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EDITORIAL

WHICH PATIENT SUBSET IS BEST SUITED FOR CABG

Coronary artery bypass graft surgery (CABG) has been the standard of care for revascularisation of patients with complex coronary artery disease since its introduction in 1968. When percutaneous coronary intervention (PCI) was introduced in 1977, it was thought to be appropriate only for patients with single vessel disease, but as operator ability and device technologies have advanced, the use of PCI has expanded to treat patients with increasingly complex disease, such as multivessel and left main coronary disease. The optimum method for revascularisation has been a matter of debate, with many published trials comparing outcomes of CABG and PCI with drug-eluting stents (DES). Most of these trials have been limited by non-randomised patient selection, inclusion of less complex disease, or insufficient statistical power.

The SYNergy between percutaneous coronary intervention with TAXus and cardiac surgery (SYNTAX) trial assessed the optimum revascularisation treatment for patients with de-novo left main coronary disease or three-vessel disease (or both), by randomly assigning patients to either PCI with a first-generation paclitaxel-eluting stent or CABG. For the primary endpoint of major adverse cardiac and cerebro vascular events (MACCE) at 1 year, PCI did not meet the goal of non-inferiority compared with CABG, because the PCI group had a significantly higher rate of repeat revascularisation than did the CABG group. Rates of death and myocardial infarction were similar between the two groups, and stroke was significantly increased in the CABG group compared with the PCI group. At 3 years, rates of MACCE, myocardial infarction, and repeat revascularisation were significantly higher in the PCI group than in the CABG group, whereas rates of the composite safety endpoint of death or stroke or myocardial infarction, and stroke alone, were not significantly different between treatment groups.

5-year results of the **SYNTAX trial,** which compared coronary artery bypass graft surgery (CABG) with percutaneous coronary intervention (PCI) for the treatment of patients with left main coronary disease or three-vessel disease, were reported, to confirm findings at 1 and 3 years. 1800 patients were randomly assigned to CABG (n=897) or PCI (n=903). More patients who were assigned to CABG withdrew consent than did those assigned to PCI (50 vs 11). After 5 years' follow-up, Kaplan-Meier estimates of MACCE were 26.9% in the CABG group and

37.3% in the PCI group (p<0.0001). Estimates of myocardial infarction (3.8% in the CABG group vs 9.7% in the PCI group; p<0.0001) and repeat revascularization (13.7% vs 25.9%; p<0.0001) were significantly increased with PCI versus CABG. All-cause death (11.4% in the CABG group vs 13.9% in the PCI group; p=0.10) and stroke (3.7% vs 2.4%; p=0.09) were not significantly different between groups. 28.6% of patients in the CABG group with low SYNTAX scores had MACCE versus 32.1% of patients in the PCI group (p=0.43) and 31.0% in the CABG group with left main coronary disease had MACCE versus 36.9% in the PCI group (p=0.12); however, in patients with intermediate or high SYNTAX scores, MACCE was significantly increased with PCI (intermediate score, 25.8% of the CABG group vs 36.0% of the PCI group; p=0.008; high score, 26.8% vs 44.0%; p<0.0001). CABG should remain the standard of care for patients with complex lesions (high or intermediate SYNTAX scores). For patients with less complex disease (low SYNTAX scores) or left main coronary disease (low or intermediate SYNTAX scores), PCI is an acceptable alternative. All patients with complex multivessel coronary artery disease should be reviewed and discussed by both a cardiac surgeon and interventional cardiologist to reach consensus on optimum treatment. The application of the SYNTAX score has created a new era in the objective assessment of coronary artery disease complexity, making interpretation of previous trials with more crude assessment of coronary severity difficult.

ASCERT, a large comparative-effectiveness study derived from **Medicare** and professional society databases, found that CABG surgery provides better four-year survival odds than PCI in high-risk stable patients with two- or three-vessel disease. **Society of Thoracic Surgeons** (STS), the **American College of Cardiology** (ACC), and the **Centers for Medicare & Medicaid Services** (CMS) collaborated to develop ASCERT. The ASCERT high-risk subset results, show a long-term survival benefit for surgery over percutaneous intervention. This confirms, in current real-world practice, the results of other studies, from the New York state data to the randomized trials like **SYNTAX.** The study combines PCI data from the **National Cardiovascular Data Registry** (NCDR), bypass surgery data from the STS database, and up to four years of Medicare outcomes data (average 2.67 years) from CMS **(Centers for Medicare & Medicaid Services).** Overall, the study includes 86 244 bypass-surgery patients and 103 549 PCI patients treated from 2004 through 2007. The mean age was 74 years. The high-risk subset represented about 2% of the patients in the trial. Survival rates favored percutaneous intervention within one year--about 1% vs 2% mortality for percutaneous intervention vs surgery, respectively. But after one year, bypass surgery was associated with progressively better survival than percutaneous intervention. For high risk patients: 75 or older, diabetic, ejection fraction <50%, and glomerular filtration rate <60 mL/min/1.73m2, bypass surgery was associated with lower four-year mortality than PCI (risk ratio=0.72) However, this analysis is limited by a lack of prospective randomization and the

unanswered question of whether selection bias can be adequately compensated for via propensity adjusted statistical analyses. Additionally, the ASCERT study did not use a measure of coronary disease severity, such as the SYNTAX score, and is thus limited in its ability to provide comparative information for the optimum revascularisation method for a given level of coronary anatomic complexity. In the SYNTAX trial, a significant difference in outcomes depending on base line severity of coronary artery disease was noted.

The recently published FREEDOM (Future REvascularization Evaluation in patients with Diabetes mellitus: Optimal management of Multivessel disease) trial, assessed CABG versus PCI in 1900 patients with multivessel disease and diabetes. In the overall population of that study, patients in the CABG group had significantly lower rates of the composite endpoint of all-cause death, cerebrovascular accident, or myocardial infarction compared with patients in the first-generation DES group (18•7% in the CABG group vs 26•6% in the PCI group; p=0•005). However, as in the SYNTAX study, the FREEDOM trial reported no difference between treatment groups for the composite endpoint of all-cause death, cerebrovascular accident, or myocardial infarction for patients with SYNTAX scores of lower than 22, and a mortality benefit associated with CABG in patients with SYNTAX scores of 23–32. However, for patients with SYNTAX scores of 33 or higher in the FREEDOM trial, no significant diference between treatment groups for this endpoint was reported. The reason for this difference in outcomes is unclear, but might be related to statistical power, since less than 20% of patients in the FREEDOM trial had a SYNTAX score of 33 or higher.

It is unclear how the overall results would differ with the use of fractional flow reserve or newer-generation DES (with lower repeat revascularisation and associated stent thrombosis rates) or improvements in antiplatelet therapy and CABG techniques (eg, more arterial revascularisation, improved perioperative care). The EXCEL trial is investigating use of newer-generation DES versus CABG in 2600 patients with low-risk or intermediate-risk left main lesions, and results are expected to provide additional insight into the optimum revascularisation technique in this subgroup of patients.

Diabetic patients experience more extensive atherosclerosis and a worse clinical outcome following revascularization procedures. In recent years, technical advances have resulted in improved outcomes after coronary revascularization with PCI or CABG. Much of the evidence comparing PCI with CABG comes from older studies of PTCA, which did not use current recommended antiplatelet therapies and aggressive secondary preventive strategies post-revascularization. Data to guide decision making are limited regarding the current choice between CABG and PCI using DES and newer antiplatelet agents in diabetic patients with

multivessel CAD. Although CABG remains the standard of care for most diabetic patients with multivessel CAD, the paradigm may begin to shift. Further follow-up from the initial stent versus CABG studies will offer insight; however, the field has already begun to move beyond these trials. Data from randomized controlled trials comparing DES with CABG in patients with diabetes, such as FREEDOM , CARDia and ARTS II – may help clarify this issue. Additionally, greater and more sustained use of both intravenous and oral antiplatelet agents, and the use of hybrid operative and PCI procedures will also change practice patterns in the coming years.

In conclusion, all patients should be reviewed and discussed by a team of both a cardiac surgeon and an interventional cardiologist to reach a consensus on optimum treatment. Treatment advice for an individual patient should take into account patient preferences, as well as the risks and benefits of the respective treatment options. **However, the delimma remains: PCI vs CABG?**

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