



Editorial

Are all stents equal – Need for scoring system to evaluate stents?



A B S T R A C T

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Stent scoring system
Price fixation

Currently drug eluting stents (DES) have reached a high degree of sophistication where there seems very little scope of improvement. Even so every year or so there is some advancement in technology and a new version is released, which is claimed to be a new generation (rather than pipeline innovation). It is really important to define what pipeline extension is and what is new innovation (generation)? This classification would not only be useful from regulatory perspective but also determining the true value of a product allowing for a correct pricing, which should ideally be able to mark-up for a real innovation.
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1. First things first – are current generation DES all equal?

Stents (as they are available in cath lab) are essentially composed of 4 components: Bare stent, anti-restenotic drug, polymer, and delivery system. The stent itself has several components relevant to clinical outcome; stent material, strut thickness, and stent design. Evolution occurs in all these components so much so that latest generation stents are quite different from the so called “first generation” stents in technical specifications. But leave aside technicalities, even outcomes of current generation DES are much superior to first generation DES and this has led to extinction of some earlier stent.^{1,2} SPIRIT-II trial (300 patients) revealed that Xience V stent (3rd generation) was superior to Taxus stent (1st generation) effecting significant reduction in late loss (0.12 vs. 0.37 for Taxus, $p < 0.001$) and a numerical reduction in binary restenosis. (1.3% vs. 3.5%; $p = 0.194$), and target lesion revascularization [TLR] (2.7% vs. 6.5%; $p = 0.157$). In addition, cardiac death, myocardial infarction [MI] and stent thrombosis was also numerically less (although did not reach statistical significance).³ Subsequently, the SPIRIT-III, a randomized controlled, multi-centric study, comparing Xience V with Taxus stent also revealed that at the end of 2 years, Xience V showed superior results; target vessel failure [TVF] showed a 32% reduction (10.7 vs. 15.4%, hazard ratio [HR] 0.68, 95% confidence interval [CI] 0.48–0.98; $p = 0.04$) and a 45% reduction in major adverse cardiac events [MACE] (7.3 vs. 12.8%, HR 0.55, 95% CI 0.36–0.83; $p = 0.004$).⁴ SPIRIT IV randomized 3690 patients to receive the Xience V or Taxus stent. At 1 year follow-up the stent thrombosis was lower with Xience V (0.29% vs. 1.06%, $p = 0.003$). At 3 years there was a 43% and 39% reduction in MACE and TLR.⁵ Another real-world trial compared Xience V with Taxus, randomizing 1800 patients (pts.). The primary end-point was a composite of all-cause mortality, non-fatal MI and target vessel revascularization [TVR] within 12 months and was significantly less in the

Xience group (6% vs. 9%, relative risk 0.69, 95% CI 0.50–0.95; $p = 0.02$ for superiority). Further, Xience V stent was also associated with significantly less stent thrombosis ($p = 0.002$).⁶ Thus evolution of stents represents not only marked improvement in efficacy but also in safety (stent thrombosis, MI at one year). These differences in outcomes could be explained by differences in the underlying stent platforms, the anti-restenotic drug or the polymer eluting the drug.⁷

1.1. Definitions

Pipeline products: pipeline products are those medical device technologies currently in the pipeline for commercialization. Regulation wise, pipeline products work on the concept of “substantial equivalency” i.e. if a product is similar enough to one already on the market and proven to be safe, it can gain approval without clinical trials. But pipeline products do represent an advance in the field whether it is improved efficacy or safety but mostly ease of use. Improvement in device delivery technology represents a good example of pipeline extension.

Next-generation products (aka platform products) are innovations which should satisfy 4 criteria⁸:

1. Address the felt-needs in a particular field.
2. Lead to substantial improvement in the range and efficiency of a product.
3. Incorporate significant improvements in performance and cost over the preceding generation.
4. Provide a path for current users to migrate from the older product.

Thus next-generation products require a major commitment of resources by the innovators but they are expected to inspire and support a whole new line of derivative products by the competitors.

2. How to establish the real clinical value of a stent?

The proof of the pudding is in eating and the bottom-line for any medical technology is if it can be proven to benefit the recipient or end-user. In other words outcome data is the most valuable proof of usefulness of any stent. However, in clinical situations particularly in context of medical devices there are several limitations to an approach purely based on data acquisition.

1. The most important limitation is that it takes a huge amount of time for data to accrue; typically hard data is obtained only after minimum of three–five years follow-up, but by this time several innovations have already happened and the older device that has accumulated this kind of data may already be antiquated. A case in point is Cypher/Taxus stent, which probably have the maximum amount of data but are no longer in use.
2. The second limitation is number of pts. required for a meaningful outcome may be huge especially if hard end-points are considered, making the study not only very expensive but a logistics nightmare as well.
3. Variability of end-points chosen; late loss, event rate, TLR, TVR, re-stenosis, TVF, mortality, etc. Some of these end-points, e.g. late loss are soft but some others like stent thrombosis or mortality are hard. The value of each study whether observational or randomized control trial will also be different depending on these variables.
4. The quality of study may also be different, randomized controlled trial, observational study, case report have different connotations.
5. The quality of data can also be widely variable, unpublished data is inferior to published data but in a non indexed journal, which is inferior to that published in peer-reviewed indexed journal.

Clearly one cannot totally rely on data alone or technical features alone. There is a need to integrate both technical features and data to come out with a score determining the real value of a stent (innovation). In choosing data the quality of data is very important; at the minimum it should be obtained from peer-reviewed, indexed journals. In choosing the technical specifications, those features should be chosen which have a proven impact on clinical outcome or interventionist's ease of use.

3. Clinical outcomes vs. ease of use

Clinical outcomes can be efficacy or safety. They vary from late loss, event rate, TLR, TVR, re-stenosis, rate of coronary artery bypass grafting to stent fracture, stent thrombosis, stroke rate, bleeding risks to mortality. End-user usability characteristics can vary from visibility of stent while implantation (radio-opacity), deliverability, ability to implant without vessel preparation, need for imaging modalities. There could be some cost outcomes as well, for example ability to deploy one long stent instead of two short ones can save on cost.

4. What about US FDA and European CE?

US FDA and European CE Mark also look at the efficacy and safety data before certifying a stent for clinical use in their respective countries, so is there a need to re-invent the wheel? The reality is that FDA and European CE are approvals for marketing, are focused on safety and but no indicators of relative clinical value of different stents. Further, FDA is constrained by several limitations. Foremost is a long time in the approval process, it even requires repetition of study in US sites, even if similar data is already available from other countries. However, a major limitation is that there is no mechanism of recall, so much so that the stents remain approved even if they have long over-lived their usefulness and even become obsolete. On the other hand, the major limitation of CE mark is the wide variability in the quality, depending on the country of marking.

5. How to classify/score a stent

To understand the value of a given stent and for the purpose of comparison between various available stents it is imperative to develop an objective scoring system. For classification of stents considerations of both technical aspects and outcome data should be made. Among technical features those that have a bearing on outcome should be considered. Each point can be scored according to degree of advancement and potential clinical/user benefit. [Table 1](#) proposes a simple objective scoring system to achieve such an outcome. The maximum score possible is 20. Stent can be classified according to scores achieved, [Table 2](#). For first generation score is <6, second generation a score between 6–11, third

Table 1
Score for stent classification.

Stent		Polymer		Data (meta-analysis of all studies available), %	
Material				No data	0
Stainless steel	0	Biocompatible $\geq 10 \mu$	0	MACE – 1 year	
Cobalt chromium	1	Biocompatible $< 10 \mu$	1	>9	0
Platinum chromium	2	Bio-resorbable $\geq 10 \mu$	2	6–9	1
Bio-absorbable	3	Bio-resorbable $< 10 \mu$	3	<6	2
Stent strut thickness				Target vessel failure – 1 year	
$\geq 150 \mu$	0			≥ 5	0
$\geq 100 \mu$	1			3–5	1
$\geq 80 \mu$	2			<3	2
$<80 \mu$	3				
Design				Stent thrombosis – 1 year	
Spiral	0			>1	0
Slotted tube	1			0.5–1	1
Hybrid	2			<0.5	2
Advanced special design features	3			Mortality – 1 year	
				>2	0
				1–2	1
				<1	2

Table 2
Stent classification based on score.

	Score
1st generation	<6
2nd generation	6–11
3rd generation	12–16
4th generation	>16

generation 12–16 and fourth generation 17 and above. This classification categorizes stents according to contemporary usefulness and can serve as a mechanism for fixing their appropriate prices.

6. Future validation

This score will require validation in future studies but this will take a long time and it is important to have something in place to solve immediate needs.

7. Conclusions

As stent technology evolves there is improvement in efficacy and safety. However, there is a need to objectively establish usefulness of stents. This may have impact on rational pricing of these devices.

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