Diabetes journals

Using stents to reduce restenosis

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The cardiovascular burden of diabetes is well established. Coronary artery disease is more prevalent, more extensive, and more lethal in patients with diabetes than in their non-diabetic counterparts.

Because of very high event rates, pharmacological therapies for coronary artery disease are, if anything, more effective in patients with diabetes compared to those without the disease, with a larger reduction in absolute risk. The same is not true for interventional procedures, and the outcomes following coronary artery bypass grafting and coronary angioplasty are less successful in those with diabetes.

In patients with diabetes, coronary angioplasty has been associated with a higher rate of restenosis, requiring further intervention. Stents are now frequently used to try and reduce restenosis. The timely meta-analysis by Gilbert et al, summarised on the right, compares the rates of restenosis following coronary angioplasty with stenting between patients with and without diabetes. Six studies were identified that met the specified criteria for the meta-analysis.

The average restenosis rate was higher in patients with diabetes, but these people were older, and when the restenosis rates were controlled for age, a much smaller restenosis rate was evident in people with diabetes.

There have been rapid advances in coronary angioplasty, and the current best treatment involves the use of drug-eluting stents. It is still early days, but the use of these devices is said to have virtually eliminated the development of restenosis.

In the future, a new meta-analysis will no doubt compare restenosis rates among patients with diabetes receiving coronary angioplasty with these drug-eluting stents.

DIABETES CARE

Reassessing the effect of diabetes on restenosis rates

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

1 In patients without diabetes, coronary angioplasty is an established method of treating coronary artery disease. After treatment, restenosis rates are typically 25–50%. Furthermore, stenting has been shown to be an effective method of reducing restenosis.

2 For patients with diabetes, it has previously been reported that restenosis rates are higher (47–71%). Various studies have been carried out to assess whether stenting is also advantageous for people with diabetes, but results were inconclusive.

3 This study aimed to assess the overall effect of diabetes on angiographic restenosis rates in patients undergoing stenting.

4 The meta-analysis combined data from six studies previously published in the medical literature. The researchers investigated the relationship between age and restenosis rate, the proportion of the individuals who were male and the number of idividuals who were using insulin.

5 On average, rates were higher among patients with diabetes than those without the disease. However, after controlling for age, the odds ratio of restenosis associated with diabetes decreased.

6 The researchers therefore concluded that, although diabetes is a risk factor for restenosis, its effect has been exaggerated in the previously published literature.

Gilbert J, Raboud J, Zinman B (2004) Meta-analysis of the Effect of Diabetes on Restenosis Rates Among Patients Receiving Coronary Angioplasty Stenting. *Diabetes Care* **27**: 990–94

DIABETIC MEDICINE

Diabetes and increased muscular artery stiffness

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

1 Arterial stiffness and endothelial vascular dysfunction are observed in insulin-resistant conditions such as type 2 diabetes.

2 At present, it is not known whether insulin-resistance is directly linked to these symptoms, or whether it contributes indirectly through other aspects of the metabolic syndrome.

3 This study compared muscular arterial stiffness (measured non-invasively by monitoring carotid-radial pulse wave velocity [crPWV]) in the healthy offspring of people with type 2 diabetes with a control group. Furthermore, the researchers measured serum levels of intercellular celluar adhesion molecule 1 (sICAM-1; a marker of endothelial signalling pathway activation).

4 The offspring and control groups were carefully matched for various parameters, including age, BMI, waist circumference, and systolic blood pressure. However, in the offspring of the patients with type 2 diabetes, crPWV measurements were 10% higher than the control group. The offspring also exhibited higher concentrations of sICAM-1, closely correlated with crPWV measurements.

5 The researchers concluded that people at higher risk of developing diabetes exhibited vascular dysfunction in the form of increased muscular arterial stiffness at an early stage. This finding might be a secondary effect of restricted activation of endothelial signalling pathways associated with insulin resistance.

McEleavy OD, McCallum RW, Petrie JR, et al (2004) Higher carotid-radial pulse wave velocity in healthy offspring of patients with Type 2 diabetes. *Diabetic Medicine* **21**: 262–66

'The researchers reviewed literature on the STOP-NIDDM trial and assessed them with respect to bias or contradictory information.'

'The authors discovered significant shortcomings in the STOP-NIDDM study; in particular, biases in patient selection, data analysis and potentially also sponsorship.'

DIABETOLOGIA

STOP-NIDDM data reported to be seriously flawed

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

1 Cardiovascular complications are the major health threat to people with diabetes.

2 A relationship between post-prandial glycaemia and the risk of developing diabetes, hypertension and cardiovascular complications has been positively indicated by epidemiological studies.

3 Therefore, if a causal link existed between these factors, treatments that enable a reduction in post-prandial glycaemia could be of major significance for future treatment of patients with and without diabetes.

4 In the recent STOP-NIDDM (Study to Prevent Non-Insulin Dependent Diabetes Mellitus) study, the drug Acarbose was used to lower post-prandial glycaemia, and a significant reduction in the risk of diabetes, hypertension and cardiovascular complications was reported. This study aimed to test the validity of these findings.

5 The researchers reviewed literature on the STOP-NIDDM trial and assessed them with respect to bias or contradictory information.

6 The authors discovered significant shortcomings in the STOP-NIDDM study; in particular, biases in patient selection, data analysis and potentially also sponsorship.

7 The paper concludes that the trial is significantly flawed, and that Acarbose has no proven effect on reducing the risk of diabetes, hypertension or cardiovascular complications.

Kaiser T, Sawicki PT (2004) Acarbose for prevention of diabetes, hypertension and cardiovascular events? A crtical analysis of the STOP-NIDDM data. *Diabetologia* **47**: 575–80

DIABETES, OBESITY AND METABOLISM

Pioglitazone efficacy linked to adiponectin

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

1 A positive correlation between insulin sensitivity index and plasma level of adiponection (a protein found in fat tissue) has previously been reported.

2 This study aimed to test the hypothesis that pioglitazone would be more effective in patients with diabetes who have a low plasma concentration of adiponectin and impaired insulin sensitivity.

3 Glycated albumin levels were recorded as a measure of glycaemic control in patients with diabetes treated with pioglitazone over an eight-week period. Before-treatment levels of adiponection were significantly lower in those patients whose glycated albumin concentrations were decreased by more than 10% over the study.

4 Lower plasma adiponectin concentrations promote the pioglitazone-mediated improvement of glycaemic control.

Hiramatsu S, Tajiri Y, Karashima T (2004) Lower plasma adiponection concentration predicts the efficacy of pioglitazone in diabetic patients. *Diabetes, Obesity and Metabolism* **6**: 231–33

DIABETES CARE

CHD death linked to diabetes duration

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

1 People with type 2 diabetes are 2–3 times more likely to develop coronary heart disease than those without.

2 This study aimed to assess the importance of diabetes duration on the risk of death from CHD among people with diabetes.

3 Original and offspring cohorts of the Framingham Heart Study who had diabetes were assessed for the duration of the disease. Hazard ratios of CHD-related events or death were calculated.

4 After adjusting for age, sex and known CHD risk factors, it was found that, for each 10-year duration of diabetes, the risk of developing CHD increased by a factor of 1.38. For CHD death, the risk increase was 1.86.

5 The researchers concluded that the duration of diabetes leads to an increase in the risk of death from CHD.

Fox CS, Sullivan L, D'Agostino RB, Wilson PWF (2004) The significant effect of diabetes duration on coronary heart disease mortality. *Diabetes Care* **27**: 704–08

DIABETIC MEDICINE

Spironolactone and cilazapril: effect on albuminuria

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

1 While many studies focus on the eplerenone, a new aldosterone antagonist, there is still much to be learnt from research on the parent drug spironolactone.

2 The researchers aimed to quantitatively study the drug's effects.

3 A randomised study of 60 female patients with diabetes, albuminuria and hypertension was carried out. Patients were treated with either spironolactone or cilazapril for 24 weeks. Both groups then received a combination treatment for 24 weeks.

4 Cilazapril was not as effective as spironolactone at reducing albuminuria, and the combined treatment was more effective than either drug alone.

Rachmani R, Slavachevsky I, Amit M et al (2004) The effect of spironolactone, cilazapril and their combination on albuminuria in patients with hypertension and diabetic nephropathy is independent of blood pressure reduction: a randomized controlled study. *Diabetic Medicine* **21**: 471–75

DIABETES CARE

Risk associated with percutaneous coronary intervention

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

1 Previous studies have elucidated that patients with diabetes who undergo percutaneous transluminal coronary angioplasty have reduced long-term survival compared with patients without diabetes.

2 Since then percutaneous coronary intervention (PCI) techniques including the use of coronary stents and the introduction of inhibitors of the platelet glycoprotein (GP) IIb/IIIa receptor have become standard.

3 Therefore, the study aimed to assess whether patients with diabetes still have reduced long-term survival prospects after PCI.

4 Information on patients undergoing PCI was contributed by three hospitals. After a mean follow-up period after PCI of 3 years, the mortality rate in patients with diabetes was higher than those without (13% compared to 8%). After adjusting for baseline condition differences, diabetes remained a significant lethal risk factor

4 Following PCI, patients with diabetes continue to have worse long-term survival than those without the disease.

Wilson SR, Vakili BA, Sherman W, Sanborn TA, Brown DL (2004) Effect of diabetes on long-term mortality following contemporary percutaneous coronary intervention. *Diabetes Care* **27**: 1137–42

DIABETIC MEDICINE

Rosiglitazone benefits patients with persistent IGT

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

1 Previous studies have shown that rosiglitazone promotes better glycaemic control in patients with type 2 diabetes.

2 This study examined the effects of the drug on patients with persistent impaired glucose tolerance.

3 Rosiglitazone or matching placebo were admistered to patients over a 12-week period. Insulin sensitivity, blood pressure, and OGTT test results were monitored.

4 As in patients with type 2 diabetes, rosiglitazone successfully improved whole body insulin sensitivity in patients with persistent IGT. The results of OGTT and meal tolerance tests were also improved.

Bennett SMA, Agrawal A, Elasha H et al (2004) Rosiglitazone improves insulin sensitivity, glucose tolerance and ambulatory blood pressure in subjects with impaired glucose tolerance. *Diabetic Medicine* **21**: 415–22

DIABETIC MEDICINE

Benefits of ECG and scintigraphy testing

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

1 Previous studies indicate that silent coronary stenoses and silent myocardial ischaemia (SMI) are common in patients with diabetes, and may explain their poor prognosis for coronary death.

2 Successfully detecting SMI is therefore a major challenge, and this study aimed to investigate the effectiveness of a myocardial scintigraphy test followed by an electrocardiogram (ECG) test.

3 The above tests were performed over a period of approximately 3 years on patients with diabetes and no history of myocardial infarction.

4 The combined tests were effective at predicting cardiac events and enabled the identification of more patients with coronary stenoses. However, routinely performing both tests may not be feasible.

Cosson E, Paycha F, Paries J eta l (2004) Detecting silent coronary stenoses and stratifying cardiac risk in patients with diabetes: ECG stress test or exercise myocardial scintigraphy? *Diabetic Medicine* **21**: 342–48

DIABETES RESEARCH AND CLINICAL PRACTICE

The lethal effects of low heart rate variability

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

1 Sudden death among patients with type 2 diabetes has been previously reported and ascribed to conditions including long Q-T syndrome and coronary atherosclerosis.

2 Low heart rate variability (HRV) has also been implicated as a risk factor, although no clear association has been previously demonstrated.

3 This study aimed to test the association between sudden cardiac death (SCD) and low HRV in patients with and without type 2 diabetes. Furthermore, the researchers tested whether low HRV is a predictive of SCD in people with type 2 diabetes

4 Oral glucose tolerance tests and electrocardiography were performed on nearly 9000 people aged 35–69. HRV was calculated by measuring the variance of 100 R-R intervals on ECG traces.

5 SCD occurred in 56 of the tested individuals (33 of whom had diabetes) in an average time period of just over 5 years.

6 After correction for various factors (including blood pressure, smoking history, age, gender and cholesterol), it was found that, in patients with diabetes, those wih a low HRV (<2.2%) were more than twice as likely to die from SCD compared to those with a higher HRV (≥2.2%) .

7 This study is the first to demonstrate that low HRV is a risk factor for SCD in people with type 2 diabetes.

Kataoka M, Ito C, Sasaki H, Yamane K, Kohno N (2004) Low heart rate variability is a risk factor for sudden cardiac death in type 2 diabetes. *Diabetes Research and Clinical Practice* **64**: 51–58

'This study aimed to test the association between sudden cardiac death and low heart rate variability in patients with and without diabetes.'

'This study is the first to demonstrate that low heart rate variability is a risk factor for sudden cardiac death in people with type 2 diabetes.'