CME Article

A stent is not just a stent: stent construction and design do matter in its clinical performance

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ABSTRACT

The undisputed superiority of stents over conventional balloon angioplasty has resulted in a plethora of stents in clinical use. Recent data, however, have indicated not all stent models are the same. Nuances in stent design and construction have impacted significantly on the immediate and long-term clinical outcome. Among the stainless steel stents, those with multicellular or tubular designs have proven to be superior to coiled or hybrid stent models, and thin-strut stents perform better than thicker-strut stents. Coating stainless steel stents with gold, carbide, phosphorylcholine or heparin do not appear to confer any additional benefit, compared with bare metal stents. In contrast, randomised trials have demonstrated that drug-eluting stents coated with various anti-proliferative drugs, with or without a carrier polymer, afford unparalleled restenosis rates compared with non-drug-eluting stents. Drug-eluting stents, however, are expensive, and their long-term durability and safety remain undefined. Notwithstanding these unresolved issues, it is likely that the majority of percutaneous coronary interventions will involve the use of drug-eluting stents once a more attractive balance between their cost and clinical effects is reached.

Keywords: balloon angioplasty, coronary restenosis, coronary stents, coronary thrombosis, stents

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INTRODUCTION

Stent technology, its deployment technique and peri-stenting medical regimen have evolved substantially since the introduction of stents in interventional cardiology by Sigwart et al 15 years ago[1]. Its impact in the field of medicine has been enormous; it is estimated that about 70% to 80% of all percutaneous coronary interventional procedures involve the use of stents. For several reasons, cardiologists worldwide have embraced this technology enthusiastically. Firstly, robust data from several randomised trials comparing stent placement with conventional balloon percutaneous transluminal coronary angioplasty (PTCA) have incontrovertibly demonstrated the superiority of the former procedure[2-5]. Stent placement for the treatment of simple coronary lesions yields better short- and long-term anatomical and clinical outcome compared with PTCA. Secondly, the use of high-pressure post-stent dilatation to ensure optimal stent expansion and aggressive post-stent non-anticoagulant, antiplatelet medical regimens have resulted in a dramatic diminution of stent thrombosis[6-10]. The latter complication no longer remains a daunting problem. Thirdly, the constant improvement in stent technology has produced stents with more flexibility, trackability, radiopacity and scaffolding properties compared with earlier stent models, thereby enabling more difficult lesions to be treated successfully. Lastly, the experience accrued has resulted in greater operator confidence and has expanded the indications for stent placement to include more complex non-STRESS/BENESTENT lesions. The result is that we now have a plethora of at least 40 newer stent models with widely disparate structural characteristics to choose from in our clinical practice. But do all stents behave similarly and do they produce the same anatomical and clinical outcome? This article hopes to provide insight into the impact of stent design and construction on clinical-driven outcomes.

ACUTE CLINICAL OUTCOME

It is abundantly clear to high-volume interventional cardiologists that the acute performance of different stent models differ. The meshwire stent design is mounted on a high-profile rigid delivery platform, making it unsuitable for tortuous vessels. In addition, its high metal density makes the stent very prone to thrombosis and restenosis[10,11]. The coil and hybrid (with mixed features of coil and tubular) stents are more flexible and trackable but have a high degree of elastic recoil and poorer radial strength (hence, less scaffolding support) than tubular or multicellular stents[12-14]. Their immediate angiographical and

Table I. Stent versus stent randomised trials.

Trial	Stent type	No. of patients	Early ST rate (%)	RS rate (%)	p-value
RENEWAL[11]	NIR	82	2.3	26	*NS
	Wallstent		4.8*	46ξ	ξ0.1
Lansky et al[12]	GR-II	755	3.9	47.3	*<0.001
	PS		0.3*	20.6*	
Yoshitomi et al[13]	ML	100	0	4	*0.003
	GFX		0	26*	
Thuesen et al[14]	NIR	111	0.9	17	*NS
	Crossflex	112	0*	26*	
NIRVANA[19]	NIR	849	0.5	19.3	*NS
	PS		0.5	22.4*	
ASCENT[20]	ML	1040	0.6	16	*0.04
	PS		1.8*	22ξ	ξ0.31
Miketic et al[21]	NIR	203	0	22.0	*0.4
	Crown		0	18.4*	
Kastrati et al[22]	Inflow	1147	1.8	35.0	*0.724
	ML		1.3	25.3	ξ0.145
	NIR		1.7	28.6	
	PS		3.0	35.9	
	PURA-A		1.8*	29.4ξ	
Kastrati et al[27]	Gold Inflow	731	2.5	49.7	*0.08
	Steel Inflow		0.8*	38.1ξ	ξ0.003
Park et al[29]	Gold NIR	216	0	46.7	*<0.05
	Steel NIR		0	26.4*	
NIRTOP[30]	Nirflex	147	0	17.8	*0.002
	Nirflex Royal	158	0	33.1*	

*, ξ: p-values for comparison between stent types.

GR: Gianturco-Roubin stent; ML: Multilink stent; NA: not available; NS: not significant; PS: Palmaz-Schatz stent; RS: restenosis; ST: stent thrombosis.

ultrasonographical luminal results tend to be inferior to those observed with the latter stent models. Gurbel et al[15] recently demonstrated that stent design can also affect the degree of platelet activation. Stent thrombosis may thus be higher with coil than tubular stents. The coil-related stent design, however, has a looser configuration compared with tubular/multicellular stent design. There is also less plaque shift ("snow-plough") and greater side-branch access. Side-branch protection and accessibility assumes importance when the side-branch is large and subtends a large amount of myocardium.

LONG-TERM CLINICAL OUTCOME

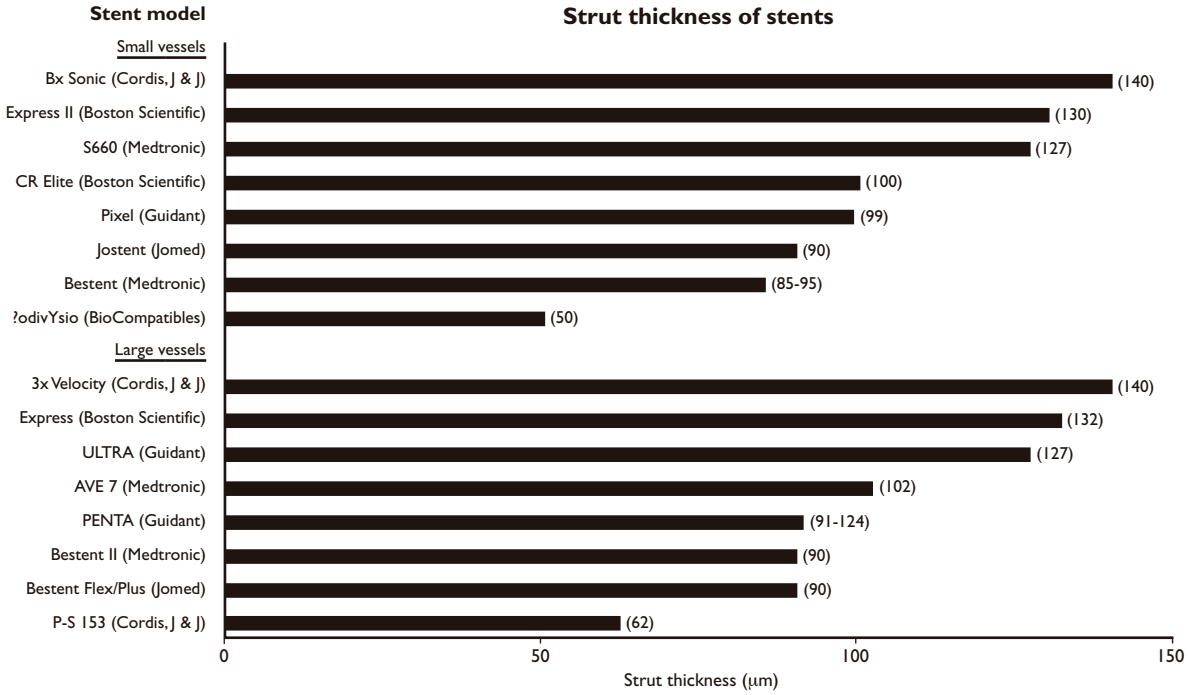
A number of stent-related properties, including stent configuration, strut thickness and stent coating can impact on the long-term clinical outcome.

Stent configuration

Animal studies have indicated that stent design does indeed exert a profound tissue effect[16-18]. Stent implantation, unlike PTCA, may cause more severe and prolonged vascular injury, thereby creating a chronic stimulus for proliferative intimal growth. Neointimal proliferation after stenting is, in fact, more exuberant than after PTCA. In an elegant animal study comparing two stent models with the same metal density but distinctly different configurations (corrugated versus slotted tube), Rogers and Edelman[17] were able to show that the corrugated stent design with its lesser number of strut-strut intersections was associated with less vascular damage and accordingly, less neointimal hyperplasia (the cornerstone mechanism for in-stent restenosis) compared with the slotted tube stent design. In a subsequent animal study[18] by the same group of investigators, it was demonstrated that the immediate luminal geometry which, in turn, is dictated by stent design, determines the vascular response independent of vascular injury. A uniformly circular post-stent lumen shape with evenly-spaced struts was found to elicit less vessel wall reaction than a less circular lumen.

Numerous randomised trials[11-14,19-22] comparing the various stent designs have since been published (Table I). It is clear that the meshwire and coil-related stent designs suffer from a significantly higher risk of restenosis compared with the tubular or multicellular stent design. A higher restenosis rate equates to a higher recurrent ischaemic event rate and a higher repeat interventional rate. In fact, because of this adverse outcome, the meshwire Wallstent (Boston Scientific, Bulach, Switzerland) and the Gianturco-Roubin coil stent (Cook, Bloomington, IN, USA) are no longer used by cardiologists for coronary

Fig. 1 Bar chart shows strut thickness of various stents in clinical use.



interventions. The Multilink stent (Guidant, Santa Clara, CA, USA) has the same radial support property as the slotted tube stent type, but with less strut-strut intersections. These characteristics appear to have a favourable impact on the vascular response by triggering less intimal hyperplasia and hence a lower restenosis rate. In the large ASCENT trial[20], patients who were randomly assigned to receive the Multilink stent showed a trend towards a lower restenosis rate compared with that observed in tubular Palmaz-Schatz stent (Johnson & Johnson, Warren, NJ, USA) treatment arm. In another randomised trial evaluating five different stent models, the Multilink stent was associated with the most favourable 6-month angiographical outcome and 1-year clinical outcome compared with the other four stent designs[22].

Strut thickness

Current stents have widely disparate strut thickness (Fig. 1). There is a delicate balance between the strut thickness of the stent and its long-term outcome. Although immediate stent performance may be improved by increasing strut thickness which in turn increases radiovisibility; radial strength and arterial wall support, excessive strut thickness, on the other hand, may impart more vascular injury, trigger more intimal hyperplasia, and engender a higher risk of restenosis than thinner struts[23]. Clinical studies appear to confirm this direct relationship between strut thickness and arterial wall reaction. In the ISAR-STEREO study[24], in which two stent types of similar design with different strut thickness were randomly implanted in 651 patients with lesions in large coronary arteries (>2.8mm reference diameter), the 6-month binary restenosis rate (25.8% versus 15.0%, respectively, p=0.003) and 1-year target vessel revascularisation rate (13.8% versus 8.6%, respectively, p=0.03) were higher following treatment with the Duet stent (strut thickness of 0.14mm) than with the Multilink stent (strut thickness of 0.05mm). A similar finding for small vessel (reference size <3.0mm) stenting was observed in a retrospective analysis by Briguori et al[25] in which strut thickness was observed to be an independent predictor of instent restenosis. The restenosis rate was significantly higher following implantation of stents with struts ≥0.1mm in thickness compared with thinner strut-stents (36.6% versus 28.5%, p=0.009). In an effort to further reduce strut thickness while maintaining adequate radiovisibility and radial strength, novel metallic materials such as cobalt-chromium alloy are being used for the production of stents. Preliminary data from the VISION registry on the use of cobalt-chromium stents are encouraging with a binary restenosis rate of 15.7%[26].

Stent coating

Stent coating has also been shown to have a great influence on the angiographical and clinical outcome of stents. Coating stainless steel with gold, a highly-radiovisible and biocompatible material, has been demonstrated in four randomised trials[27-30] to be inferior to plain stainless steel stents. A higher stent thrombosis and restenosis rate was observed with gold-coated stents compared with bare metal stents

Table II. Randomised trials of drug-eluting stents (DES) versus bare metal stents (BMS).

Trials	No.of patients	Agent	RVD (mm)	Mid-term results			p-value
				Late loss (mm)	RS rate (%)	MACE rate (%)	
RAVEL[36]	DES 120 Control 118	Sirolimus	2.5-3.5	0 0.8*	0 26.6*	5.8 28.8*	*<0.001
SIRIUS[37]	DES 533 Control 525	Sirolimus	2.5-3.5	0.24 0.81*	8.9 42.3*	7.1 18.9*	*<0.001
E-SIRIUS[38]	DES 175 Control 177	Sirolimus	2.5-3.0	0.19 0.80*	5.9 41.7*	8.0 22.6ξ	*<0.0001 ξ0.0002
C-SIRIUS[39]	DES 50 Control 50	Sirolimus	2.5-3.0	0.12 1.02*	2.3 52.3*	4 18.3ξ	*<0.001 ξ0.029
TAXUS I[40]	SR 31 NIR 30	Paclitaxel	3.0-3.5	0.36 0.71*	0 10ξ	3 7ξ	*0.008 ξNS
TAXUS II[41]	SR 131 MR 135 Control 270	Paclitaxel	3.0-3.5	0.31 0.30 0.79*	5.5 8.6 20.1*	8.5 7.8 19.8ξ	*<0.001 ξ0.006
TAXUS IV[42]	SR 662 Control 652	Paclitaxel	2.5-3.75	0.23 0.61*	7.9 26.6*	8.5 15.0ξ	*<0.0001 ξ0.0002
ELUTES[43]	LD 37 Control 38	Paclitaxel	3.0-3.5	0.10 0.73*	3.0 21.0ξ	11 11	*0.002 ξ0.055
ASPECT[44]	HD 60 LD 58 Control 59	Paclitaxel	2.5-3.5	0.29 0.57 1.04*	4 12 27*	4 5 4ξ	*<0.001 ξNS
DELIVER[45]	DES 522 Control 519	Paclitaxel	2.5-4.0	0.81 0.98*	16.7 22.4ξ	10.3 13.3ϕ	*0.03 ξ0.15 ϕNS

*, ξ, ϕ: p-value for comparison between treatment group/groups and control;

HD: high dose DES group; LD: low-dose DES group; MACE: major adverse cardiac events; MR: moderate release DES group; NS: not significant; RS: restenosis; RVD: reference vessel diameter inclusion criteria in study; SR: slow release DES group.

(BMS) (Table I). Even special processing of the gold-plated stent to further reduce surface roughness and impurities did not improve upon its outcome[30]. Coating stents with silicon carbide, a potentially less thrombogenic and more compatible material than stainless steel, also did not result in any improvement in its angiographical and clinical outcome compared with BMS in two recent randomised trials[31,32]. A similar fate was observed with phosphorylcholine[33] and heparin coating[34,35], where there was no anatomical or clinical benefit over BMS.

Coating stents with anti-proliferative drugs with or without a carrier polymer, however, have produced unparalleled results with an overall reduction in mid-term in-segment restenosis rate of between 70% to 85% and in major adverse cardiac events of about 60%, compared with BMS[36-45] (Table II). In the RAVEL trial in which 238 patients were randomised to receive either the sirolimus-coated stent (SES) or BMS, mid-term neointimal hyperplasia was virtually absent in the SES group[36]. Correspondingly, 6-month in-segment (instent and within 5mm of the stent margins) restenosis was significantly lower in the SES group compared with the BMS group (0% versus 26.6%, respectively, p<0.001). In the SIRIUS trial[37] which recruited more "real world" patients with more complex lesions than the RAVEL trial, the superiority of SES was again evident. Not only was the overall 8-month in-segment restenosis rate (8.9% versus 36.3%, respectively, p<0.001) lower in the SES group compared with the BMS group, this benefit was also apparent consistently across all patient and lesion subgroups, including those traditionally linked with a heightened risk of in-stent restenosis such as small vessel size, long lesions, and diabetics. The more recently completed European[38] and Canadian[39] SIRIUS trials have reaffirmed and extended the findings in the RAVEL and SIRIUS trials by clearly demonstrating the efficacy of this new novel device in smaller vessels without an increased risk of stent thrombosis. Similarly, restenosis rates for the paclitaxel-eluting stent (PES) cohort have also been significantly lower than those in BMS cohort in several randomised trials[40-45]. The results emanating from the TAXUS I[40], TAXUS II[41], TAXUS IV[42], ELUTES[43], and ASPECT[44] trials were impressive and appeared comparable to those obtained with SES, with the exception of the DELIVER trial[45] where an unusally higher restenosis rate (16.7%) was observed in the PES group (Table II).

Despite the excellent results observed with drug-eluting stents (DES), there remain a number of unresolved issues with this stent model. Firstly, are they cost-effective for all or only selected clinico-anatomical settings deemed to be at high risk of

in-stent restenosis? Given their unrivalled restenosis results in the aforementioned comparative randomised trials, it is anticipated that there will be extensive and rapid worldwide adoption of this technology. For example, in Singapore, the euphoria for DES has been overwhelming with a near-complete "take-up" rate of this stent technology by interventional cardiologists in the private hospitals where the hospital and procedural costs are paid for by either the patients, their insurance companies, or both. Is this exuberance scientifically or economically justifiable? Opponents to the high usage of DES would argue that DES has only been shown to reduce the "soft" end-points of restenosis and repeat intervention, and not harder end-points such as myocardial infarction and death. DES should thus be reserved for lesions at high risk of restenosis. Proponents, on the other hand, would argue that these hard clinical end-point benefits in patients who have received DES may never be achievable in any single randomised controlled trial as it would require thousands of patients to be recruited. Similar hard end-points (with the exception of diabetics with multivessel disease who received internal mammary arterial grafts) were not even demonstrated for coronary bypass surgery in at least six randomised trials comparing PTCA and coronary bypass surgery in more than 6,500 patients collectively[46-51]. It can also by argued that no patient would relish the thought of suffering the pain and inconvenience of a repeat interventional procedure for in-stent restenosis. Furthermore, in-stent restenosis after BMS is more frequently diffuse and occlusive in morphology (as opposed to the more common focal type of in-stent restenosis observed with DES). They are thus more difficult to treat, have a high recurrence rate after the second intervention, or worse still, may longer be amenable to PCI and treatable only with bypass surgery. The latter unpleasant situation may have been avoided if DES was used in the first instance. Understandably, proponents of DES would argue that patients should thus be informed of the availability of DES and its cost during consent taking, and be given the choice to select the device if they can afford it. Softer end-points such as the quality of life and individual productivity are important and valid considerations when one is considering cost-effectiveness.

DES, however, have created substantial increases in costs, not only for the patients but also for the entire healthcare delivery system. This financial limitation has resulted in a DES utilisation rate of about 12% of all coronary stent devices in Europe[52]. The health implications of DES have also prompted the U.S. Department of Health and Human Services and the Centers for Medicare and Medicaid Services to exercise an unprecendented move in creating a new International Classification of Diseases-Ninth Edition (ICD-9) code for DES and two new diagnosis-related groups (DRGs) for the use of DES in acute myocardial infarction and in those without myocardial infarction in August 2002, even before the use of DES was approved by the U.S. Food and Drug Administration[53]. The use of the new DES DRGs will result in additional payment to hospitals by Medicare of about US $2,100 compared with the payment for BMS. This move by the U.S. health authority occurred because of compelling clinical data supporting the superiority of DES over BMS and evidence that in the long-term, DES procedures may emerge as either more, equally or at worst, slightly less cost-effective than BMS procedures. A preliminary cost-effectiveness analysis of the SIRIUS trial revealed that the initial cost difference between a DES and a BMS procedure was about US$2,800. However, because of the significantly reduced rate of target vessel revascularisation with the use of DES, by one year, the difference had narrowed down to only US$309 per patient[54]. It is anticipated that the advent of more DES models in the market in the near future will force the companies to lower their pricing for DES to a more reasonable and manageable level. For the moment, however, reconciling cost containment with the superior clinical outcome of DES remains a matter between the DES-producing companies, hospitals, third-party payers for cardiovascular care, physicians and patients.

Secondly, are they safe and can their early profound salutary effects be maintained for several years after implantation? To date, 2-year follow-up data in the SIRIUS trial on patients who have received DES appear to indicate that their clinical benefit and superiority over BMS are durable[55]. Overlapping SES appear to be safe[37,38,56]. In contrast, because of the potential danger of local paclitaxel toxicity with multiple overlapping stents[57,58], this practice should be avoided and a single long PES used whenever possible, until there is evidence to indicate otherwise. Chronic, low-grade inflammatory and delayed wound healing responses have also been observed in porcine coronary arteries treated with paclitaxel-coated stents[58].

Thirdly, the role of the basic design and structure of underlying stent platform on which the anti-proliferative drugs are coated also remains unclear at this stage. The ideal DES design may need to have a large surface area of contact with the vascular wall, minimal interfilament gaps, robust radial support and symmetrical expansion to ensure uniform drug elution. At the same time, it would need to be slim, flexible and conformable to enable successful deployment in complex

lesions. For drugs with a narrow toxic-therapeutic index, customised stent platform may be required.

Lastly, the potential for long-term adverse effects of the synthetic polymers often used as carriers for anti-mitotic drugs is a major concern. Synthetic polymers may induce an enhanced inflammatory reaction and possibly a prothrombotic response[59-62]. Late stent thrombosis, late stent apposition and coronary aneurysm formation are thus real possibilities[63].

CONCLUSION

The place of stents as a device in the treatment of narrowed coronary arteries is irrefutable. However, there is now compelling experimental and clinical evidence to indicate that a stent is not just a stent. Different stent models have different structural properties, with their own inherent advantages. The design, material composition and surface features of the stent, as well as the stent deployment technique, impact strongly on the acute performance of the stent, risk of stent thrombosis, degree of vascular response and subsequent risk of in-stent restenosis. Tubular or corrugated stents are better than coil or meshwire stents, in terms of a better acute and midterm outcome. Stents with thinner struts and lower metal density yield a lower risk of restenosis than those with thicker struts, and should be used for high-risk lesions such as those located in small vessels where the risk of restenosis is often magnified. The availability of new, highly-biocompatible and more radiovisible alloys with the same if not superior tensile strength than stainless steel will enable the production of low metal density stents that may further improve the anatomical and clinical outcomes of current stainless steel stents. Gold-plated stents are best avoided because of their enhanced risk of restenosis. Coating stents with phosphorylcholine and heparin also do not appear to confer any advantage over BMS. In contradistinction, stents coated with highly anti-proliferative agents, in particular, sirolimus and paclitaxel, hold considerable promise. They produce restenosis rates that are unrivalled by other BMS models. However, several important questions regarding their cost-effectiveness, long-term safety and durability need to be addressed first before any dramatical and marked alteration of our interventional cardiology practice patterns. It is however entirely foreseeable that most interventional procedures in the near future will involve DES in one form or another, perhaps one containing sirolimus, paclitaxel or an even more effective drug with both anti-mitotic and anti-thrombotic actions, impregnated onto a highly-biocompatible carrier vehicle, and mounted onto a stent design with uniform expansion and with programmable, controllable drug-eluting capability.

REFERENCES

1. Sigwart U, Puel J, Mirkovitch V, Joffre F, Kappenberger L. Intravascular stents to prevent occlusion and restenosis after transluminal angioplasty. N Engl J Med 1987; 316:701-6.
2. Serruys PW, de Jaegere P, Kiemeneij F, Macaya C, Rutsch W, Heyndricks G, et al. A comparison of balloon-expandable-stent implantation with balloon angioplasty in patients with coronary artery disease. N Engl J Med 1994; 331:489-95.
3. Fischman DL, Leon MB, Baim DS, Schatz RA, Savage MP, Penn I, et al. A randomized comparison of coronary-stent placement and balloon angioplasty in the treatment of coronary artery disease. N Engl J Med 1994; 331:496-501.
4. Macaya C, Serruys PW, Ruygrok P, Suryapranata H, Mast G, Klugmann S, et al. Continued benefit of coronary stenting versus balloon angioplasty: one-year clinical follow-up of Benestent trial. J Am Coll Cardiol 1996; 27:255-61.
5. Betriu A, Masotti M, Serra A, Alonso J, Fernandez-Aviles F, Gimeno F, et al. Randomized comparison of coronary stent implantation and balloon angioplasty in the treatment of de novo coronary artery lesions (START): a four-year follow-up. J Am Coll Cardiol 1999; 34:1498-506.
6. Nakamura S, Colombo A, Gaglione A, Almagor Y, Goldberg SL, Maiello L, et al. Intracoronary ultrasound observations during stent implantation. Circulation 1994; 89:2026-34.
7. Colombo A, Hall P, Nakamura S, Almagor Y, Maiello L, Martini G, et al. Intracoronary stenting without anticoagulation accomplished with intravascular ultrasound guidance. Circulation 1995; 91:1676-88.
8. Moussa I, Di Mario C, Di Francesco L, Reimers B, Blengino S, Colombo A. Subacute stent thrombosis and the anticoagulation controversy: changes in drug therapy, operator technique and the impact of intravascular ultrasound. Am J Cardiol 1996; 78:13-7.
9. Schomig A, Neumann FJ, Kastrati A, Schuhlen H, Blasini R, Hadamitzky M, et al. A randomized comparison of antiplatelet and anticoagulant therapy after the placement of coronary-artery stents. N Engl J Med 1996; 334:1084-9.
10. Serruys PW, Strauss BH, Beatt KJ, Bertrand ME, Puel J, Rickards AF, et al. Angiographic follow-up after placement of a self-expanding coronary artery stent. N Engl J Med 1991; 324:13-7.
11. Nageh T, de Belder AJ, Thomas MR, Williams IL, Wainwright RJ. A randomized trial of endoluminal reconstruction comparing the NIR stent and the Wallstent in angioplasty of long segment coronary disease: results of the RENEWAL study. Am Heart J 2001; 141:971-6.
12. Lansky AJ, Roubin GS, O'Shaughnessy CD, Moore PB, Dean LS, Raizner AE, et al. Randomized comparison of GR-II stent and Palmaz-Schatz stent for elective treatment of coronary stenoses. Circulation 2000; 102:1364-8.
13. Yoshitomi Y, Kojima S, Yano M, Sugi T, Matsumoto Y, Saotome M, et al. Does stent design affect probability of restenosis? A randomized trial comparing Multilink stents with GFX stents. Am Heart J 2001; 142:445-51.
14. Thuesen L, Andersen HR, Krusell LR, Botker HE, Jorgensen E, Kelback H, et al. Randomized comparison of the coil-design Crossflex and the tubular NIR stent. Catheter Cardiovasc Interv 2003; 59:8-12.
15. Gurbel PA, Callahan KP, Malinin AI, Serebruany UL, Gillis J. Could stent design affect platelet activation? Results of the platelet activation in stenting (PAST) study. J Invas Cardiol 2002; 14:584-9.
16. Barth KH, Virmani R, Froelich J, Takeda T, Lossef SV, Newsome J, et al. Paired comparison of vascular wall reactions to Palmaz stents, Strecker tantalum stents, and Wallstents in canine iliac and femoral arteries. Circulation 1996; 93:2161-9.
17. Rogers C, Edelman ER. Endovascular stent design dictates experimental restenosis and thrombosis. Circulation 1995; 91:2995-3001.
18. Garasic JM, Edelman ER, Squire JC, Seifert P, Williams MS, Rogers C, et al. Stent and artery geometry determine intimal thickening independent of arterial injury. Circulation 2000; 101:812-8.
19. Baim DS, Cutlip DE, O'Shaughnessy CD, Hermillar JS, Kereiakes DJ, Giumbartolomei A, et al. Final results of a randomized trial comparing the NIR stent to the Palmaz-Schatz stent for narrowings in native coronary arteries. Am J Cardiol 2001; 87:152-6.
20. Baim DS, Cutlip DE, Midei M, Linnemeier M, Schreiber T, Cox D, et al. Final results of a randomized trial comparing the Multilink stent with the Palmaz-Schatz stent for narrowings in native coronary arteries. Am J Cardiol 2001; 87:157-62.
21. Miketic S, Carlsson J, Tebbe U. Randomized comparison of J & J Crown stent versus NIR stent after routine coronary angioplasty. Am Heart J 2001; 142:e8.

22. Kastrati A, Dirschinger J, Boekstegers P, Elezi S, Schuhlen H, Pache J, et al. Influence of stent design on 1-year outcome after coronary stent placement: a randomized comparison of five stent types in 1,147 unselected patients. Catheter Cardiovasc Interv 2000; 50:290-7.
24. Kastrati A, Mehilli J, Dirschinger J, Dotzer F, Schuhlen H, Neumann FJ, et al. Intracoronary stenting and angiographic results: strut thickness effect on restenosis outcome (ISAR-STEREO) trial. Circulation 2001; 103:2816-21.
25. Briguori C, Sarais C, Pagnotta P, Liistro F, Montorfano M, Chieffo A, et al. Instent restenosis in small coronary arteries: impact of strut thickness. J Am Coll Cardiol 2002; 40:403-9.
26. Kereiakas DJ, Cox DA, Hermiller J, Midei M, Bachinsky W, Nukta D, et al. First use of a novel cobalt-chromium coronary stent in humans: clinical and angiographic outcomes (abstract). J Am Coll Cardiol 2003; 41:57A.
27. Kastrati A, Schomig A, Dirschinger J, Mehilli J, von Welser n, Pache J, et al. Increase risk of restenosis after placement of gold-coated stents; results of a randomized trial comparing gold-coated with uncoated steel stents in patients with coronary artery disease. Circulation 2000; 101:2478-83.
28. Reifart N, Morice MC, Silber S, Benit E, Hauptmann KE, de Sousa E, et al. The NUGGET trial: NIR ultimate gold-gilded equivalency trial. Catheter Cardiovasc Interv 2004; 62:18-25.
29. Park SJ, Lee CW, Hong MK, Kim JJ, Park SW, Talik SJ, et al. Comparison of gold-coated NIR stents with uncoated NIR stents in patients with coronary artery disease. Am J Cardiol 2002; 89:872-5.
30. Silber S. Final results of the NIRTOP trial (abstract). EuroPCR Symposium, Paris, France, 2003.
31. Unverdorben M, Sippel B, Degenhardt R, Sattler K, Fries R, Abt B, et al. Comparison of a silicon carbide-coated stent versus a noncoated stent in human beings: the Tenax versus Nir stent study's long-term outcome. Am Heart J 2003; 145:e17.
32. Tanajura LF, Abizaid AA, Feres F, Pinto I, Mattos L, Staico R, et al. Randomized intravascular ultrasound comparison between patients that underwent amorphous hydrogenated Silicon-Carbide coated stent deployment versus uncoated stents (abstract). J Am Coll Cardiol 2003; 41:58A.
33. Moses JW, Buller CEH, Nukta ED, et al. The first clinical trial comparing a coated versus a noncoated coronary stent: The Biocompatibles BiodivYsio stent in randomized control trial (DISTINCT) (abstract). Circulation 2000; 101:II-664.
34. Wohrle J, Al-Khayer U, Grotzinger U, Schindler C, Kochs M, Hombach V, et al. Comparison of the heparin-coated versus the uncoated Jostent – no influence on restenosis or clinical outcome. Eur Heart J 2001; 22:1808-16.
35. Haude M, Kononza TFM, Kalnins U, Erglis A, Saunamaki K Glogar HD, et al. Heparin-coated stent placement for the treatment of stenoses in small coronary arteries of symptomatic patients. Circulation 2003; 107:1265-70.
36. Morice MC, Serruys PW, Sousa JE, Fajadet J, Ban Hayashi E, Perin M, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. N Engl J Med 2002; 346:1773-80.
37. Moses JW, Leon MB, Popma JJ, Fitzgerald PJ, Holmes DR, O'Shaughnessy C, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. N Engl J Med 2003; 349:1315-23.
38. Schofer J, Schlüter M, Gershlick AH, Wijns W, Garcia E, Schampaert E, et al. Sirolimus-eluting stents for treatment of patients with long atherosclerotic lesions in small coronary arteries: double-blind, randomised controlled trial (E-SIRIUS). Lancet 2003; 362:1093-9.
39. Schampaert E, Cohen EA, Schluter M, Reeves F, Traboulsi MD, Title LM, et al. The Canadian study of the sirolimus-eluting stent in the treatment of patients with long de-novo lesions in small native coronary arteries (C-SIRIUS). J Am Coll Cardiol 2004; 43:1110-5.
40. Grube E, Silber SM, Hauptmann KE, Mueller R, Bueuesfeld L, Gerckens U, et al. TAXUS I: six- and twelve-month results from a randomized, double-blind trial on a slow-release paclitaxel-eluting stent for de novo coronary lesions. Circulation 2003; 107:38-42.
41. Colombo A, Drzewiecki J, Banning A, Grube E, Hauptmann K, Silber S, et al. Randomized study to assess the effectiveness of slow- and moderate-release polymer-based paclitaxel-eluting stents for coronary artery lesions. Circulation 2003; 108:788-94.
42. Stone GW. TAXUS IV: the pivotal, perspective, randomized trial of the slow-rate release polymer-based paclitaxel-eluting TAXUS™ Stent (abstract). Transcatheter Therapeutics, Washington, DC, 2003.
43. Gershlick AH, De Scheerder I, Chevalier B, Stephens-Lloyd A, Camenzind E, Vrints C, et al. Inhibition of restenosis with a paclitaxel-eluting polymer-free coronary stent. The European evaluation of paclitaxel eluting stent (ELUTES) trial. Circulation 2004; 109:487-93.
44. Park SJ, Shim WH, Ho DS, Raizner AE, Park SW, Hong MK, et al. A paclitaxel-eluting stent for the prevention of coronary restenosis. N Engl J Med 2003; 348:1537-45.
45. O'Neill WW. The DELIVER Trial: a randomized comparison of paclitaxel-coated versus metallic stents for treatment of coronary lesions (abstract). Annual Scientific Session of the American College of Cardiology, Chicago, IL, 2003.
46. The randomized intervention treatment of angina (RITA) trial: coronary angioplasty versus coronary artery bypass surgery: Lancet 1993; 341:573-80.
47. Rodriguez A, Boullon F, Perez-Balino N, Paviotti C, Liprandi MI, Palacios IF, et al. Argentine randomized trial of percutaneous transluminal coronary angioplasty versus coronary artery bypass surgery in multivessel disease (ERACI): in-hospital results and 1-year follow-up. J Am Coll Cardiol 1993; 22:1060-7.
48. Hamm CW, Reimers J, Ischinger T, Rupprecht HJ, Berger J, Bleifeld W. A randomized study of coronary angioplasty compared with bypass surgery in patients with symptomatic multivessel coronary disease. N Engl J Med 1994; 331:1037-43.
49. King SB III, Lembo NJ, Weintraub WS, Kosinski AS, Barnhart HX, Kutner MH, et al. A randomized trial comparing coronary angioplasty with coronary bypass surgery. N Engl J Med 1994; 331:1044-50.
50. CABRI trial participants. First-year results of CABRI (Coronary Angioplasty versus Bypass Revascularization Investigation). Lancet 1995; 346:1179-84.
51. The Bypass Angioplasty Revascularization Investigation (BARI) investigators. Comparison of coronary bypass surgery with angioplasty in patients with multivessel disease. N Engl J Med 1996; 335:217-25.
52. Kereiakas DJ. The evidence for drug-eluting stents (editorial). Circulation 2003; 107:3012-4.
53. Holmes DR, Firth BG, Wood DL. Paradigm shifts in cardiovascular medicine. J Am Coll Cardiol 2004; 43:507-12.
54. Cohen DJ, Bakhai A, Shi C, Gilthiora L, Berezin RH, Caputo RP, et al. Cost-effectiveness of sirolimus drug-eluting stents for the treatment of complex coronary stenoses: results from the randomized SIRIUS trial (abstract). J Am Coll Cardiol 2003; 41:32A.
55. Kereiakes D, Moses JW, Leon MB, O'Shaughnessy C, Caputo RP, Brown C, et al. Durable clinical benefit following Cypher coronary stent deployment: SIRIUS study 2-year results (abstract). Circulation 2003; 108 (Suppl-IV):532.
56. Weisz G, Moses JW, Popma JJ, Mishkel G, Wilensky RL, Cohen B, et al. Do overlapping multiple Sirolimus-eluting stents impact angiographic and clinical outcomes? Insights from the SIRIUS trial (abstract). J Am Coll Cardiol 2003; 41:33A.
57. Kornowski R, Hong MK, Ragheb AO, Brarnwell O, Leon MB. Slow-release taxol coated GR-II stents reduce neointimal formation in porcine coronary instent restenosis model (abstract). Circulation 1997; 96:I-341.
58. Farb A, Heller PF, Shroff S, Cheng L, Kolodgie FD, Carter AJ, et al. Pathological analysis of local delivery of paclitaxel via a polymer-coated stent. Circulation 2001; 104:473-9.
59. Lincoff AM, Furst JG, Ellis SG, Tuch RJ, Topol EJ. Sustained local delivery of dexamethasone by a novel intravascular eluting stent to prevent restenosis in the porcine coronary injury model. J Am Coll Cardiol 1997; 29:808-16.
60. Zidar J, Lincoff AM, Stack R. Biodegradable stents. In: Topol EJ (ed). Textbook of Interventional Cardiology. 2nd ed. Philadelphia: WB Saunders, 1994; 787-802.
61. van der Giessen WJ, Lincoff AM, Schwartz RS, van Beusekom MM, Serruys PW, Holmes DR Jr, et al. Marked inflammatory sequelae to implantation of biodegradable and nonbiodegradable polymers in porcine coronary arteries. Circulation 1996; 94:1690-7.
62. Murphy JG, Schwartz RS, Edwards WD, Camrud AR, Vlietstra RE, Holmes DR Jr. Percutaneous polymeric stents in porcine coronary arteries. Initial experience with polyethylene terephthalate stents Circulation 1992; 86:1596-604.
63. Lau KW, Hung JS, Sigwart U. The current status of stent placement in small coronary arteries <3.0mm in diameter. J Invas Cardiol (in press).

SINGAPORE MEDICAL COUNCIL CATEGORY 3B CME PROGRAMME

Multiple Choice Questions (Code SMJ 200407A)

	True	False
Question 1. Bare metal stents are generally preferred over balloon angioplasty for the treatment of obstructive coronary artery disease because:		
(a) Stenting is associated with less arterial injury than balloon angioplasty.	❑	❑
(b) Stents are associated with a significantly lower risk of restenosis compared with balloon angioplasty in multiple randomised trials.	❑	❑
(c) The risk of stent thrombosis is only 1-2% with current strategy of aggressive antiplatelet therapy and high-pressure dilatation after stent deployment.	❑	❑
(d) There is less intimal hyperplasia with stenting than with balloon angioplasty.	❑	❑
Question 2. The following statements explain why different stent designs have different clinical outcomes:		
(a) Stents with high metal density are less prone to stent thrombosis.	❑	❑
(b) Gold-coated stents are superior to uncoated stainless steel stents.	❑	❑
(c) Self-expanding mesh stents are associated with low stent thrombosis and instent restenosis rates.	❑	❑
(d) Regardless of the stent design, exaggerated neointimal hyperplasia remains the main underlying mechanism leading to instent restenosis.	❑	❑
Question 3. Drug-eluting stents have recently become an integral tool in interventional cardiology because:		
(a) All drug-coated stents have been shown to be superior to bare metal stents in reducing the risk of instent restenosis.	❑	❑
(b) Paclitaxel-eluting stents have a significantly lower rate of instent restenosis compared with bare metal stents.	❑	❑
(c) Drug-eluting stents have been demonstrated to reduce myocardial infarction and mortality compared with bare metal stents.	❑	❑
(d) Heparin-coated stents are associated with a lower instent restenosis rate compared with bare metal stents.	❑	❑
Question 4. The strut thickness of stents appear to have a strong impact on the clinical performance of stents because:		
(a) Increasing strut thickness increases radiovisibility.	❑	❑
(b) Increasing strut thickness decreases radial strength and arterial wall support.	❑	❑
(c) Thin strut stents are associated with lower restenosis rates than thicker strut stents.	❑	❑
(d) Decreasing strut thickness increases arterial wall injury.	❑	❑
Question 5. In the randomised trials comparing sirolimus-eluting and paclitaxel-eluting stents with bare metal stents, it was found that:		
(a) There was significantly less intimal proliferation in the coronary segments treated with drug-eluting stents compared with those treated with bare metal stents.	❑	❑
(b) Restenosis rates following treatment with drug-eluting stents were generally in the single digit range.	❑	❑
(c) Stent thrombosis rate was similar between drug-eluting and bare metal stents.	❑	❑
(d) Drug-eluting stents did not offer any clinical benefit to patients.	❑	❑

Doctor's particulars:

Name in full: _____

MCR number: _____ Specialty: _____

Email address: _____

Submission instructions:

A. Using this answer form

1. Photocopy this answer form.
2. Indicate your responses by marking the "True" or "False" box ☑
3. Fill in your professional particulars.
4. Either post the answer form to the SMJ at 2 College Road, Singapore 169850 or fax to SMJ at (65) 6224 7827.

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1. Log on at the SMJ website: URL http://www.sma.org.sg/cme/smj
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Deadline for submission: (July 2004 SMJ 3B CME programme): 25 August 2004

Results:

1. Answers will be published in the SMJ September 2004 issue.
2. Successful candidates will be notified by email in September 2004.
3. Passing mark is 60%. No mark will be deducted for incorrect answers.
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