) significantly reduced sCD40L serum levels by 8.1% within the first 2 weeks, further decreasing them by 18.4% after 6 weeks and by 27.5% after 12 weeks

Treatment with PPARy-activating thiazolidinedione rosiglitazone reduces sCD40L serum levels in people with type 2 diabetes and CAD.

An anti-inflammatory and potentially antiatherogenic effect of thiazolidinediones is supported.

Marx N. Imhof A. Froehlich J et al (2003) Effect of rosiglitazone treatment on soluble CD40L in patients with type 2 diabetes and coronary artery disease. Circulation 107: 1954-7

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY



CAC levels are increased in people with diabetes

Readability Applicability to practice ✓ ✓ WOW! factor

This study examines the age and gender distribution of coronary artery calcium (CAC) in people with and without diabetes.

A total of 30 904 asymptomatic people stratified by their selfreported diabetes status, gender and age were screened for CAC by

electron-beam tomography (EBT).

People with diabetes (n=1075) had higher median CAC scores across all but two age groups (women 40-44 years old and men and women ≥ 70 years old) than people without diabetes (n=29 829).

The likelihood of having a CAC score in the highest age/gender quartile was 70% greater for people

Young people with diabetes have calcified plaque burden similar to that of older people with diabetes.

Hoff JA, Quinn L, Sevrukov A et al (2003) The prevalence of coronary artery calcium among diabetic individuals without known coronary artery disease. Journal of the American College of Cardiology 41: 1008-12

CIRCULATION



Changes in LDL size affect fenofibrates

Readability Applicability to practice 🗸 🗸 🗸 WOW! factor 1111

The Diabetes Atherosclerosis Intervention Study (DAIS) showed that treatment with fenofibrate decreases progression of coronary atherosclerosis in people with type 2 diabetes.

This study examined whether changes in LDL particle size contribute to the favourable effect of fenofibrate on coronary artery disease (CAD) progression in DAIS participants.

People with type 2 diabetes (n=418) were assigned to 200 mg micronised fenofibrate daily or placebo and followed up for a mean of 39.6 months.

Fenofibrate increased LDL particle size and HDL-C concentration and decreased plasma triglyceride, total and LDL-C, and lipoprotein B concentrations compared with placebo.

When the groups were combined small LDL size was associated with progression of CAD.

Changes in LDL size and plasma lipid levels account for part of the antiatherogenic effect of fenofibrate in type 2 diabetes.

Vakkilainen J, Steiner G, Ansquer JC et al (2003) Relationships between low-density lipoprotein particle size, plasma lipoproteins, and progression of coronary artery disease. *Circulation* **107**: 1733–37

interventions (elective and urgent) compared with patients without diabetes. 7

^C Patients with

diabetes have an

increased risk of

early death after

precutaneous

coronary

Cardiovascular disease

Clinical **DIGEST**

CIRCULATION

Fish reduces CHD in women with diabetes

Research has shown an inverse association between fish consumption and risk of CHD or sudden cardiac death in the general population, but limited data are available in people with diabetes.

This prospective study examined the association between fish and long-chain ω -3 fatty acid intake and incidence of CHD and total mortality in

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Mechanism of fluid retention after TZD still undefined

Fluid retention is an adverse effect of thiazolidinedione (TZD) which has been attributed to exacerbation of heart failure (HF).

This study sought to define the characteristics of fluid retention after TZD initiation in people with HF.

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Hyperglycaemia has a key role in vascular dysfunction

Readability Applicability to practice WOW! factor

This study examined if the type and severity of coronary vascular function associated with diabetes is similar in people with type 1 and type 2 diabetes.

The study group comprised 35 people with diabetes (18 type 1 and 17 type 2) who were free from

women with diabetes.

The study group comprised 5103 female nurses with type 2 diabetes who were free of CHD and cancer at baseline.

From 1980–96, 362 cases of CHD (141 CHD deaths and 221 nonfatal MI) and 468 deaths from all causes were documented.

A higher consumption of fish and ω -3 fatty acids was associated with a lower incidence of CHD and total mortality, even after adjusting for established cardiovascular risk factors. Hu FB, Cho E, Rexrode KM, Albert CM, Manson JE (2003) Fish and long-chain ω -3 fatty acid intake and risk of coronary heart disease and total mortality in diabetic women. *Circulation* **107**: 1852–7

A total of 111 people with diabetes and chronic systolic HF and treated with TZD were examined; 17.1% developed fluid retention which reversed after drug withdrawal and presented mainly as peripheral oedema.

More females and insulin users developed TZD-related fluid retention. No direct association between the risk of fluid retention and the severity of HF was observed.

Fluid retention after treatment with TZD in people with diabetes with chronic systolic HF occurs but the mechanism is undefined.

Wilson Tang WH, Francis GS, Hoogwerf BJ, Young JB (2003) Fluid retention after initiation of thiazolidinedione therapy in diabetic patients with established chronic heart failure. Journal of the American College of Cardiology 41: 1394–8

overt cardiovascular complications, and 11 age-matched healthy controls.

The increase in myocardial blood flow (MBF) with adenosine and during the cold pressor test was similar in people with type 1 and type 2 diabetes, but lower than in the control group.

The reduced endothelium-dependent and independent coronary vasodilator function in people with type 1 and type 2 diabetes suggests a key role of chronic hyperglycaemia in the pathogenesis of vascular dysfunction in diabetes.

Di Carli MF, Janisse J, Grunberger G, Ager J (2003) Role of chronic hyperglycemia in the pathogenesis of coronary microvascular dysfunction in diabetes. *Journal of the American College of Cardiology* **41**: 1387–93



Nurse counselling progammes are as successful as GP care

Prevention of CHD through lifestyle modification has been attempted through counselling and eduction in community and primary care settings but has not been uniformly successful.

In this randomised controlled trial, trained nurse counsellors delivered cognitive behavioural programmes which aimed to reduced cardiovascular risk in people with hypertension, type 2 diabetes or CHD.

The 212 participants were randomised to one of three groups.

The low intervention group consisted of monthly telephone contact for 1 year followed by a one face-to-face counselling session; the high intervention group comprised individual face-to-face counselling for 1 hour on a monthly basis for 1 year; the control group received usual care only.

Total fat intake fell by 9, 12 and 15% in the high, low and control groups, respectively at 12 months, and by 2, 10 and 5% at 18 months.

Total serum cholesterol fell by 3, 3 and 2% in the high, low and control groups, respectively at 12 months, and by 7, 5 and 8% at 18 months.

Change in fat intake and serum cholesterol did not significantly differ between the groups, and BMI increased in all groups with no significant changes related to the programme.

Programmes using nursecounsellors were not significantly more successful than usual care from GPs.

Wollard J, Burke V, Beilin LJ, Verheijden M, Bulsara MK (2003) Effects of a general practice-based intervention on diet, body mass index and blood lipids in patients at cardiovascular risk. *Journal of Cardiovascular Risk* 10: 31–40

⁽ A higher consumption of fish and ω-3 fatty acids was associated with a lower incidence of CHD and total mortality, even after adjusting for established cardiovascular risk factors. ³

¹ Programmes using nurse-counsellors were not significantly more successful than usual care from GPs. ³

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