Interventional Cardiology:
Update on Percutaneous Coronary Intervention

What should you know about new stent technologies and adjunctive drug therapies for coronary intervention? Learn more about these, as well as new innovations in the field of interventional cardiology.

Anita W. Asgar, MD, FRCPC; and Michael P. Love, MB, ChB, MRCP(UK), MD

Coronary artery disease is a leading cause of death and disability. Obstructive coronary lesions are increasingly treated by percutaneous coronary intervention (PCI), a procedure which typically involves balloon dilatation and intracoronary stent deployment (Figures 1, 2). Technologic, as well as pharmacologic advances have seen the scope and popularity of PCI evolve rapidly during the last decade. Indeed, more than 1 million PCI procedures are now performed worldwide each year, surpassing the number of coronary artery bypass procedures.

What can be said about stents?

Stents, which have arguably been one of the most important advancements in the field of interventional cardiology, improve the safety and efficacy of PCI. They are now used in 80% to 90% of all PCI procedures. Stent deployment improves lumen size, and minimizes the risk of early, abrupt vessel closure. Compared with plain balloon angioplasty, stents reduce the risk of vessel restenosis through their ability to prevent elastic vessel recoil and negative remodelling.1

Despite their success, the major limitation of stents is that they have not eliminated the problem of restenosis. In-stent restenosis (ISR) occurs because stent deployment triggers a complex biologic process in the vessel wall that leads to neointimal proliferation.2 Between 10% to 15% of stented patients develop sufficient proliferation of neointimal tissue that ISR occurs, resulting in the requirement for repeat revascularization. This sequence of events causes considerable patient inconvenience and additional health-care resource utilization.3

What about drug-eluting stents?

Targeting neointimal proliferation in an attempt to prevent ISR has been the rationale for the recent evolution of drug-eluting stents (DES).4 DES use the stent as a vehicle for prolonged intramural delivery of a drug aimed at reducing neointimal proliferation. The amount and rate of drug release is typically regulated by a polymer.5 Several different agents have been evaluated, two of which have emerged as leaders in the
field, and are currently approved for use in Canada—sirolimus and paclitaxel (Table 1).

Despite promising initial studies of DES, there are many important coronary lesion types for which DES have yet to be tested in randomized clinical trials (RCTs), such as:

- ostial lesions,
- bifurcation lesions,
- degenerate saphenous vein grafts,
- left main stem lesions,
- bare metal stent restenosis, and
- acute myocardial infarction (MI).

Regardless, it is widely anticipated that DES will quickly become the preferred technology for most PCI procedures.

Cost is the biggest impediment to the mass utilization of DES. In Canada, DES currently cost between four and six times more than bare metal stents. The incremental up-front cost of converting to universal DES use would be tens of millions of dollars annually. However, it is likely that some of

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**Table 1**

**Leading polymer-coated, drug-eluting stents**

<table>
<thead>
<tr>
<th>Properties</th>
<th>Sirolimus</th>
<th>Paclitaxel</th>
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<tbody>
<tr>
<td></td>
<td>Anti-proliferative,</td>
<td>Agent with proven reduction in cell proliferation and migration</td>
</tr>
<tr>
<td></td>
<td>immunosuppressive macrolide antibiotic&lt;sup&gt;6&lt;/sup&gt;</td>
<td></td>
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<tr>
<td>Related trial</td>
<td>Sirolimus-eluting stent for de novo lesions (SIRIUS) trial: 1,058 randomized patients&lt;sup&gt;7&lt;/sup&gt;</td>
<td>TAXUS IV trial: 1,314 randomized patients&lt;sup&gt;8&lt;/sup&gt;</td>
</tr>
<tr>
<td>Primary end point</td>
<td>Target vessel failure</td>
<td>Ischemia-driven target vessel revascularization</td>
</tr>
<tr>
<td></td>
<td>(composite of cardiovascular, death, MI, and repeat target vessel revascularization)</td>
<td></td>
</tr>
<tr>
<td>End point reduction</td>
<td>Reduced from 21% with standard stent to 8.6% (at 270 days)</td>
<td>Reduced from 12% with standard stent to 4.7% (at 9 months)</td>
</tr>
<tr>
<td>Effectiveness in patients at high risk of ISR (patients with diabetes, small diameter vessels, and long lesions)</td>
<td>Yes</td>
<td>Yes</td>
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**About the authors...**

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the up-front DES costs will be offset by reductions in repeat hospitalizations and revascularization procedures. Preliminary cost analyses suggest that DES may be cost-effective for most patients undergoing PCI, and possibly cost-neutral for high-risk patients.9

Some concerns persist about the long-term safety of DES, specifically the possible increased risk of delayed stent thrombosis, rebound intimal hyperplasia, aneurysm formation, or stent malapposition. Two-year followup after sirolimus-eluting stent implantation has confirmed continued efficacy of the sirolimus stent, with no evidence of late vessel toxicity.10 Concerns about delayed vessel healing and re-endothelialization have resulted in a recommendation for more prolonged treatment with acetylsalicylic acid (ASA) and clopidogrel following DES implantation (three months following sirolimus, and six months following paclitaxel-eluting stent implantation).

Several other drug coatings have yielded encouraging results in preliminary clinical DES trials, but further studies are required. Importantly, although DES significantly reduce the need for repeat revascularization, they have no effect on clinical end points such as death and MI.

Are biodegradable stents possible?

An exciting future possibility is that of biodegradable stents, in which the metallic component of a stent is replaced with a biodegradable polymer. Ideally, the biologically inert polymer component would resorb completely once its job of preventing early recoil and negative remodelling is completed.

Early clinical studies with a biodegradable poly-L-lactic acid stent have yielded encouraging preliminary results.11

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Alzheimer Disease

Dispelling the myths

Myth: Alzheimer Disease is preventable.

Reality: Because there is no known cause for Alzheimer Disease, there is no conclusive evidence that Alzheimer Disease can be prevented. There is, however, a growing amount of evidence that lifestyle choices that keep mind and body fit may help reduce the risk. These choices include physical exercise, a healthy diet including fresh fruits, vegetables and fish, as well as keeping your brain active.
What about adjunctive pharmacology?

Thrombotic complications during PCI have become much less common in the current era of high-pressure stent deployment and aggressive anticoagulation with heparin and combination antiplatelet therapy.

Thrombin plays a key role in thrombus formation and platelet activation. It is well-established that antithrombin therapy significantly reduces thrombotic complications during PCI. Unfractionated heparin (UFH) remains the most widely used antithrombin agent in the cardiac catheterization laboratory, but is increasingly being challenged by the low-molecular-weight heparins (LMWHs). The advantages of LMWH include the following:

- a more predictable anticoagulant effect,
- easier administration, with no required monitoring of activated partial thromboplastin time,
- a lower incidence of heparin-induced thrombocytopenia, and
- a decreased tendency to cause platelet activation.

Recent RCTs have confirmed that LMWHs are as safe and effective as UFH in a range of patients undergoing PCI. Accumulating evidence that some LMWHs may reduce adverse outcomes more than UFH in acute coronary syndromes may lead to the preferential use of these antithrombin agents during PCI. Various other novel alternatives to heparin under clinical investigation include direct thrombin inhibitors, such as bivalirudin and argatroban, and inhibitors of activated factor X, such as fondaparinux.

Antiplatelet therapy is an integral part of PCI to minimize the risk of stent thrombosis. The synergistic benefits of combination therapy with ASA and thienopyridines, such as ticlopidine and clopidogrel, are well-established and have been confirmed in several RCTs. Clopidogrel has become the drug of choice because of its favourable side-effect profile and more rapid onset of action. RCTs suggest...
that long-term combination therapy with ASA and clopidogrel following PCI may be associated with a reduction in adverse cardiac events at the expense of an increased risk of bleeding. Potential bleeding complications may be minimized by using a low ASA dose. 

Activation of the platelet glycoprotein (GP) IIb/IIIa integrin receptor complex constitutes the final common pathway for platelet aggregation. When administered parenterally (in addition to heparin, ASA, and clopidogrel), GPIIb/IIIa receptor antagonists reduce thrombotic complications and improve clinical outcomes following PCI. Three such receptors have been approved for use in Canada: abciximab, eptifibatide, and tirofiban. There are compelling data to support the routine use of these agents during elective and emergent PCI. However, their cost often results in administration being targeted in patients with clinical or angiographic features which suggest an increased risk of an adverse outcome, such as presence of diabetes, angiographic evidence of thrombus, or complex lesion morphology.

Are there any other novel inventions?

The important complication of procedural MI secondary to distal embolization of atherothrombotic debris from the site of PCI led to the development of distal protection devices. Two main types of distal protection device have been developed (Figure 3). The first of these devices protects the distal circulation by inflating an occlusion balloon downstream from the site of PCI. Embolized debris is trapped within a stagnant column of blood and can be aspirated via a specially designed catheter.

The other type of distal protection device uses a porous filter positioned downstream from the site of PCI. The filter pores are large enough to allow continued antegrade vessel perfusion but small enough to catch any embolic debris (Figure 4). Preliminary clinical trials with each type of device have yielded encouraging results in the two most common settings of distal embolization: degenerate saphenous vein graft intervention, and primary PCI for acute MI.

In summary, interventional cardiology is an ever-changing field with new advances that promise to improve the quality of patient care.

References