CHAPTER

7

Bare Metal Stents – Role in Drug Eluting Stent Era

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Introduction

When angioplasty was introduced in the late 1970's, it was estimated that only 5% of patients with coronary artery disease (CAD), would be acceptable candidates. Since then, the development of circulatory support systems, advances in catheter technology, and increased operator experience have extended the application of percutaneous techniques – and, the single most important advance being the coronary stent.

A Few Facts

1. Recently most Percutaneous Transluminal Coronary Angioplasty (PTCA) procedures have involved the use of stents. Percutaneous Coronary Interventions (PCI) is a generic term to encompass PTCA with or without adjunctive techniques.
2. The major problem with balloon angioplasty is restenosis of the artery.
3. A repeat procedure is consequently required in approximately 20% of patients with simple lesion. This rate of reintervention is much higher (upto 50%) for arteries with small diameter, saphenous vein grafts, long lesions, total occlusions and in people with diabetes mellitus (DM).
4. Stents have been repeatedly shown to reduce the need for repeat procedures when compared to balloon angioplasty alone.
5. One of the main criteria for assessing the clinical effectiveness of stents compared with standard balloon angioplasty is their ability to reduce the incidence of subsequent attacks of angina as well as adverse events, which include death, myocardial infarction (MI), and the need for further reinterventions.
6. Drug eluting stents (DES), release cytostatic or cytotoxic drugs locally to reduce the incidence of restenosis. In the era of 'Bare Metal' stenting (BMS), it was anticipated that 20–30% of lesions would recur warranting repeat interventions, which has fallen to about 5% since DES introduction.
7. Any foreign object placed in blood vessel can cause thrombosis. The consequence of this is MI and rarely sudden death. Both BMS and DES can result in the above events – which necessitates need for dual antiplatelet therapy with aspirin and clopidogrel for variable amount of time after stent implantation.
8. There is evidence that stopping all antiplatelet therapy, at any time, after any type of stent may lead to stent thrombosis. This risk is probably higher with use of DES as shown in Basket – Late study.[1]

9. The risk of bleeding associated with use of longterm antiplatelet therapy needs to be considered for each patient.
10. While the efficacy of DES has been demonstrated by several clinical trials, the impact of DES on health care costs and recipient quality of life (QOL) is debatable.

The Evidence

1. Numerous clinical studies and systematic reviews have established that first generation DES reduce **angiographic restenosis** by 60–80%, and the need for **repeat revascularisation** procedures by 50 – 60 % compared to BMS[2]. However, observational studies [1] and followup trials comparing DES with BMS, and meta analysis of randomized trials,[2,3] suggested that very late stent thrombosis (ST), (more than 1 year after stent implantation) was more common with DES than BMS.

   A 15 month follow up study, which used western Denmark heart registry and western Denmark's healthcare databases covering the region's entire population found that the risk of ST, 15 month cumulative incidence of MI and mortality were similar in BMS & DES treated patients. Very late ST was seen more commonly in DES than with BMS (p value=0.03) and Target Lesion Revascularisation(TLR) within 15 months occurred less frequently in DES patients than in patients with BMS (p value < 0.0001).[4]

   Another large registry study, the Swedish coronary angiography and angioplasty registry (SCAAR)[5] showed similar findings to those in Danish study. The SCAAR data suggested that the rates of death and MI were similar for patients with DES and BMS during the first 6 months following stent implantation, but rates of MI and death increased in DES group after 6 months. There was no difference between the two stent groups in cardiac or noncardiac mortality during 15 months of followup.

   The new SCAAR analysis reported at ESC, Vienna September 2007, showed no overall increased deaths with DES at 4 years and found no difference with the BMS treated group.
2. **Late stent thrombosis** (ST) exists in both DES and BMS. Retrospective analysis of ST, applying the Academic research consortium definitions in randomized controlled trials, does not reveal a different rate of late ST between BMS and DES upto 4 years. But, the chronology and circumstances of occurrence seem different. In DES, late ST occurs later than in BMS and seems to appear as primary thrombosis; Whereas in BMS, a certain number of late ST are related to repeat interventions of target lesions.[6]
3. Treatment of **Instent Restenosis** (ISR) with further implantation of BMS did not show improved outcomes; Whereas in ISAR Desire and Ribs II trials,[7] DES was associated with > 50% reduction in recurrent restenosis.
4. **Diabetes Mellitus** (DM) is not only a major risk factor for CAD, but also is associated with poorer results in patients treated with coronary revascularisation procedures. Several factors are involved in the higher rate of subsequent revascularisation in diabetics when treated with PCI – such as high frequency of incomplete revascularisation, progression of disease in nontreated segments and higher rate of restenosis . Several randomized trials (ARTS 1, SoS, MASS 2, AweSome, Eraci 2) in patients with DM and **multivessel disease**(MVD) compared PCI with coronary artery bypass graft surgery(CABG) in the BMS Era, and showed that the treatment with coronary stents was associated with higher incidence of recurrent ischemia and new revascularisation procedures.[8]
5. Even in the Era of DES, the best treatment for patients with **DM and MVD** remains controversial.[9] Randomised trials comparing CABG and DES are ongoing (SYNTAX,

FREEDOM, and CARDIA). Though the Research registry[10] and ARTS II[11] have demonstrated beneficial effects in reducing major adverse coronary events (MACE) with DES in MVD than with BMS.

6. A meta analysis [12] of all randomized trials on use of DES in **Acute Myocardial Infarction** (AMI) (which included TYPHOON,[13] PASSION,[14] and STRATEGY[15] trials), showed significant reduction in TLR without any significant change in the incidence of death and MI compared to BMS (p value < 0.0001). Use of DES was not associated with increased risk of ST upto 1 year followup – a finding similar to that noted with use of BMS. However sirolimus eluting stents(SES) showed lower restenosis and TLR compared to paclitaxel eluting stents(PES).
7. Procedural complexity and longterm recurrence remain major concerns when stents are implanted in **complex lesions**. It seems that the combined use of Rota-DES has a favorable effect when dealing with heavily calcified lesions in both the angiographic and clinical outcomes at 9 months as compared to BMS implantation after rotablation.[16]
8. A clinical followup results from German Cypher stent registry on implantation of SES in **Saphenous Vein Grafts** (SVG's) , showed high target vessel revascularisation (TVR) and MACE rates with use of SES.[17]
9. Given the modest gains in both MACE and TVR in addition to increased rates of ST with **'off label'** use of DES, its use for non FDA approved indications should be undertaken with caution.[18]

As yet unanswered questions

1. Which stent ?
2. How much Antiplatelet therapy ?
3. How effectively are we deploying the stents ?
4. Is thin strut BMS comparable to DES ?

The trial data and statistics only seem to confound the issues !

The messages from the data:

1. Importance of antiplatelet regimens and adjunctive benefits of glycoprotein IIb/IIIa inhibitors.
2. Pooled data comparing DES with BMS do not show any significant difference between the 2 treatment arms in rates of death/MI/ST.
3. Stent Thrombosis is more common with DES than BMS after 1 year.
4. DES definitely reduces TVR.
5. DES use is associated with increased rate of death after 6 months compared to BMS, but seems to level off by 4 years.
6. DES is better for high risk lesions and ISR following BMS use.
7. For left mainstem disease and MVD especially in diabetic population, surgery should remain the treatment of choice until trials prove efficacy and safety of use of DES in these situations.
8. **Some patients might be better treated with BMS (and not DES)**. For example –
   - The very elderly
   - Those who will need a surgical procedure within 1-2 years .
   - Those with prior bleeding problems who are at risk from dual antiplatelet therapy.
   - Acute MI and Acute coronary syndromes with heavy thrombus burden.
   - Venous graft disease.
   - Large coronary artery size (more than 3.5 mm diameter vessel)

The Future

Should focus on :

- New BMS designs
- Head to Head trials of BMS & DES

- Bioabsorbable stents
- The need for reinterventions which are clinically driven and not protocol driven (as in trials) .

Conclusion

During the twothirds of a century since Forssmann's experiment, the introduction, development and deployment of invasive and interventional approaches to diseases of the heart and vasculature have taken us on an extraordinary journey. Since the first intracoronary stent placement in 1986, coronary stenting has become the most commonly performed percutaneous coronary intervention around the world.

Despite the phenomenal pace of stent design technology and adjunctive therapies, much has yet to be learned, as regards longterm outcome of patients treated with intravascular stents.

The ongoing trials are certain to show '**the light at the end of the tunnel**'.

Yes, DES is good

But, BMS is not bad either.

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