Recent Advances in Percutaneous Coronary Intervention (PCI)

Dr. Michael KY Lee
MBBS(HK), MRCP(UK), FRCP(Glasg), FHKCP, FHKAM(Medicine)
Specialist in Cardiology

It has been 30 years since the introduction of coronary angioplasty by Andreas Gruntzig in 1977. It started with only balloon angioplasty to dilate coronary artery narrowing and thus it was initially termed Percutaneous Transluminal Coronary Angioplasty (PTCA). In 1987, Sigwart and his colleagues first described the use of coronary stents to treat threatened vessel closure during balloon angioplasty, with a view to scaffolding the intimal dissection flap and preventing the elastic recoil of the vessel. Percutaneous Coronary Intervention (PCI) encompasses balloon, stent and the assisted devices used in coronary angioplasty procedures. With the improvement in stent design and refinement of anti-platelet regimen, explosive use of coronary stents has been witnessed leading to markedly improved outcomes of PCI. Over the last 4 years, coronary stents have been used in 94% of PCI procedures done in HA hospitals in Hong Kong.

Drug-Eluting Stent (DES)

The escalating use of coronary stents is not without its problem. Repeat revascularisation still occurred in 15-20% of patients implanted with bare-metal stents (BMS). In-stent restenosis (ISR) has long been regarded as the "Achilles' heel of PCI". The introduction of drug-eluting stents (DES) in 2001 has changed the landscape of interventional cardiology. This involves the delivery of anti-proliferative drugs via polymers coated on the stent surface locally to the diseased coronary artery to prevent restenosis by inhibiting the neointimal proliferation of the vessel wall. Compared to BMS, the absolute risk reduction of DES ranges from 10-50% in terms of restenosis reduction (2.0% vs. 31.9%, p<0.001), Major Adverse Cardiac Events (MACE) reduction (43.3% vs. 29.3%, p<0.001) and a trend towards less stent thrombosis at 6 months (0.6% vs. 3.1%, p=0.15). Different stenting strategies have been suggested to tackle bifurcation lesions. However, the two stents technique (one over the main vessel and one over the side-branch) has not been shown to have advantage over stenting of one vessel while performing balloon angioplasty of the other. In fact, Colombo et al. have shown a 6-month restenosis rate of 28.0% for double stenting (main vessel and side-branch) as compared to 18.7% for provisional side-branch stenting (stenting the main vessel, balloon angioplasty to the side-branch and stenting only if necessary) with SES for bifurcation lesions. The current consensus is to adopt a simple strategy of stenting the main vessel, balloononing the side-branch and finishing with a final "kissing balloons" technique (one balloon in the main vessel and one in the side-branch, inflating simultaneously). For unprotected left main coronary artery stenosis, there have been registry data showing a potential role of DES as an alternative to coronary artery bypass graft surgery (CABG) and the ongoing randomised Synergy between Percutaneous Coronary Intervention with Taxus stent and Cardiac Surgery (SYNTAX) Study will further delineate the role of DES vs. CABG for left main disease.

BMS in-stent restenosis. The treatment of BMS in-stent restenosis (ISR) has always been unsatisfactory with balloon angioplasty and BMS-in-BMS technique. Vascular brachytherapy has brought some light to this area but its effectiveness is limited by the development of late stent thrombosis. In a meta-analysis by Dibra et al., involving 4 randomised trials comparing DES vs. balloon angioplasty or vascular brachytherapy in 1,230 patients with BMS ISR, the angiographic restenosis rate was markedly lower in patients treated with DES. They suggested DES should be considered as the first-line treatment for patients with BMS in-stent restenosis.

Stent thrombosis. Although DES is highly effective in reducing restenosis and future repeat revascularisation, it brings with it a potential complication of stent thrombosis even years after DES implantation. This might tilt the balance from a more benign stent restenosis in which the patients might present with increasing effort angina to a more sinister and fatal problem of stent
thrombosis in which the patient might develop acute vessel closure with large MI or death.\textsuperscript{13,14} According to the Academic Research Consortium (ARC) definition\textsuperscript{15}, stent thrombosis is further classified on the basis of timing (acute 0-24 hours after stent implantation, subacute >24 hours to 30 days, late >30 days to 1 year and very late >1 year) and certainty (definite, probable and possible). In comparing the incidence of stent thrombosis between 2,602 patients implanted with DES and 2,428 patients with BMS, no difference was observed in the overall (0.6% vs. 0.5%) and late (0.2% vs. 0.3%) incidence of stent thrombosis.\textsuperscript{16} However, very late (>1 year) stent thrombosis is significantly more common in DES than BMS. In a meta-analysis on 14 contemporary clinical trials randomising 6,675 patients to DES or BMS with follow-up from 8 to 48 months, a significantly higher rate of very late stent thrombosis was observed in the DES group (0.5% vs. 0%) while no difference was observed in the overall incidence (0.1% vs. 0.07%).\textsuperscript{17} In December 2006, the FDA has convened an Advisory Panel meeting on the issue of DES stent thrombosis and concluded that there seemed to be an excess of stent thrombosis with DES, especially with off-label use but they were uncertain about the magnitude of the problem.\textsuperscript{18} They suggested future DES trials to look specifically at the incidence of stent thrombosis over a longer follow-up period and involving more patients. Discontinuation of anti-platelet therapy has emerged as one of the most important predictors of stent thrombosis.\textsuperscript{19} Other contribution factors include stent malapposition (mismatch between the stent and the vessel), hypersensitivity, abnormal re-endothelialisation and resistance to aspirin or clopidogrel\textsuperscript{20}. To prevent such catastrophic events, patients must be reminded to adhere to their regimen of dual anti-platelet therapy and, on completion, take aspirin monotherapy.\textsuperscript{20} Patients with DES who require surgery, elective or otherwise, irrespective of the time since implantation, must continue to take aspirin perioperatively unless it is absolutely contraindicated.\textsuperscript{5} Attention to PCI technical details may also improve DES outcomes. This includes avoidance of too many stents, especially overlapping stents, use the shortest stent length wherever possible, fully expand the stent over its entire length, particularly in calcified lesions, and residual dissections should be avoided.\textsuperscript{18}

**Primary PCI for AMI**

Patients presenting with acute myocardial infarction (AMI) carry a high mortality and morbidity. It has been shown that acute reperfusion therapy to restore coronary blood flow can improve the survival and decrease the long-term complications of AMI.\textsuperscript{21} In the 1980s, fibrinolytic drugs have been the main modality of treatment for ST-elevation myocardial infarction (STEMI). However, numerous randomised trials and meta-analysis have shown that primary PCI (to open up an occluded coronary artery by PCI) for STEMI is associated with higher rate of reperfusion, lower risks of reocclusion and reinfarction and improved survival.\textsuperscript{22,23} The RIKS-HIA Registry is a large registry of 26,205 consecutive STEMI patients who received reperfusion therapy within 15 hours of symptom onset between 1999 and 2004.\textsuperscript{27} 7,084 patients received primary PCI, 3,078 pre-hospital thrombolysis (PHT) and 16,043 in-hospital thrombolysis (IHT). After adjusting for age and comorbidity, primary PCI was associated with lower mortality than PHT and IHT at 30 days (4.9% vs. 7.6% vs. 11.4%) and at 1 year (7.6% vs. 10.3% vs. 15.9%). The benefits of primary PCI persisted regardless of treatment delay and it was associated with shorter hospital stay and less reinfarction.

The routine practice of performing delayed PCI for persistently occluded coronary artery after STEMI has been questioned. In the Occluded Artery Trial (OAT),\textsuperscript{28} 2,166 high-risk patients (with ejection fraction <50% or proximal occlusion) who had total occlusion of the infarct-related artery 3-28 days after MI were randomised to receive PCI or medical therapy. The median time to randomisation was 8 days. PCI did not reduce the occurrence of death, reinfarction or heart failure (17.2% vs. 15.6%, p=0.2) and there was a trend towards non-fatal reinfarction in the PCI group (6.9% vs. 5.0%, p=0.08). Thus, primary PCI should be done as early as possible after symptom onset and late restoration of coronary blood flow does not improve the left ventricular function, death, reinfarction or heart failure.

For STEMI, an invasive strategy with primary PCI is generally preferred if the door-to-balloon time can be achieved within 90 minutes or fibrinolysis is contraindicated.\textsuperscript{29} Fibrinolysis is preferred if <3 hours have elapsed from symptom onset, there is an anticipated delay that decreases the potential advantage of PCI, or an invasive strategy is not an option (e.g. owing to vascular access difficulties or lack of access to a skilled PCI laboratory with skilled operators). To ensure timely primary PCI service involves the organisation of a cooperative network for STEMI. After such reorganisation in the Vienna STEMI Registry, there was a substantial increase in the use of primary PCI with significant decrease of in-hospital mortality from 16% to 9.5%.\textsuperscript{30} More than 900 hospitals in the US have so far signed on to the D2B Alliance, representing more than 60% of US PCI hospitals. The aim is to reduce the door-to-balloon time for primary PCI to <90 minutes.

**Unstable Coronary Lesions - Vulnerable Plaque**

Acute coronary syndrome and sudden cardiac death originates from rupture of a non-flow limiting coronary atherosclerosis with superimposed thrombus formation\textsuperscript{31,32} These vulnerable plaques consist of a thin fibrous cap and a large lipid core with abundant macrophage infiltration.\textsuperscript{33} Proper identification of these plaques with appropriate treatment can theoretically prevent the catastrophic event of AMI or even sudden death.

Intravascular ultrasound (IVUS) has been used to identify coronary atherosclerotic plaque burden and assess vessel size. Spatial analysis of the IVUS signal (IVUS-Virtual Histology (VH)) can provide further details of the composition of the plaque, which can be categorised into necrotic, fibro-fatty, fibrous and calcified tissue.\textsuperscript{34} By using IVUS-VH, Gaston et al. could identify a significantly higher prevalence of IVUS-derived thin-cap fibroatheroma (TCFA) in patients presenting as acute coronary syndrome, as compared to stable angina patients.\textsuperscript{35} Ruptured TCFA...
was the culprit for 60% of the coronary artery thrombi.

Kubo et al. evaluated the ability of optical coherence tomography (OCT) for assessment of the culprit lesion morphology in AMI as compared to IVUS and coronary angiography (CAS). The incidence of plaque rupture observed by OCT was significantly higher than CAS and IVUS (73% vs. 47% vs. 40%). Fibrous cap erosion and intracoronary thrombus were also more readily identified by OCT. Further standardisation on OCT classification of plaque composition to minimise intra- and inter-observer variability will prove OCT to be a powerful tool for identification of vulnerable plaques.

Once a vulnerable plaque is identified, it is reasonable to cover the lesion and reinforce the cap by a stent which can also release pharmaceutical agents targeting to stabilise the necrotic core. Ongoing studies will provide more information on this mechanical treatment but aggressive medical therapy including anti-platelet and lipid-lowering agents will surely play an important role.

Way Forward

The development of PCI has been moving in a fascinating speed. It has been estimated that more than 1 million PCI procedures are being performed in the United States and about 2 million worldwide every year. The introduction of DES has greatly reduced the incidence of in-stent restenosis but in return increases the incidence of very late stent thrombosis. Hopefully, the next generation DES with a biodegradable polymer, together with optimal pharmacological therapy can expand the scope to treat more complex patient and lesion subsets while keeping stent thrombosis and restenosis to the minimum. The mortality benefit of primary PCI for STEMI is beyond doubt. It might involve structural organisational changes for proper implementation of the programme. However, if vulnerable plaques can be detected early and appropriate treatment initiated, significant number of ACS and AMI can be prevented. This in turn will improve the overall health of the general population.

References

MCHK CME Programme Self-assessment Questions

Please read the article entitled "Recent Advances in Percutaneous Coronary Intervention (PCI) " by Dr. Michael KY Lee, and complete the following self-assessment questions. Participants in the MCHK CME Programme will be awarded 1 CME credit under the Programme for returning completed answer sheets via fax (2865 0345) or by mail to the Federation Secretariat on or before 31 January 2008. Answers to questions will be provided in the next issue of The Hong Kong Medical Diary.

Questions 1-10: Please answer T (true) or F (false)

1. Repeat revascularisation occurred in 40% of patients implanted with bare-metal stent?
2. Angiographic restenosis occurred in 6-9% of patients 9 months after implantation of a DES?
3. In the SCANDSTENT trial, the use of sirolimus-eluting stent to treat the more complex lesion subsets, significantly reduced restenosis and MACE?
4. In the treatment of bare-metal stent in-stent restenosis, vascular brachytherapy is more effective than DES to prevent further restenosis?
5. The use of DES is associated with significantly more very late (>1 year) stent thrombosis while the overall incidence of stent thrombosis is the same as BMS?
6. To prevent DES stent thrombosis, patients should be reminded to continue dual anti-platelet agents for the pre-specified period of time and then continue Aspirin as monotherapy for life.
7. Primary PCI cannot improve the survival of patients presenting as ST-elevation MI.
8. The goal of the door-to-balloon time for primary PCI for AMI should be <90 minutes?
9. IVUS-derived thin-cap fibroatheroma (TCFA) by using Virtual Histology is more prevalent in patients with stable angina than acute coronary syndrome?
10. Acute coronary syndrome originates from rupture of a non-flow limiting coronary vulnerable plaque?

ANSWER SHEET FOR JANUARY 2008

Please return the completed answer sheet to the Federation Secretariat on or before 31 January 2008 for documentation. 1 CME point will be awarded for answering the MCHK CME programme (for non-specialists) self-assessment questions.

Recent Advances in Percutaneous Coronary Intervention (PCI)

Dr. Michael KY Lee

MBBS(HK), MRCP(UK), FRCP(Glasg), FHKCP, FHKAM(Medicine)
Specialist in Cardiology


Name (block letters):____________________________________ HKMA No.: ____________________________

HKID No.: ____ ___ - ___ ___ ___ ___ X X (x) Other Membership No. (please indicate): ____________________________

Contact Tel No.: _______________________________________

Answers to December 2007 issue

Laboratory Diagnosis of Community-associated Methicillin-resistant *Staphylococcus aureus*