Pitfalls in coronary stenting

A review of current strategies

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Coronary stenting has evolved rapidly since the first implantation of a stent to treat abrupt vessel closure of the left anterior descending (LAD) human coronary artery in 1986. Many lessons have been learnt in the last 10 years, leading to high rates of implantation success with an ever-falling incidence of stent thrombosis. Planning of each case is an important part of ensuring a successful short-, medium- and long-term outcome. Important issues in this planning process can be divided into: (i) patient selection/clinical indication; (ii) lesion selection; (iii) equipment; (iv) which stent?; (v) deployment strategy; (vi) post-deployment treatment; (vii) treatment of in-stent restenosis.

Patient selection/clinical indication

There are no data to suggest that any particular patient groups should not receive an intra-coronary stent. Specifically, elderly patients do well, especially since anticoagulation regimens have been reduced. Despite the apparently unfavourable coronary environment of unstable angina a number of studies have indicated that, given optimal stent deployment, the clinical outcome is similar to when stents are inserted in stable angina. In the case of the deployment of stents in the presence of angiographically visible coronary thrombus the results remain encouraging, although there does appear to be a small increase in myocardial infarction perhaps indicative of distal embolisation. It will be interesting to see the influence of the IIb/IIIa platelet receptor inhibitors such as ReoPro on the results of stenting in this clinical situation. Although the data on the use of ReoPro are established in the setting of balloon angioplasty in unstable clinical syndromes, the data on stents are less clear. Recently there has been great interest in the use of primary stenting for the treatment of acute myocardial infarction. No controlled data are available in this clinical setting, but some observational studies have given encouraging results and the PAMI 3 study will aim to delineate the role of stenting in acute myocardial infarction.

Intra-coronary stents may be used in four situations within the cardiac catheter laboratory: (i) elective; (ii) suboptimal balloon result; (iii) threatened vessel closure (pain, dissection and reduced TIMI flow); (iv) acute vessel closure (TIMI 0 - 1 flow).

There does appear to be a clear difference in outcome if stents are placed in the 'bail-out' situation (with altered TIMI flow) rather than for a suboptimal balloon result or in the elective situation. In the bail-out situation the incidence of subacute stent thrombosis, myocardial infarction, coronary artery bypass grafting, death and angiographic restenosis is significantly increased. Most of these data predate the routine use of ticlopidine, aspirin regimens and high-pressure balloon deployment and may need to be revisited. However, the clear message from these clinical trials is that stents should be deployed at an early stage before there is an alteration in TIMI flow within the vessel.

Lesion selection

It is important to decide on the rationale for stenting in any particular situation. Stents may be delivered electively, either in an attempt to reduce restenosis or to ensure a good primary
angiographic result. The Benestent and STRESS trials pro-
vided the data for so-called 'restenosis stenting' with
angiographic restenosis rates in the stent arms being 22 - 32%
compared with 32 - 42% in the balloon angioplasty arms. It is,
however, important to remember that the patients and
lesions in these trials were very carefully selected. Entry crite-
ria for the Benestent study included the presence of stable
angina, a single lesion in a native coronary artery of less than
15 mm (actual mean lesion length 7.06 mm) and a vessel size
of greater than 3 mm supplying normal myocardium. Only
3% of patients were undergoing angioplasty of an occluded
coronary artery. In our own institution the number of patients
who would be eligible for the Benestent study make up only
20% of the total number of patients receiving an intra-coron-
ary stent.

The results of stenting 'non-Benestent type lesions' (e.g.
small vessels, long lesions, ostial lesions and saphenous vein
grafts) compared with 'Benestent-type' lesions are signifi-
cantly different, with angiographic restenosis rates of
30 - 40% compared with around 11%. Although the in-stent
restenosis rates in this type of lesion may be high, it may well
be that these will be lower than with balloon angioplasty but
this has not yet been proven in a randomised trial. Subgroup
analysis of the Benestent study also suggests that the greatest
benefit of stenting appears to be in the LAD artery (angio-
graphic restenosis reduced from 43% to 27%), with less
impressive results in the right coronary artery (32% reduced to
23%) and the circumflex coronary artery (32% reduced to
25%).

There is now good evidence that the elective deployment
of a coronary stent following the successful reopening of an
occluded coronary artery will improve both angiographic and
clinical events at 6 months, with a significant reduction in re-
occurrence and restenosis rates. Coronary stents have also
allowed patients with unprotected left main to be considered
for angioplasty-type procedures. However, the medium-term
results appear disappointing with a high follow-up cardiac
mortality rate of 17%. Although these data should be inter-
preted with the knowledge that the majority of patients had a
contraindication to bypass surgery, further work appears
necessary before this becomes an established treatment
modality for left mainstem disease.

There are currently no randomised studies comparing dif-
ferent stents in specific lesion subgroups, but given the cur-
rent variation in stent design and properties the following
recommendations can be made:

1. Ostial lesions. The critical properties of a given stent in
this situation are accuracy of stent placement and high radial
strength. For this reason a slotted-tube or zigzag wire type of
design, with markers on the balloon indicating the stent posi-
tion, can be recommended.

2. Calcified lesions. For this type of lesion high radial
strength is most important. The slotted tube type of design
may therefore be favoured. The concept of debulking with
rotational atherectomy prior to stent deployment (so-called
'stent synergy') may well aid optimal stent deployment and
this approach is currently under clinical evaluation.

3. Long lesions. An increasing number of stents of
> 20 mm are available. Data on the procedural and medium
outcome of these devices are currently limited and there are
certainly no randomised data comparing one device with
another. Future studies of the user-friendliness and restenosis
rates of the various long stents should indicate if a particular
stent design has an advantage in any given subset of lesions.

4. Tortuous proximal anatomy. Wire coil stents appear
to have advantages if there is marked proximal tortuosity but
these stents do tend to have less radial strength. The zigzag
wire stent (AVE Microstent) combines high tractability with
adequate radial strength and may be the best stent currently
available for this subset of lesions.

Equipment

Despite the advances in stent technology the addition of an
intra-coronary stent to an angioplasty balloon inevitably leads
to a device that is generally more bulky and a little less flexi-
ble. Because of this, optimisation of the guiding catheter and
guidewire remains important for successful stenting proce-
dures. Guiding catheters with smooth curves are therefore
preferable. This is particularly the case if long stents are being
used. Occasionally the use of 'Amplatz'-type curves can be
difficult in this situation. It is always important to keep in
mind that an intra-coronary stent may eventually be deployed,
even if this is not the initial strategy planned. Most stents can
now be deployed through a 6F guiding catheter but this is not
always the case if large-diameter (> 3.5 mm) stents are to be
deployed. Advance planning is important. The use of 'support'
type wires improves the trackability of most stents, the
only disadvantage being the relatively frequent occurrence of
coronary spasm in the wire.

Which stent?

Over 15 coronary stents are now available in Europe (most in
variable lengths). These can broadly be divided into: (i) slotted-
tube (Johnson and Johnson Palmaz-Schatz, ACS Multilink, Scimed NIR, ACT ONE, Biotronik Tensum 3 and Bard Angiomed); (ii) wire coil ( Cordis, Medtronic Wiktor, Cook Gianturco-Rubin, Global Therapeutics Freedom and Angiodynamics Angiostent); (iii) wire braid ( Schneider Wallsten); (iv) spiral coil (Innolink Cardiocoil); (v) zigzag wire (AVE Microstent).

All of these stents have their own potential advantages and
disadvantages. To assess which stent is best suited to a parti-
cular lesion the following should be considered: (i) the need
for radial strength in calcified or ostial lesions; (ii) low metal
to vessel coverage when large side branches are associated
with the primary lesion; (iii) high metal coverage for friable
lesions such as those within a vein graft; (iv) flexibility of the
stent for tortuous lesions; (v) the specific length of the lesion
and the length of stent required to cover the entire lesion.

There is certainly evidence in the animal model that stent
design ( strut design, surface characteristics, foreign body
reaction, deformability, radial strength and endothelial preser-
vation) can influence issues such as thrombogenicity and sub-
sequent intimal hyperplasia but the relevance of this to clini-
cal practice has yet to be established. No large-scale
'head-to-head' stent studies have yet been reported but many of these are currently underway in the USA, under the auspices of the FDA.

**Deployment strategy**

The initial era of coronary stenting was dogged by the two major complications of subacute stent thrombosis and bleeding secondary to the excessive anticoagulation regimens that were thought necessary to try to prevent subacute stent thrombosis. Nakamura et al., using intravascular ultrasound, showed in 1994 that many stents with a satisfactory angiographic appearance were in fact suboptimally deployed. Intravascular ultrasound showed that 80% of patients needed further dilatation, either with higher pressures or larger balloons when the angiographic appearance appeared optimal. Intravascular ultrasound was required to: (i) appreciate stent under-expansion; (ii) show incomplete strut apposition; and (iii) allow accurate balloon sizing. Nakamura et al. went on to show that with intravascular ultrasound-guided stent deployment using high-pressure balloon dilatation a very low stent thrombosis rate could be achieved using aspirin and ticlopidine rather than the usual anticoagulation regimens. The French Multicentre Registry (MUST) has also indicated the low subacute stent thrombosis rates that can be obtained with the aspirin/ticlopidine regimen. The concept that optimal stent deployment, using high-pressure balloon inflations, was the most important factor in preventing stent thrombosis (rather than anticoagulation regimens) was a major advance in eliminating the major complications of elective coronary stenting. Whether routine intravascular ultrasound following stent deployment is a cost-effective strategy remains controversial. With high-pressure balloon deployment and subsequent aspirin/ticlopidine antiplatelet regimens subacute stent thrombosis rates are now 0.5-1.5% in most series. It will be difficult to demonstrate that additional intravascular ultrasound can influence this low rate. The MUSIC study was designed to show the impact of intravascular ultrasound on stent deployment and may help to answer this question. A newer concept is that intravascular ultrasound-guided deployment may influence subsequent 'in-stent' restenosis but there are currently no data to support this.

**Post-deployment treatment**

The ISAR study has provided compelling evidence that the regimen of aspirin and ticlopidine has major advantages over the previous standard regimen of intravenous heparin and warfarin. In this randomised study subacute stent thrombosis (0% v. 5.4%), cardiac events (1.6% v. 6.2%) and non-cardiac events (including significant bleeding) (1.2% v. 12.3%) were significantly lower on the aspirin/ticlopidine regimen. It is now difficult to see any indication for the standard anticoagulation regimen. In the presence of angiographic thrombus post-stent deployment should be used or if optimal stent deployment cannot be achieved it may well be more logical to use ReoPro although no data on this are currently available.

**The treatment of in-stent restenosis**

Because most units will be placing stents in many situations that do not meet the criteria of the Benestent and STRESS studies it is likely that subsequent in-stent restenosis rates will be higher than those seen in these two trials. There is currently no agreed optimal strategy for the treatment of this condition. The Washington Group (Mintz et al.), using serial intravascular ultrasound studies, have elegantly demonstrated that the pathology of in-stent restenosis is very different from that after conventional balloon angioplasty. When restenosis occurs following balloon angioplasty 73% of the late loss is due to remodelling (vessel shrinkage) and only 23% to intimal hyperplasia. The logical treatment for this condition would therefore appear to be to place a stent and the REST study’s provisional results appear to support this, with re-intervention rates reduced from 37% to 11.7% by elective stenting. However, with in-stent restenosis, virtually 100% of the late loss is due to intimal hyperplasia; the stent prevents vascular remodelling. Balloon dilatation within the stent appears to have variable results. If there is localised stent-border or intra-stent restenosis then balloon angioplasty has acceptable re-restenosis rates of 15 - 20%. However, if there is diffuse in-stent restenosis then balloon angioplasty leads to an unacceptably high re-restenosis rate of 50 - 85%. Alternative treatment options would appear to be laser angioplasty, rotational atherectomy or directional atherectomy. There is currently little information on recurrence following these treatment regimens. However, if these do become the preferred method of treatment it is highly likely that intravascular ultrasound will be essential for these procedures in order to: (i) assess initially the pathology within the stent; and (ii) assess the safety of the intervention, so that no trauma occurs to the stent struts.

**Conclusion**

Intra-coronary stenting has advanced rapidly over the last 10 years. Percutaneous interventional techniques are now a very real alternative treatment strategy to arterial grafting. Randomised trials comparing the outcome of coronary angioplasty and bypass grafting in multivessel coronary artery disease (in the current era of coronary stenting and arterial grafting) are about to start (the SOST study). Major advances in stenting technique have led to high rates of initially successful deployment, with very low subsequent stent thrombosis rates. Careful planning of each interventional case remains vital for a successful outcome. Continued research and stent development will be needed to lower the restenosis rates in non-Benestent type lesions. This will probably involve changes in stent design including coatings along with adjunctive therapies such as radiation delivery and growth factor suppression. The major challenge currently, however, is likely to be the treatment of in-stent restenosis. Unless an effective treatment strategy is found for this newly created disease process an unacceptable number of stent patients will eventually progress to coronary artery bypass grafting.
References


