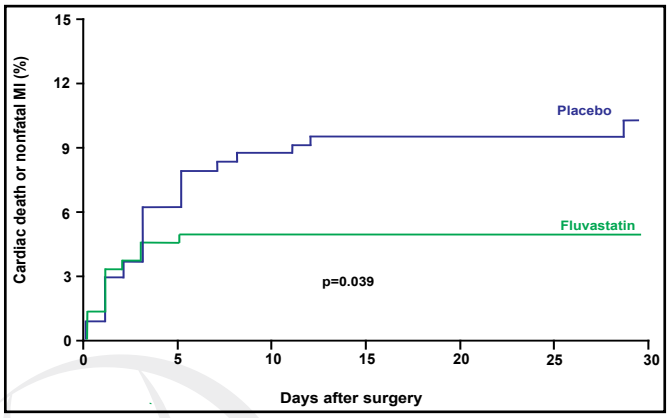
reduction in the incidence of the combined secondary endpoint of cardiovascular death or MI (OR 0.48; 95% CI, 0.24 to 0.95; p=0.039;Figure 2). The NNT for the secondary composite endpoint of cardiovascular death or nonfatal MI was 19.

Figure 2. Secondary Endpoint of Cardiovascular Death or MI Within 30 Days After Surgery.



The proportion of patients who experienced any adverse event was similar between the fluvastatin and placebo groups. The percentage of patients who experienced a CK rise >10X the ULN was 4.1% in the fluvastatin group versus 3.0% in the placebo group (p=0.8). The percentage of patients who had a significant increase (>3X the ULN) in ALT levels was 3.1% in the fluvastatin group and 5.2% in the placebo group (p=0.3). Similar rates of study drug discontinuation were observed between the groups, and there were no cases of myopathy or rhabdomyolysis.

Commenting on the results of this study, Marc E. Shelton, MD, Prairie Heart Institute, Springfield, IL, expressed the opinion that extended-release fluvastatin should be considered for statin-naïve patients who undergo major peripheral vascular procedures and that, in light of the safety profile of fluvastatin, future studies of other statins should consider avoiding a placebo arm.

Of note, many of the patients who were enrolled in this study met current indications for aggressive lipid-lowering therapy due to the presence of prior CAD, stroke, or peripheral vascular disease, for whom the target LDL was <2.5 mM/L (optional target < 2.0 mM/L). While the study excluded patients who were on statins at the time of randomization, it is not clear how much of the benefit of extended-release fluvastatin that was observed in the trial was derived from those patients who should have been taking a statin prior to randomization. Nonetheless, the results of this trial are consistent with prior studies that have observed a beneficial effect of perioperative statin therapy in patients who are undergoing noncardiac surgery.

Coronary Artery Bypass Graft Surgery Superior to Percutaneous Coronary Stenting in Patients with Left Main or Three-Vessel Coronary Disease

Percutaneous coronary intervention (PCI) with Taxus (paclitaxel-eluting) stenting was inferior to coronary artery bypass graft (CABG) with respect to the primary composite of death, stroke, myocardial infarction (MI), or repeat revascularization among patients with left main or 3-vessel coronary artery disease (CAD), as reported by researchers from the international SYNTAX trial (The SYNergy between Percutaneous Coronary Intervention with TAXus and Cardiac Surgery; NCT00114972) at the European Society of Cardiology Congress 2008 in Munich.

"In the randomized cohort, we saw comparable overall safety outcomes in terms of MI, cerebrovascular accident, or death for CABG and PCI," said investigator and copresenter Patrick Serruys, MD, PhD, Interuniversity Cardiological Institute, Rotterdam, The Netherlands. "But there was a significantly higher rate of revascularization in the PCI group and a significantly higher rate of stroke in the CABG group," he added.

The trial was conducted at 62 sites in Europe and 23 sites in the United States and had an "all-comers" design instead of a highly selected patient population to reflect, as much as possible, real-world conditions. Patients had either left main stenosis or 3-vessel CAD with the intent to revascularize all 3 vascular territories. The investigators relied on a cardiologist and surgeon consensus to determine whether each subject was eligible for both coronary interventions. Limited exclusion criteria included previous interventions, acute MI with creatine phosphokinase (CPK)-myocardial band >2X, or concomitant cardiac surgery.

After establishing eligibility for either intervention, investigators randomized 1800 subjects to CABG (n=897) or PCI (n=903). Approximately 28% had diabetes, 33% prior MI, and 29% recent unstable angina. The average number of lesions was 4.4, with 66% qualifying on the basis of 3-vessel disease only, 3% with left main only, and 31% with both left main and 3-vessel disease.

The primary endpoint of the trial, the rate of MACCE (Major Cardiovascular or Cerebrovascular Event Rate) as defined by all-cause death, cerebrovascular accident (CVA), documented MI, or any repeated revascularization (PCI or CABG) at 12 months, occurred in more patients who were undergoing PCI than CABG (17.8% vs 12.1%;

p=0.0015). There was a significantly higher rate of revascularization in the PCI group (13.7% vs 5.9%; p<0.0001) but a significantly higher rate of CVA in the CABG group (2.2% vs 0.6%; p=0.003). The composite rates of all-cause death, CVA, and MI were nearly identical (7.6% for PCI vs 7.7% for CABG; p=0.98). Individual rates of death, MI, and thrombosed vessel (bypass graft vs stented vessel) at 12 months were each similar in both cohorts. Among the subgroups that were presented, patients with diabetes, isolated 3-vessel CAD, and left main plus involvement of an additional 2 or 3 vessels tended to have better outcomes with CABG, while outcomes in patients with isolated left main disease and left main plus a single additional vessel tended to favor PCI. A possible explanation is that the risk of complication with PCI is more closely related to the number of vessels undergoing revascularization than to the risk of complication with CABG.

SYNTAX Registries

Friedrich Mohr, MD, PhD, University of Leipzig, Leipzig, Germany, presented the results of the registries. There were 1275 patients who were eligible for only one of the interventions, of which 649 were enrolled in the CABG registry and 198 in the PCI registry.

"The treatment schedule and follow-up visits in the registries were identical with the subjects in the randomized groups, and major adverse cardio- and cerebrovascular events were completely monitored," Prof. Mohr said. "No statistical comparisons between the randomized and registry groups were performed," he added.

For the 12-month endpoint, Prof. Mohr reported a total MACCE rate for PCI registry subjects of 20.4%. This included all-cause death (7.3%), stroke (0%), MI (4.2%), death by stroke or MI (10.5%), and revascularization (12.0%).

For the same endpoint, he reported a total MACCE rate for CABG registry subjects of 8.8%. This included all-cause death (2.5%), stroke (2.2%), MI (2.5%), death from stroke or MI (6.6%), and revascularization (3.0%).

"While repeat revascularization drove the higher MACCE for the PCI group, it is notable and surprising that there were no strokes reported in the PCI group," Prof. Mohr said.

Prof. Mohr noted that SYNTAX showed that CABG remains the only interventional option for one-third of patients but that for patients who are not eligible for CABG, PCI is a good option instead of medical therapy. "Likewise, for patients who are not candidates for PCI, surgery results are excellent."

PCI is a "Reasonable" Strategy For Diabetic Patients With Multivessel Disease: The CARDia Trial

At 1 year following intervention, there apparently is no difference between coronary artery bypass grafting (CABG) and percutaneous coronary intervention (PCI) in treating diabetic patients with multivessel disease, as measured by the incidence of a composite of death, myocardial infarction (MI), and stroke.

The CARDia (Coronary Artery Revascularization in Diabetes Trial; ISRCTN19872154) trial results were presented in Munich at the 2008 European Society of Cardiology Congress by Akhil Kapur, MD, London Chest Hospital, Barts and the London NHS Trust, London, UK.

"We saw more repeat revascularization in the PCI group, but with similarity in other major outcomes at 1 year, we can now consider PCI a reasonable strategy in diabetic patients with multivessel disease. But longer follow-up is still needed," said Dr. Kapur.

Dr. Kapur emphasized that even though the trial was designed to test the hypothesis that PCI is noninferior to CABG (n=254) in these patients, the targeted enrollment of 600 subjects was not met, and the noninferiority of PCI could not be formally, statistically established by the outcome of the trial. "The trial was, finally, underpowered to test this endpoint," he said. Noninferiority trials are intended to show that the effect of one treatment, in this case PCI, is not worse than that of an active control, in this case CABG, by a statistically significant margin. Investigators randomized 510 diabetic patients (mean age 64 years, 74% men, average weight 84 kg) with multivessel disease to CABG (n=254) or PCI (n=256). Nearly one-quarter of the admissions were considered acute (23.7% CABG group vs 21.5% in the PCI cohort). Similar numbers of patients required insulin to treat diabetes (31.4% of CABG vs 30.6% of PCI). All patients in the PCI group were treated with aspirin, clopidogrel, and GP IIb/IIIa inhibitors.

Of the CABG group, 229 underwent the procedure. Of the PCI group, 252 underwent the procedure. There was 96% (n=245) subject follow-up at 1 year in the CABG group and 98% (n=251) in the PCI group.

The investigators reported that for the composite primary endpoint of death, MI, and stroke at 1 year, there was a rate of 10.2% for CABG veruss 11.6% for PCI (OR=1.15, 95% CI, 0.65–2.03; p=0.63). This result was not statistically significant enough to establish the noninferiority of PCI.