Cardiovascular journals

Insulin treatment in CAD patients predicts CVD risk, but early glucose-lowering treatment helps!

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The Euro-Heart Survey on Diabetes and the Heart has reported that abnormal glucose regulation exists in at least 50% of patients with coronary artery disease (Bartnik et al, 2004). The same study also showed that people with existing diabetes or those newly diagnosed with the condition had a significant increase in mortality and cardiovascular events. This new report (summarised alongside) focuses on the mode of glucose-lowering therapy and its effect on cardiovascular events in coronary artery disease patients with existing or newly diagnosed diabetes.

Overall, 4676 individuals with coronary artery disease were assessed. Of these, 1425 had known diabetes and 452 were newly diagnosed with the condition. This is interesting in itself as it shows that over 40% of those with coronary artery disease have diabetes. At 1 year follow up, around 75% were on beta-blockers and statin therapy, 80% were using ACE inhibitors or ARBs and 90% were taking aspirin. Insulin-treated individuals had a 123% increased risk of mortality and 27% increased risk of a cardiovascular event compared to those on oral glucose-lowering therapies. Moreover, the hazard ratio for cardiovascular events events in people newly diagnosed with diabetes on glucose-lowering agents was only 0.22 compared with people newly diagnosed with diabetes not only using glucose-lowering agents.

What does this mean clinically? A straightforward answer cannot be given. However, it is reasonable to assume that those individuals on insulin would be expected to have a higher mortality with a longer duration of diabetes. Clinically, the most important finding is that patients not on a glucose-lowering agent had the higher mortality. Patients on metformin alone had a lower all-cause mortality, myocardial infarction, combined cardiovascular events and revascularization rates than those on sulphonylureas.

Patients with coronary artery disease often have, quite rightly, a great deal of attention paid to their statin treatment, aspirin, ACE inhibitors and further investigations such as coronary angiography. Early implementation of glucose-lowering therapy appears to be cardioprotective. It is therefore imperative that, firstly, we actually test patients with coronary artery disease (but not known diabetes) using a standard oral glucose-tolerance test to establish whether diabetes is present or not. If present, it should be treated. Current evidence recommends that metformin should be used.

Bartnik M, Rydén L, Ferrari R et al (2004) The prevalence of abnormal glucose regulation in patients with coronary artery disease across Europe. The Euro Heart Survey on diabetes and the heart. *European Heart Journal* **25**: 1880–90

EUROPEAN HEART JOURNAL

Earlier drug approach to glucose lowering may be beneficial

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

1 The Euro Heart Survey on Diabetes and the Heart enrolled 4676 people with coronary artery disease, of whom 1425 had existing and 452 had newly detected diabetes.

2 The impact of differing glucose-lowering treatments on cardiovascular events (death, myocardial infarction or stroke) was monitored.

3 People with diabetes who were using insulin had an adjusted 1 year hazard ratio for mortality of 2.23 and for cardiovascular events of 1.27 compared with those on oral glucose-lowering treatment.

4 Of those individuals newly diagnosed with diabetes, 77 began glucose lowering treatment and, by study-end, none of them died, whereas 25 of those people newly diagnosed with diabetes without glucose lowering treatment died.

5 The authors of the study conclude that insulin therapy may be linked to a more serious prognosis in those individuals with coronary artery disease and diabetes.

6 It is suggested that in people newly diagnosed with diabetes, an early pharmacological approach to glucose lowering may be beneficial.

Anselmino M, Ohrvik J, Malmberg K, Standl E, Rydén L on behalf of the Euro Heart Survey Investigators (2008) Glucose lowering treatment in patients with coronary artery disease is prognostically important not only in established but also in newly detected diabetes mellitus: a report from the Euro Heart Survey on Diabetes and the Heart. *European Heart Journal* **29**: 177–84

EUROPEAN HEART JOURNAL

BP strong predictor of type 2 diabetes in healthy women

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

1 A prospective cohort study evaluated the relationship of blood pressure (BP) and BP progression with the subsequent development of type 2 diabetes.

2 Participants comprised 38 172 women with no diabetes or cardiovascular disease at baseline; all were classified into four categories according to self-reported BP, and further classified according to progression to a higher BP category during the first 48 months of follow up.

3 In 10.2 years of follow up, 1672 women developed type 2 diabetes; results indicated that baseline BP and BP progression are independent and strong predictors of type 2 diabetes in initially healthy women.

Conen D, Ridker PM, Mora S, Buring JE, Glynn RJ (2007) Blood pressure and risk of developing type 2 diabetes mellitus: the Women's Health Study. *European Heart Journal* **28**: 2397–43

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

CAC progression is affected by glycaemic control

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

1 The relationship between cardiovascular risk factors, selected biomarkers and the progression of coronary artery calcification (CAC) in type 2 diabetes was evaluated.

2 A total of 398 people with type 2 diabetes and no prior coronary disease or symptoms were evaluated by CAC imaging.

3 Of these, 211 people had CAC at baseline; 118 people had CAC progression and three people had regression at a mean follow up of 2.5 years. A multivariate model indicated that independent predictors of CAC progression were baseline CAC, HbA_{1c} >7% and statin use.

4 Severity of baseline CAC and suboptimal glycaemic control are strong risk factors for CAC progression in type 2 diabetes.

Anand DV, Lim E, Darko D et al (2007) *Journal of the American College of Cardiology* **50**: 2218–25

AMERICAN JOURNAL OF CARDIOLOGY

MS may account for CVD risk in apparently healthy women

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

1 The importance of body mass index (BMI) and metabolic syndrome (MS) related risk factors in predicting future risk of cardiovascular disease (CVD) in women was investigated.

2 Women (n=25 626) aged ≥45 years with no CVD, cancer or diabetes at baseline were classified into six groups according to three BMI categories and the presence or absence of MS.

3 During the median 10-year follow up, 724 CVD events were recorded.

4 When compared to lean women with no MS, multivariate relative risks of CVD were 2.40 for lean women with MS, 1.08 for overweight women with no MS, 3.01 for overweight women with MS, 1.58 for obese women with no MS and 2.89 for obese women with MS; similar associations were found for total coronary heart disease.

5 The increased risk of CVD associated with BMI in apparently health women may be largely accounted for by MS.

Song Y, Manson JE, Meigs JB et al (2007) *American Journal of Cardiology* **100**: 1654–58

AMERICAN JOURNAL OF HYPERTENSION

Heart protection offered by dual blood pressure treatment

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

1 The impact of 12 months' treatment of dual blockade with candesartan and lisinopril vs high-dose lisinopril monotherapy on ambulatory pulse pressure (PP) in people with hypertension and type 2 diabetes was examined.

2 Participants comprised 51 people with type 2 diabetes and hypertension randomised for treatment with high-dose lisinopril or dual blockade with candesartan and lisinopril and followed up for 12 months.

3 Compared with lisinopril monotherapy, dual blockade treatment caused a highly significant reduction in 24-hour ambulatory pulse pressure levels, but the difference in the blood pressure (BP) lowering effect between the groups did not differ significantly for 24-hour systolic or diastolic BP.

4 Dual blockade treatment significantly lowered 24-hour systolic BP, but not 24-hour diastolic BP, but the reverse effect was seen in the lisinopril group.

5 The authors speculate that this finding may translate into more protection of the heart from dual treatment than ACE inhibition alone, and suggest further studies are carried out.

Knudsen ST, Andersen NH, Poulsen SH et al (2008) Pulse pressure lowering effect of dual blockade with candesartan and lisinopril vs. high-dose ACE inhibition in hypertensive type 2 diabetic subjects: a CALM II study post-hoc analysis. *American Journal of Hypertension* **21**: 172–76

> *'Dual blockade treatment significantly lowered 24-hour systolic BP, but not 24-hour diastolic BP, but the reverse effect was seen in the lisinopril group.'*

"Aldosterone blockade treatment could help prevent renal injury in hypertensive people with aldosterone breakthrough."

"Type 2 diabetes and hypertension increase the risk of CHD independently, and when combined the risk is dramatically increased, particularly in women."

EUROPEAN HEART JOURNAL

Type 2 diabetes combined with hypertension increases CHD risk dramatically

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

1 The joint effects of history of hypertension at baseline and type 2 diabetes at baseline and during follow up on the incidence of CHD and CHD mortality were examined.

2 Participants comprised 49 775 people aged 25–74 years with no history of stroke and CHD.

3 The multivariable-adjusted hazard ratios of CHD incidence in men and women, respectively, when compared to those without either were: hypertension I (1.25, 1.52; defined as BP<160/95mmHg); hypertension II (1.69, 2.37; BP≥160/95mmHg); incident diabetes during follow-up (1.25, 2.45); hypertension I and incident diabetes (1.83, 3.78); hypertension II and incident diabetes (1.85, 4.56); history of diabetes at baseline (2.39, 5.63); hypertension I and history of diabetes (2.15, 6.10); and hypertension II and history of diabetes (3.31, 7.41).

4 The impact of CHD mortality was almost the same between the different groups in the study.

5 Type 2 diabetes and hypertension increase the risk of CHD independently, and when combined the risk is dramatically increased, particularly in women.

Hu G, Jousilahti P, Tuomilehto J (2007) Joint effects of history of hypertension at baseline and type 2 diabetes at baseline and during follow-up on the risk of coronary heart disease. *European Heart Journal* **28**: 3059–66

AMERICAN JOURNAL OF HYPERTENSION

Aldosterone breakthrough equal in candesartan or valsartan treatment

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

1 A total of 95 people with diabetes and hypertension were treated with candesartan or valsartan for 15 months, and measurements were taken at 3, 6, 12 and 15 months.

2 Plasma aldosterone concentration significantly decreased in each group, but eventually increased in 21 participants (11 candesartan and 10 valsartan).

3 Urinary albumin excretion (UAE) decreased in people with or without aldosterone breakthrough at 6 months, but increased at 15 months of treatment in people with aldosterone breakthrough. Further treatment with spironolactone reduced UAE in this group.

4 Aldosterone blockade treatment could help prevent renal injury in hypertensive people with aldosterone breakthrough.

Yoneda T, Takeda Y, Usukura M (2007) Aldosterone breakthrough during angiotensin II receptor blockade in hypertensive patients with diabetes mellitus. *American Journal of Hypertension* **20**: 1329–33

JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

Another option for the statin intolerant

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

1 Researchers investigated the effect of ezetimibe (10mg/day) alone or in combination with atorvastatin (10mg twice/week) on hypercholesterolemia in 56 people at high risk and intolerant to daily statin use.

2 Ezetimibe monotherapy was well tolerated and induced a mean reduction in LDL cholesterol of 20% at the third month, but only 9% met LDL cholesterol goals.

3 Atorvastatin was added and the combination reduced LDL cholesterol by 37% compared with baseline, and 84% of participants reached the LDL cholesterol targets.

4 For high-risk people intolerant to daily statin monotherapy, the combination of ezetimibe and a statin could be a treatment option.

Athyros VG, Tziomalos K, Kakafika AI, Koumaras H, Karagiannis A, Mikhailidis DP (2008) Effectiveness of ezetimibe alone or in combination with twice a week atorvastatin (10 mg) for statin intolerant high-risk patients. *American Journal of Cardiology* **101**: 483–85

EUROPEAN HEART JOURNAL

CV mortality risk is not determined by diabetes treatment

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

1 The impact of glucose lowering treatment on prognosis in people with diabetes and myocardial infarction (MI) was investigated.

2 A total of 1181 people with type 2 diabetes discharged after MI were followed for a median of 2.1 years and the impact of various treatment regimens analysed.

3 Controlling for confounding factors showed that cardiovascular mortality was not influenced by metformin, sulphonylureas or insulin.

4 The risk of non-fatal MI and stroke significantly increased in people on insulin, but was lower for those on metformin and unchanged with sulphonylureas.

Mellbin LG, Malmberg K, Norhammar A et al (2008) *European Heart Journal* **29**: 166–76