Updates on Percutaneous Coronary Intervention

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Ever since the invention of percutaneous coronary intervention (PCI) to treat coronary artery disease (CAD) around twenty years ago, its clinical use has been expanded dramatically. According to overseas and local experiences, the number of 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 the latest advance in the field of intervention cardiology and the different indications of PCI.

Percutaneous Transluminal Coronary Angioplasty (PTCA)

Andreas Gruentzig performed the first balloon angioplasty in human in 1977, using a prototype fixed-wire balloon catheter. Balloon angioplasty expands the coronary lumen by stretching the vessel wall and taring the atherosclerotic plaque. Meanwhile, longitudinal redistribution of the atherosclerotic plaque contributes to the increase in vessel lumen. PTCA is able to improve coronary flow and hence reduces coronary ischaemia in selected patients. However, the uncontrolled tearing of the atherosclerotic plaque may result in flow-limiting coronary dissections that results in abrupt closure in 5 to 8% of patients. These patients may need urgent CABG in order to salvage ischemic myocardium. On the other hand, elastic recoil of the stretched vessel wall left an average residual stenosis of 30 to 35%, with higher residual stenoses correlated with higher subsequent recurrence rates. Repeat revascularisation by either repeat PTCA or CABG was in the range of 20 to 40%. Hence, the long-term efficacy of PTCA is significantly limited by restenosis. Nowadays, in the era of stent, standalone PTCA is now reserved only for cases such as smaller (<2.5mm) vessels and early anastomotic lesions in saphenous vein grafts in which the long-term benefits of coronary stenting are limited.

Coronary Atherectomy

By removing the obstructing atherosclerotic plaque in the coronary arteries, a larger vessel lumen can be obtained. This may improve the vessel wall compliance and render the vessel more dilatable. Different atherectomy devices are available including directional coronary atherectomy (DCA), rotational atherectomy, transluminal extraction atherectomy and excimer laser coronary angioplasty. DCA uses a directional cutting device to remove the atheroma while rotational atherectomy uses a rotating burr to remove calcified atheromatous plaque. Before the availability of coronary stents, there was huge enthusiasm in the use of these devices in the hope of improving both short and long-term outcomes. However, multiple studies showed standalone coronary atherectomy did not improve the restenosis rate compared with PTCA. In a contemporary cardiac catheterisation laboratory, coronary atherectomy is now being used in less than 10% of cases. DCA may still be used for bulky lesions in the left main and proximal left anterior descending arteries whereas rotablator is occasionally needed to pre-treat rigid and calcified lesions for subsequent stenting.

Coronary stents

The first implantation of coronary stent in human in 1986 has revolutionised the practice of intervention cardiology. By providing a scaffold to the dilated coronary lesion, coronary stents almost completely eliminate elastic recoil which is the major cause of restenosis after PTCA. Achieving a larger vascular lumen, coronary stenting effectively reduces angiographic and clinical restenosis. By tagging up uncontrolled dissection, it also significantly reduces acute closure of the vessel after PTCA. This significantly decreases early ischaemic complications and improves the safety of the procedure.

A large number of randomised trials demonstrated clear benefits of coronary stents over PTCA in different subsets of patients. These included de novo or restenotic lesions, abrupt or threatened closure (i.e. bailout situation), saphenous vein grafts, chronic total occlusion and acute coronary syndromes. Hence these devices are now used in more than 80% of all PCIs.

Despite the improvement in early outcomes, 10 to 20 percent of patients had recurrent symptoms within 12 months after stent implantation. Repeat angiogram usually revealed new tissue formation (neointimal hyperplasia) within the stent. Histological analyses revealed that a great deal of the volume of the in-stent restenotic lesion is made up of "myxomatous" tissue.
comprising occasional stellate smooth muscle cells embedded in a loose and highly hydrated extracellular matrix.

The major risk factors for restenosis are longer lesion length (>30mm), longer stent length, small vessel diameter (<2.5mm), smaller post-treatment lumen diameter, reopened chronic total occlusion, ostial and bifurcation lesions, and the presence of diabetes. If multiple risk factors are present, the restenosis rate may be up to 40 to 50%. Even though restenosis seldom causes acute coronary syndrome or cardiac death, patients often need repeated admissions and revascularisation to relieve symptoms. Different systemic medications were tested in clinical trials to lower the restenosis rate but without avail. Radiation treatment (intracoronary brachytherapy), presumably targeting smooth muscle cell proliferation and preventing the neointima from recanalising, was utilised to treat in-stent restenosis. In several randomised, placebo-controlled trials, intracoronary brachytherapy showed significant improvement in angiographic and clinical outcome in native coronary arteries and in SVGs. However, recent data showed that there was a late increase in restenosis and clinical events among those received brachytherapy. Most if not all interventionist had stopped using brachytherapy for a few years already.

Drug eluting stent, as described below, is now the mainstay of therapy for restenosis.

Drug Eluting Stent (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. As said before, 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. Some DES systems (e.g. sirolimus, everolimus, polymer-delivered paclitaxel) have, in clinical studies, significantly reduced restenosis whereas other had no or a limited effect (e.g. batimastat, dexamethasone, stent-based paclitaxel) or were clinically detrimental (e.g. actinomycin D, 7-hexanoyltaxol). It demonstrated the important interaction between the stent design, the drugs used to deliver the drug, and the types of agents that are delivered to the vessel wall.

The dramatic reduction in restenosis allowed interventionist to expand the application of PCI to different subsets of patients. Patients who were at high risk for restenosis in the bare metal stent era (e.g. diabetic patients with multivessel diseases, left main disease) may now consider PCI as an option to CABG figures. Indeed, a recent study showed that multivessel PCI with DES might be as good as, if not better than, CABG.

Recently, there is a hot debate around the issue of late stent thrombosis associated with the use of DES. By implanting a metallic stent in the blood stream, there will be continuous activation of the flowing platelets which may result in platelet clump and then blood clot formation. This may cause acute closure of the stent and patient would then present with ST elevation MI. The risk is substantially reduced when endothelialisation (i.e. the stent luminal surface was covered by a thin layer of endothelium) is completed. This will take around four weeks for a bare metal stent. The use of dual anti-platelet agents (i.e. aspirin plus ticlopidine or clopidogrel) has been proven to reduce the incidence of stent thrombosis significantly. For DES, the anti-proliferative drug will act on not only smooth muscle cells but also endothelial cells. Hence, the process of endothelialisation for DES is much prolonged. For bare metal stent, it is recommended to take both aspirin and clopidogrel for at least 4 weeks. On the other hand, the recommended duration of dual anti-platelet agents for DES is 6 to 12 months.

Distal Embolic Protection Devices

Although distal embolization of atherosclerotic debris was thought not to be a problem during the early years of catheter-based intervention, it is now recognised as a potential cause of distal myocardial necrosis after PCI. The role of distal embolisation is particularly important in SVG and acute coronary syndrome. It is also now recognised as a cause of neurological complication after carotid stenting.

There are three different types of distal protection devices. The first involves distal occlusion using a low pressure balloon. Any debris liberated by intervention remains trapped in the stagnant column of blood and can be aspirated before the occlusion balloon is deflated to restore antegrade flow. The second class consists of distal filters that are passed across the target lesion in their smaller collapsed state, opened to approximate the edges of the filter material against the vessel wall, and remain in place to catch any liberated embolic material larger than the filter pore size, until they are collapsed after stent deployment, thereby removing the captured embolic material from the body. The third type involves proximal occlusion of the treated vessel with balloon. Any debris liberated can then be aspirated from the guiding catheter.

These devices have been studied in SVG and been proven to reduce post-procedure complication significantly. However, data on ST elevation MI were inconsistent. The use of these devices in carotid stenting is under extensive study right now. In short, there are mounting evidence that distal atherosclerotic debris commonly embolises from lesions in many vascular
territories during PCI, that it can be recovered using any of the three types of embolic protection device, and that use of those devices reduces the incidence of end-organ injury.

**Indications for PCI**

**Patients with No or Mild Angina**

Patients who are asymptomatic or have only mild symptoms are best treated with medical therapy unless one or more significant lesions subtend a moderate to large area of viable myocardium, the patient prefers to maintain an aggressive life style or has a high-risk occupation, and the procedure can be performed with a high chance of success and low likelihood of complications. PCI should not be performed in patients with absent or mild symptoms if only a small area of myocardium is at risk, if no objective evidence of ischaemia can be found, or if the likelihood of success is low or the chance of complications is high.

There is no evidence so far that PCI of a haemodynamically insignificant ‘vulnerable’ plaque prevents a subsequent MI.

**Patients with Moderate or Severe Angina**

Patients with moderate or severe angina are suitable candidates for PCI provided that the lesion subtends a moderate to large area of viable myocardium. PCI should be offered even if they have a higher risk for an adverse outcome with revascularisation.

**Patients with Unstable Angina or Non-ST elevation Myocardial Infarction**

Before the availability of glycoprotein IIb/IIIa inhibitors and coronary stents, clinical studies could not document any benefit of early invasive therapy in patients presented with unstable angina or non-ST elevation MI. However, recent trials, with the use of both glycoprotein IIb/IIIa inhibitors and coronary stents, showed that early invasive treatment (i.e. cardiac catheterisation and revascularisation) could reduce the rate of death, myocardial infarction or urgent revascularisation. These benefits were highest in high risk patients (e.g. those with rest pain, cardiac enzyme elevation, or ECG changes). Hence, patients now presented with unstable angina or non-ST elevation MI are generally advised to undergo cardiac catheterisation and PCI if needed.

**Patients with ST elevation Myocardial Infarction**

Patients with ST elevation MI have thrombotic occlusion of the culprit coronary artery. It is well proven that early reperfusion by fibrinolytics could limit the infarct size and could hence prolong survival and improve prognosis. It is now generally accepted that catheter-based reperfusion (i.e. primary PCI) is preferable to fibrinolytics if facility and expertise are available. This is because primary PCI allows more rapid, complete and sustained reperfusion. Meanwhile, it also allows treating the residual coronary lesion which probably would cause myocardial ischaemia if left alone. Invasive strategy also allows better delineation of the coronary anatomy and hence better risk stratification. Most importantly, primary PCI is associated with less mechanical complication (e.g. myocardial rupture, acute mitral regurgitation, ventricular septal defect) and thrombolysis-related intracranial haemorrhage which is usually fatal.

**Conclusion**

PCI is one of the most frequently performed medical procedures. With the improvement in hardware and accumulation in clinician’s experience, its usage and indications are ever expanding. The availability of DES allows more difficult subset of patients to be treated by this catheter-based procedure. Prolonged duration (1 year) of dual anti-platelet therapy after DES is recommended. Patients with unstable angina, non-ST elevation MI, ST elevation MI and moderate to severe angina symptoms should consider PCI as the treatment of choice. Their symptoms and prognosis would be significantly improved after this 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.
This 72-year-old gentleman with history of hypertension and hypercholesterolaemia presented with typical angina. Cardiac catheterisation showed critical stenoses in proximal, mid and distal left anterior descending artery (LAD), first obtuse marginal branch (OM1) & distal left circumflex artery (1a), and subtotal occlusion of the right coronary artery (RCA) (1b). Without DES, the patient had a high restenosis rate and CABG would be a preferred option. This patient subsequently underwent PCI with deployment of 3 DES in LAD (1c), 1 DES in OM1 (1c) and 3 DES in RCA (1d). The plan was to continue life-long dual anti-platelet therapy.

References