The past 30 years witnessed a revolution in cardiovascular care with the introduction of percutaneous approaches for the treatment of patients with a variety of cardiovascular diseases. According to overseas and local experiences, the number of percutaneous coronary intervention (PCI) performed every year far exceeds the number of patients undergoing coronary artery bypass surgery (CABG). The procedural success, safety and durability of PCI have dramatically improved because of the advance in technology, refinements in periprocedural adjunctive pharmacology (e.g. glycoprotein IIb/IIIa inhibitors, alternative thrombin inhibitors), and a better understanding of early and late outcomes. Indeed, it is now one of the most frequently performed medical procedures.

In this article, I will review a few important trials in the field of intervention cardiology.

**Drug-eluting Stents (DES)**

The idea of combining a coronary stent and an anti-proliferative drug is to target the different components of restenosis. By achieving a bigger post-procedural vessel lumen, the use of bare metal coronary stent reduces both clinical and angiographic restenosis. However, 20 to 30% of these patients have recurrent symptoms due to neointimal hyperplasia which is a “normal response” to vascular injury. A number of systemic agents have been used to prevent restenosis after balloon angioplasty and stenting, but none has had a consistent effect on restenosis prevention. By local delivery of a highly efficacious anti-proliferative drug, DES is very effective at suppressing the local neointimal proliferation. Angiographic and clinical restenosis in general have been reduced to less than 10% and 5% respectively. Siroliums and paclitaxel eluting stents were the first two stent platforms studied and were available in clinical use. However, new problems specific to DES were noticed. These included delayed endothelialisation, impaired arterial wall healing and late stent thrombosis. Hence, there is a need for a new DES platform and, hopefully, DES related problems and complications could be minimised.

A thin, cobalt-chromium stent eluting the antiproliferative agent everolimus from a nonadhesive, durable fluoropolymer has been developed and it has shown promise in preliminary studies in improving clinical and angiographic outcomes in patients with coronary artery disease. SPIRIT III compared this everolimus-eluting stent (EES) with a widely used paclitaxel-eluting stent (PES) in a prospective, randomised and controlled setting. It showed less angiographic late loss (i.e. less neointimal hyperplasia which translates into less restenosis) in EES compared with PES. There were also fewer major adverse cardiac events (MACE - cardiac death, myocardial infarction, or target lesion revascularisation) during 1 year of follow-up. This was the first DES to prove superior, in a randomised clinical trial, to another DES already on the market. This EES then was granted marketing approval by the FDA in July 2008. Because this stent was more user-friendly (highly deliverable) and had favourable clinical outcomes, it had been used extensively by the US interventionist since its marketing. Similar experience was noted in Hong Kong. However, as this stent was relative new to the market, there were no long-term data in compared with the first generation DESs.

**Medical Therapy vs PCI**

The value of PCI for patients with disabling or unstable angina or myocardial infarction is well proven in clinical trials. Controversial, however, is the role of PCI for patients who are either asymptomatic or minimally symptomatic. This issue intensified after the Clinical Outcomes Utilizing Revascularization and Aggressive Drug Evaluation (COURAGE) trial, which randomised 2287 patients who had stable coronary artery disease to either optimal medical therapy plus PCI or optimal medical therapy (OMT) alone. After a median follow-up of 4.6 years, the primary end point (death and myocardial infarction) was almost identical between PCI (19%) and OMT (18.5%). However, a group of relatively low-risk patients were randomised: 12% to 13% were asymptomatic, whereas 30% had Canadian Cardiovascular Society class 1 angina; approximately 70% had 1- or 2- vessel disease; and the ejection fraction was 61%. Meanwhile, during the trial, 33% of the medical group crossed over to PCI whereas only 21% of the PCI group required repeat revascularisation. Moreover, in the PCI group, only balloon angioplasty was performed in 14.5% of lesions and DES was rarely used because of the time frame of the study.

An important substudy of COURAGE compared scintigraphic stress tests at 6-18 months follow-up with the baseline study in 314 patients. Each group had similar baseline characteristics. As measured by scintigraphy, increasing amounts of jeopardised...
myocardium at baseline indicated increased risk of end points. At follow-up scintigraphy, the reduction in ischaemic myocardium was greater with PCI than with OMT particularly in patients with moderate to severe ischaemia at baseline. Patients with ischaemia reduction had lower risk for death or myocardial infarction. Death or MI rates ranged from 0% for patients with no residual ischaemia to 39% in patients with 10% residual ischaemia on follow-up stress test. This supported the importance of recognition and treatment of ischaemic burden rather than just anatomy as the goal of interventional therapies.

The COURAGE study indeed reconfirmed what we are currently practising. For those patients with minimal symptom or no symptom, optimal medical therapy offers good control of symptom without increased risk of death or myocardial infarction. However, if there is significant inducible ischaemia on function test (e.g. stress scintigraphy), PCI could relief residual ischaemia and reduce cardiovascular events whether the patient is symptomatic or not. If medical therapy does not provide adequate angina relief, provide desired physical activity level to meet the patient's expectations, or the patient is intolerant of medical therapy, PCI is the treatment of choice. Last but not the least, OMT includes antiplatelet therapy (aspirin, clopidogrel), anti-ischaemic therapy (long-acting beta-blocker, long-acting calcium channel blocker, nitrate), lipid-lowering therapy (statin), extended-release niacin or fibrates (for low HDL) and exercise.

Multivessel Disease

The application of PCI in patients with multivessel disease remains controversial, particularly in the setting of diabetes mellitus. Multiple randomised trials have compared PCI with bare metal stents to coronary artery bypass graft surgery (CABG) in selected patients with multi-vessel coronary artery disease, and rates of survival free from myocardial infarction have been similar. Typically, patients treated with PCI require more subsequent revascularisation procedures due to restenosis or incomplete revascularisation. The need to compare the use of DES and CABG in this setting is eagerly awaited.

One-year follow-up data from the much anticipated Synergy Between PCI With Taxus and Cardiac Surgery (SYNTAX) trial was recently announced. 1800 patients were randomised to either CABG or PCI with the Taxus DES5. By 12-month, DES was statistically inferior to CABD for the primary composite end-points of all-cause death, cerebrovascular event, MI and repeat revascularisation (12.1% vs 17.8%, p=0.0015). Indeed, there was no difference between all-cause death and MI with stenting and CABG in patients with left main coronary artery disease6. However, there was a significantly higher rate of target vessel revascularisation in the PCI group.

The MAIN-COMPARE registry study which was carried out in Korea showed there was no significant difference in major outcomes (death, MI or stroke) between PCI with stenting and CABG in patients with left main coronary artery disease6. However, there was a significantly higher rate of target vessel revascularisation in the PCI group.

Left Main Coronary Artery Stenosis

Significant narrowing of the left main coronary artery has the worst prognosis of any form of coronary artery disease. CABG has been considered standard therapy because restenosis of the left main coronary artery could be fatal. However, with the availability of DES, there is a growth of interest in a percutaneous approach. Indeed, left main coronary artery lesions are routinely treated, for example, in Japan, Korea and Hong Kong.

The MAIN-COMPARE registry study showed that PCI with stenting was safe in left main disease. However, a well-designed and adequately powered prospective randomised trial of the two revascularisation strategies in patients with unprotected left main disease is eagerly needed.

Conclusion

PCI is one of the most frequently performed medical procedures. With the improvement in hardware and accumulation in clinicians' experience, its usage and indications are ever expanding. Patients with unstable angina, non-ST elevation MI, ST elevation MI and moderate to severe angina symptoms should consider PCI as an option of treatment. Their symptoms and prognosis would be improved after the invasive procedure. For those with no or minimal symptoms, they are candidates for PCI if there is objective evidence of significant myocardial ischaemia. Otherwise, medical treatment with aggressive control of cardiovascular risk factors should be considered. In the setting of multivessel disease and left main coronary disease, PCI is a viable alternative to CABG. A higher repeated revascularisation rate, however, is expected.

References