

The current role of coronary artery bypass in diabetics with multivessel coronary disease

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The recent publication of the FREEDOM Trial, which has strong evidence supporting the use of CABG rather than PCI for diabetics with multivessel coronary artery disease, has focused attention back to the most appropriate interventional treatment of diabetics with complex coronary artery disease¹. In 1996, the BARI Trial compared coronary bypass to angioplasty for patients with multivessel coronary artery disease and followed them for over five years². The authors noted that, in a subgroup of 353 patients who had diabetes being treated with oral hypoglycaemic agents or insulin and who were randomised in the trial, there was an average five-year survival rate of 80.6% for coronary bypass patients compared to 65.5% for PTCA patients ($p < 0.003$). In addition, the cardiac mortality rates were 5.8% for CABG vs. 20.6% in PTCA ($p = 0.003$)³. The survival curves diverged steadily beginning in the first year of follow-up. The coronary bypass patients included in the study all had at least one internal mammary artery graft, and the PTCA patients initially were treated with angioplasty only until stents became available, at which time bare metal stents were employed. Because of these findings, the National Heart, Lung and Blood Institute released a Clinical Alert on September 21, 1995⁴. Although the survival benefit was very significant, this study has received subsequent criticism because newer stent technology was not available at the time, and therefore some doubted the current validity of the study.

In the ARTS randomised trial comparing PCI using bare metal stents to CABG, the subgroup of 208 diabetics was analysed and revealed a five-year mortality of 13.4% in the stented patients compared to 8.3% in CABG patients, for a RR of 1.61⁵. Because of the small sample size, this 60% increase in mortality was not statistically significant. A collaborative analysis of patient data from ten randomised trials was published in 2009 comparing PCI to CABG⁶. Six studies utilised balloon angioplasty and four used bare metal stents in the PCI group. In the subgroup of diabetic patients, there was a significant reduction in long-term (5.9 years) mortality in diabetic

patients receiving coronary bypass with a mortality of 23% compared to 29% of PCI patients ($p = 0.014$, HR 0.70). Whether the patient received a balloon angioplasty or bare metal stent did not affect the outcome. This study, however, also did not utilise drug-eluting stents, creating some doubt over the current validity of the results.

In November 2012 the Freedom Trial was presented and published¹. This was a study of a diabetic population only and enrolled 1,900 patients at 140 international centres from 2005-2010, including patients with diabetics who had multivessel coronary artery disease (83% with three-vessel disease). Patients were randomised to PCI with drug-eluting stents or coronary bypass grafting. They were followed for a minimum of two years with a median follow-up among survivors of 3.8 years and, in addition, were prescribed the current recommended medical therapies for both coronary disease and diabetes. The primary outcome measure was a composite of death from any cause, non-fatal myocardial infarction or non-fatal stroke. The results were very striking in that the primary composite adverse outcome occurred at five years in 26.6% of the PCI group as compared to 18.7% of the CABG group ($p = 0.005$). Death rates and myocardial infarction were both higher for PCI patients, 26.6% vs. 18.7% ($p = 0.049$) and 13.9% vs. 6% ($p < 0.001$), respectively, whereas stroke was somewhat higher for coronary bypass patients, 5.2% vs. 2.4% ($p = 0.03$). Of interest was that the advantage for CABG was present in all three SYNTAX tertiles with a higher hazard ratio in each SYNTAX group of PCI patients, of 1.14, 1.46, and 1.46, for the low, medium and higher complexity SYNTAX scores, reflecting a greater difference in the mid and high SYNTAX score groups.

Recently, the five-year follow-up of patients in the SYNTAX Trial has been presented and published⁷ with another SYNTAX paper focusing specifically on the treatment of complex coronary disease in patients with diabetes comparing coronary bypass to percutaneous coronary intervention⁸. This was a pre-specified subgroup analysis evaluating diabetics with left main and/or three-vessel

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coronary disease and included 452 patients with diabetes and 1,348 without. The MACCE composite adverse endpoint, which included all-cause death, stroke, MI and repeat revascularisation, was significantly higher in the PCI group vs. the CABG group (46.5% vs. 29.0%, $p<0.001$), while repeat revascularisation was 35.3% in the PCI group and 14.6% in the CABG group ($p<0.001$). However, there was no difference in the composite all-cause death/stroke/MI. All-cause death, however, although not statistically significant, was higher in the PCI group at 19.5% vs. 12.9% in the CABG group ($p=0.065$), with stroke occurring in 3% of the PCI and 4.7% of the CABG patients. However, the all-cause death and MI differences, although not statistically significant, certainly favoured CABG, i.e., were lower, and could possibly be related to a beta error. Cardiac death occurred more frequently in diabetics undergoing PCI compared to CABG, HR2.01 ($p=0.034$). The authors concluded that “although PCI is a potential treatment option in patients with less complex SYNTAX scores, CABG should be the revascularisation option of choice for patients with more complex anatomic disease, particularly with concurrent diabetes.” The large ACCF/STS ASCERT “real world” observational study of approximately 190,000 patients from the ACC-NCDR Cath PCI registry and the STS Adult Cardiac Surgery Database also supports the long-term efficacy of CABG over PCI in diabetic patients with advanced two and three-vessel coronary artery disease as have the above prospective randomised trials⁹.

In summary, there are now several recent trials that have clearly demonstrated better long-term survival, a lower myocardial infarction rate and greater freedom from revascularisation benefit with coronary bypass as compared to PCI in diabetic patients. The latest trials include patients with drug-eluting stents, so are quite contemporary. The evidence, therefore, is quite solid in favour of coronary bypass for the treatment of diabetics with two and three-vessel coronary artery disease, particularly those with the more complex SYNTAX scores of 22 and greater. Although physicians have been reluctant to heed the warning from the NHLBI following the BARI Trial, the evidence at this point strongly favours coronary bypass for diabetics with complex multivessel disease. Hlatky, an accomplished cardiologist who performs neither procedure, states in his editorial accompanying the FREEDOM Trial paper¹⁰, “the results of the FREEDOM Trial suggest that the comparative effectiveness of CABG and PCI on hard outcomes remain similar whether PCI is performed without stents, with bare metal stents or with drug-eluting stents. Mortality has been consistently reduced by CABG, as compared with PCI, in more than 4,000 patients with diabetes that have been evaluated in 13 clinical trials. The controversy should finally be settled.” In another editorial accompanying the recently published VA CARDS study, Ellis states that “...it seems, on the basis of the current body of evidence, that CABG should be preferred over PCI in patients with diabetes and multivessel disease with complex anatomy exemplified by SYNTAX scores >22 , and perhaps even all patients with diabetes with multivessel disease”¹¹.

It is imperative, therefore, that both surgeons and cardiologists incorporate this evidence-based data from multiple sources into practice for diabetic patients. Each patient has individual features which

may impact that decision. For this reason, it is very important for the heart team, the cardiologists, surgeons and the primary care physician to adequately inform each patient of these data, incorporating each individual patient’s risk factors into a recommendation for a truly personalised informed consent. We must always remember to treat each patient in the most appropriate manner possible. For this reason, *ad hoc* PCI should not be performed in non-emergent diabetic patients without the heart team reviewing the data and presenting it to the patient and their families for a mutual informed decision.

Conflict of interest statement

F.L. Grover reports the following conflicts of interest: New Jersey Department of Health, Healthcare Quality Assessment; Chair of Quality, Patient Safety and Research Council for the Society of Thoracic Surgeons; Member of the ACC NCDR Board. M.J. Mack has no conflicts of interest to declare.

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