EDITORIAL

Is surgery still the preferred option for coronary revascularisation in diabetics with multivessel coronary disease?

A Kapur, I S Malik

In patients with diabetes, the choice of optimal revascularisation strategy—bypass surgery or percutaneous coronary intervention—remains controversial.

In the UK, 2.5 million people have diabetes. Three quarters of all deaths in patients with diabetes are caused by coronary artery disease. It has been projected that 25–30% of all revascularisations will be in patients with diabetes by 2010. The choice of optimal revascularisation strategy—coronary artery bypass graft (CABG) surgery or percutaneous coronary intervention (PCI)—remains controversial.

CABG is considered preferable in diabetic patients with multivessel coronary artery disease based primarily on post hoc analysis of the BARI study. While some other studies have also performed subgroup analyses in patients with diabetes, in none was that analysis prespecified. In light of recent developments in the field of revascularisation, with the advent of glycoprotein (GP) IIb/IIIa inhibitors, use of stents, and the development of off bypass and minimally invasive surgery, the data available to guide treatment in patients with diabetes are in need of reassessment.

CABG VERSUS PCI: THE MAJOR TRIALS

Several trials have compared an initial treatment strategy of PCI with a strategy of CABG in patients with multivessel coronary disease. Most of the data currently available relate to comparisons made in the late 1980s and early ‘90s although several new studies have been published recently. While not identical, each trial randomised patients who were considered suitable for both forms of revascularisation. Results have suggested that there is no difference between the two strategies in terms of mortality, non-fatal MI, and stroke although the rates of additional revascularisation were much higher in the PCI groups. PCI usually requires a short admission followed by an early return to work, but is associated with a 30% risk of further revascularisation during the first six months of follow up. Conversely, CABG is more invasive and requires a longer recovery.

IS THE PATIENT WITH DIABETES MELLITUS DIFFERENT?

It has been suggested that there might be a difference in outcome of CABG versus PCI in the subset of patients with diabetes mellitus. There are specific issues to confront in this group of patients including the problems of small calibre vessels, more extensive distal disease, greater left ventricular dysfunction, and altered platelet function. Moreover, numerous studies have shown that diabetes increases the risk of restenosis after successful PCI. At present, clinicians tend to favour surgery for diabetics requiring coronary revascularisation.

The BARI trial recruited 1829 patients with multivessel disease between 1988 and 1991. After five years, mortality (10.7% in the CABG arm v 13.7% in the PCI arm, p = 0.19) and the combined rate of death and non-fatal myocardial infarction (19.6% CABG v 21.3% PCI, p = 0.84) were similar in the two groups. Although additional revascularisation was required more often in the PCI group (8% CABG v 54% PCI, p < 0.001), 69% of PCI patients avoided CABG during this period and 45% required only one further PCI. After PCI, patients returned to work an average of five weeks earlier than those undergoing CABG, and there was no difference in long-term employment status.

The cohort of 1829 patients in BARI included 336 with diabetes. This subgroup only became a defined group for analysis part way through recruitment. While these patients were not stratified in the randomisation process, their baseline characteristics were similar. The five year mortality was 19.4% among 180 patients assigned to CABG and 34.5% among 173 patients assigned to PCI (p < 0.003). Seven year mortality in the PCI group was also higher compared to CABG (23.6% CABG v 44% PCI at seven years, p = 0.001). Despite this being a post hoc analysis the PCI and CABG arms were well matched and crossover between arms was minimal. However, the outcome of 339 non-randomised diabetics in the registry did not suggest a dramatic advantage of CABG over PCI. In addition: (1) registry data indicate that only 16%...
ADJUNCTIVE TREATMENTS IN REVASCULARISATION

While both CABG and PCI have advanced technically in recent years, the field of coronary angioplasty in its routine practice has changed more substantially than has CABG. The STRESS and BENESTENT trials demonstrated that in selected patients coronary stents reduce the risk of restenosis and subsequent clinical events.20,21 These benefits may be most pronounced in diabetic patients.22 The advent of drug eluting stents may reduce restenosis rates further.

New pharmacological interventions also appear to improve the results of PCI. Several trials have shown that abciximab and other GP IIb/IIIa receptor antagonists improve outcome, especially when combined with stents.23,24

Advances in medical treatment, such as aggressive lipid lowering with statins and the use of clopidogrel, may have differential effects post-PCI as opposed to post-CABG. The I-2D trial will compare aggressive medical treatment to revascularisation (PCI or CABG) in patients with diabetes, but will not compare PCI to CABG directly.

ADJUNCTIVE ANTIPLATELET TREATMENT IN DIABETIC PATIENTS

The role of adjunctive periprocedural pharmacotherapy has been examined in several trials, including the EPIC, EPILOG, and EPISTENT trials. In the EPILOG trial, the outcomes of 638 diabetic patients were compared to 2154 non-diabetic patients.25 Despite greater comorbidity, diabetic patients treated with abciximab during PCI suffered the same rate of in-hospital death, myocardial infarction, and urgent revascularisation as non-diabetic patients (7.1% vs 7.5%, p = ns). At six months, treatment reduced the composite of death or myocardial infarction to 8.8% in diabetic patients and 7.4% in non-diabetics (p = ns), significantly better in both groups when compared to placebo.

In the more recent EPISTENT study, the composite of death, myocardial infarction, or target vessel revascularisation was reduced from 25% to 13% (a 48% reduction, p = 0.005) in diabetics treated with abciximab and stenting as opposed to stenting alone.26 The combined death and myocardial infarction rate was reduced from 16.3% to 6.8% at one year, with cardiac event rates in the treated diabetic population being reduced to the level seen in non-diabetic patients.27 A pooled analysis of three abciximab trials (EPIC, EPILOG, and EPISTENT) showed that abciximab decreased the one year mortality in diabetics from 4.5% to 2.5% (p = 0.031) and in non-diabetic patients from 2.6% to 1.9% (p = 0.1).28

The potential role of other GP IIb/IIIa inhibitors such as eptifibatide and tirofiban remains to be determined in diabetics.29 The use of abciximab and stents among patients with diabetes undergoing PCI appears to abolish the excess risk of such procedures in patients with diabetes. Whether the results achievable with this regimen are comparable to those achieved with modern coronary artery bypass grafting can only be answered by a prospective randomised trial.

CONCLUSION

An evidence base for the preferred mode of coronary revascularisation (CABG or PCI) in patients with diabetes is lacking. Such data as are available are now more difficult to evaluate in the setting of recent major advances in adjunctive treatment for PCI. The advent of the GP IIb/IIIa inhibitors and drug eluting stents in particular may revolutionise percutaneous intervention in diabetics.

There is an obvious need for a head-to-head trial to establish whether these advances have abolished the outcome gap that was seen in the BARI trial. If one accepts that a higher rate of repeat revascularisation is a reasonable price to pay for a less invasive procedure, then the new trial has to show that “optimal PCI” is not inferior to “up-to-date CABG” in terms of the hard end points of death, non-fatal myocardial infarction, and stroke. The UK based CARDia trial addresses these
questions for the first time, and will begin recruitment in the near future. It may help provide the answer to the question posed in the title of this editorial.

References


Werner Forssmann

Werner Forssmann (1904–1979) was the pioneer of cardiac catheterisation in man. In 1929, at the age of 23, while doing his surgical training at Eberswalde, a small town near Berlin, he introduced a ureteral catheter into his own right atrium. Using a mirror he advanced the catheter under fluoroscopic control and then climbed the stairs to the x-ray department where a chest film was taken. Forssmann had two objects in mind. Firstly to use this technique in emergencies to administer drugs directly into the heart, and secondly “to study the heart and for diagnosis”. Later he catheterised his own heart on six more occasions. He also injected contrast material, Uroselectan, in 1931 in an attempt to produce an angiogram. By 1932 pulmonary angiography using a catheter in the right atrium had been done in Lisbon, Paris, and Buenos Aires.

Cardiac catheterisation made it possible to measure the cardiac output using the Fick principle and this important advance was first made in Prague in 1930. The development of Forssmann’s technique owed much to the work in New York of André Cournand and Dickinson Richards and together with Forssmann they were the joint recipients of the Nobel Prize for physiology or medicine in 1956. Werner Forssmann ended his career as chief surgeon to the Evangelical Hospital in Dusseldorf.

At St Vincent and the Grenadines a set of 48 $1.00 stamps in 1995 to commemorate the centenary of the Nobel Prize Trust Fund. These were issued in sheetlets of 12 with each stamp in the four sheetlets depicting a different recipient of a Nobel Prize. Eight of the stamps celebrated Nobel Prize winners for medicine including Konrad Lorenz, Ivan Pavlov, and Werner Forssmann.

M K Davies
A Hollman