News from the American Heart Association Scientific Sessions 2012

Highlights of the American Heart Association 2012 meeting held on 3rd–7th November 2012 in Los Angeles, USA, included a win for surgery in people with diabetes and multi-vessel disease, and intriguing results for colchicine and chelation therapy.

FREEDOM: CABG beats PCI in diabetes patients with multi-vessel disease

Coronary artery by-pass graft (CABG) surgery was associated with better outcomes than percutaneous coronary intervention (PCI) in patients with diabetes with multi-vessel coronary artery disease in the FREEDOM (Future Revascularization Evaluation in Patients With Diabetes Mellitus: Optimal Management of Multi-vessel Disease) trial.

Senior FREEDOM investigator, Dr Valentin Fuster (Mount Sinai School of Medicine, New York, USA), said the results (**table 1**) would change practice. He estimated that patients in this study represent about a quarter of patients undergoing PCI.

In the study, which was sponsored by the US National Heart, Lung, and Blood Institute, some 1,900 patients with diabetes, the majority of whom had three-vessel disease, were randomised to treatment with CABG surgery or PCI with drug-eluting stents. Dual antiplatelet therapy was recommended for at least 12 months, and patients were followed for a median of 3.8 years.

Table 1. FREEDOM: primary end point five years after randomisation

Outcome	PCI (%)	CABG (%)	P value
Primary end point (all-cause death, nonfatal MI, or nonfatal stroke)	26.6	18.7	0.005
All-cause death	16.3	10.9	0.049
MI	13.9	6.0	<0.001
Stroke	2.4	5.2	0.03
Cardiovascular death	10.9	6.8	0.12

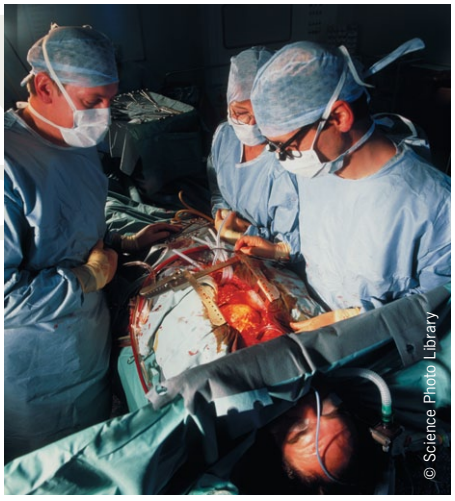
Key: CABG = coronary artery bypass graft; MI = myocardial infarction; PCI = percutaneous coronary intervention

Those undergoing bypass surgery had lower rates of death and myocardial infarction (MI). Although there were more strokes in the CABG group, this was not enough to negate the net significant benefits of fewer deaths and heart attacks, Dr Fuster said.

Previous studies in this group of patients also showed that bypass was favourable compared to PCI, but many of those studies did not use drug-eluting stents. "The cardiology community didn't know if that held true when compared exclusively to newer, drug-covered stents," said Dr Fuster, "so we are very excited to find the answer."

The researchers observed no significant interaction based on SYNTAX score, with the absolute difference in the primary end point between PCI and surgery similar in patients with a low, intermediate, and high SYNTAX score. Given the wide variability of the patients enrolled in FREEDOM, as evidenced by the wide distribution of SYNTAX scores at baseline, the trial represents real-world practice and should be considered a strength of the study, according to the investigators.

In an accompanying editorial (*N Engl J Med* 2012; doi: 10.1056/NEJMe1212278) to the study (doi: 10.1056/NEJMoa1211585), Dr Mark Hlatky (Stanford University School of Medicine, California, USA) says the controversy surrounding the optimal revascularisation strategy in patients with diabetes "should finally be settled". The results of the FREEDOM study "suggest that patients with diabetes ought to be informed about the potential survival benefit from CABG for the treatment of multi-vessel disease".



Cost-effective

CABG was also said to be cost-effective for these patients according to a cost analysis of the FREEDOM trial, presented by Dr Elizabeth Magnuson (Saint Luke's Mid America Heart Institute, Kansas City, USA). The cost of CABG surgery was calculated at US $34,467 while the cost of PCI was US $24,845, although the gap between the two narrowed from US $8,622 to US $3641 by year five.

Over the course of a lifetime, assuming a life expectancy of 12 years following the procedure, CABG was associated with 0.66 quality-adjusted life-years (QALYs) gained and approximately higher costs of US $5,400 per patient. This resulted in an incremental cost-effectiveness ratio of US $8,132 per QALY gained.

Dr Magnuson said that, even by the most conservative estimates, limiting the cost-effectiveness analysis to the five-year study period, the incremental cost-effectiveness ratio was approximately US $27,000 per QALY gained.

Flaxseed reduces blood pressure

Patients with peripheral arterial disease (PAD) who added flax seeds to their diets experienced drops in blood pressure of around 10 mmHg systolic and 7 mmHg diastolic after six months, according to a new study.

Presenting the results, Dr Delfin Rodriguez (University Hospital Holguin, Cuba) said: "This is the largest reduction of blood pressure ever shown by any dietary intervention". Such reductions would be expected to result in around a 50% fall in the incidence of stroke and a 30% reduction in myocardial infarction, he added.

Dr Rodriguez noted that around 75% of PAD patients have hypertension. Subgroup analyses of only those PAD patients with hypertension showed an even greater reduction in blood pressure.

"Flaxseed represents a particularly attractive strategy for controlling hypertension in economically disadvantaged communities and countries, and its blood pressure lowering effects compare favourably with those of antihypertensive drugs and lifestyle modifications, such as a low-salt diet and weight loss," he said.

The researchers randomised 110 patients with PAD to milled flaxseed (30 g/day) in the form of bagels, muffins, and buns or placebo products, made from wheat with a similar flavour, for one year.

The flaxseed group exhibited a two-fold increase in plasma alpha-linolenic acid and a 10-fold increase in enterolactone levels, which may have effected blood pressure.

LoDoCo: colchicine effective for secondary prevention

More data suggesting that colchicine, long used to treat gout and familial Mediterranean fever, is useful for the secondary prevention of cardiac events in patients with stable coronary disease, has come from the LoDoCo (Low-Dose Colchicine) study.

The study randomised 532 patients with stable coronary artery disease (CAD) to low-dose colchicine or placebo for a minimum of two years. During a median follow-up of three years, the primary outcome (acute coronary syndrome [ACS], out-of-hospital cardiac arrest, or non-cardioembolic ischaemic stroke) was seen in 16% of placebo patients versus 5.3% of those on colchicine, a significant 67% relative risk reduction. The number needed to treat to prevent one primary clinical outcome was 11.

Presenting the data, Dr Stefan Nidorf (Heart Research Institute of Western Australia, Perth) explained that colchicine has been shown to be effective in preventing neutrophil-mediated inflammation, as documented by its efficacy in the treatment of gout. As neutrophils are activated in culprit lesions of patients with ACS, it was proposed that inhibiting neutrophil function might reduce the risk of plaque instability and subsequently clinical instability in patients with cardiovascular disease.

Discussant of the study, Dr Shinya Goto (Tokai University School of Medicine, Kanagawa, Japan) pointed out that gastrointestinal side effects may limit the drug's use to some extent, noting that 11% of patients dropped out of the trial mainly due to these issues.

TACT: chelation therapy shows benefit post MI

The biggest surprise of the meeting was the finding that chelation therapy was associated with improved clinical outcomes in patients after an acute myocardial infarction (MI) in the randomised controlled TACT (Trial to Assess ChelationTherapy) trial.

The trial, sponsored by the US National Institutes of Health, randomised 1,708 patients to infusions of a chelation solution which included EDTA, ascorbic acid, magnesium chloride, potassium chloride, sodium bicarbonate, B vitamins, procainamide, standard heparin, and water, or placebo (saline and glucose). About 65% of the patients completed all 40 prescribed infusions; 76% completed at least 30.

Results (**table 1**) showed that the primary end point – a composite of all-cause mortality, MI, stroke, coronary revascularisation, and hospitalisation for angina – was reduced by 18% in the chelation group. The effect seemed to be stronger in diabetics.

Presenting the data, Dr Gervasio Lamas (Mount Sinai Medical Center, Miami, USA) said that chelation therapy "showed some evidence of a potentially important treatment signal in post-MI patients already on evidence-based therapy," and "appears to be safe" as given and monitored in the trial. But he added that clinical use of chelation therapy could not be recommended at this time based on these unexpected results.

Table 1. TACT: hazard ratio for primary end point with chelation therapy versus placebo

	HR (95% CI)	P value
All patients	0.82 (0.69–0.99)	0.035
Patients with diabetes	0.61 (0.45–0.83)	0.002
Patients without diabetes	0.96 (0.77–1.20)	0.725

Key: CI = confidence interval; HR = hazard ratio

However, he did suggest that such treatment should be pursued with additional research. In a statement, the American Heart Association said that TACT raised many questions

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