SCIENTIFIC LETTER

Targeting drug-eluting stents to lesions at high risk of restenosis: a flawed approach?

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Heart 2007;93:251–252. doi: 10.1136/hrt.2006.089243

Drug eluting stents (DES) reduce the risk of restenosis as compared to bare metal stents (BMS).¹ The high cost of these stents, however, makes their use in all patients undergoing percutaneous coronary intervention (PCI) problematic. In this journal 3 years ago we argued for a policy of selective implantation of DES, restricting their use to arteries of small calibre requiring a long stent, with some extra allowance for patients with diabetes.² We recommended DES for all lesions if they needed a 2.5 or 2.75 mm stent ≥ 12 mm long or a 3 mm stent ≥ 16 mm long. For diabetic patients, in addition, a DES was recommended for stent sizes 2.5 $\times$ 8 mm, 3 $\times$ 12 mm and 3.5 $\times$ ≥ 20 mm. For all other stent sizes, BMS were appropriate. These recommendations were similar in principle to the NICE guidelines.³ We estimated that the introduction of this policy would imply DES implantation in about 30% of lesions and would reduce the clinical restenosis rate in our institution by 33%.²

The aim of this study was to test the hypothesis that a policy of selectively targeted implantation of DES would lead to a significant reduction in our overall clinical restenosis rate.

METHODS

DES were available to us from July 2003 onwards. In the preceding 6-month period (January–June 2003), 485 patients underwent PCI (group 1; pre-DES). We identified an identical number of consecutive patients undergoing PCI from December 2003 onwards in whom our selective implantation policy was implemented (group 2; post-DES). We then examined our catheter-laboratory database and patient case notes to determine the rate of clinical restenosis (defined as symptom-driven re-angiography with restenosis $>50\%$ by eye) within 12 months of the index procedure in both groups.

RESULTS

The results are presented in table 1. There was no difference in the clinical restenosis rate between the two groups: 4.5% in group 1 versus 4.3% in group 2 ($p = \text{NS}$). Of the 452 patients who received a stent in group 2, 287 (64%) received BMS only (group 2a), 105 (23%) received DES only (group 2b) and 60 (13%) received both (group 2c). The only DES used was Taxus (Boston Scientific, Natick, MA). In group 2, stent length was 14.8 mm (BMS) versus 20.8 mm (DES) ($p < 0.01$) and stent width was 3.17 mm (BMS) versus 2.81 mm (DES) ($p < 0.01$). Of the 21 cases of restenosis in group 2, 18 occurred in BMS (16 in group 2a; two in group 2c) and three in DES (one in group 2b; two in group 2c).

DISCUSSION

Our main findings were that our institutional clinical restenosis rate was low (4.5%) before the introduction of DES and a policy of selective implantation of DES did not reduce this (4.3%). The clinical restenosis rate in the BMS group was substantially lower than the target vessel revascularisation (TVR) rates in the

BMS arms of the randomised controlled trials of DES versus BMS (typically 10–20%), reflecting both the fact that clinical restenosis is less than angiographically driven TVR⁴ and, possibly, improvements in BMS technology.

This study raises several questions. Why was the clinical restenosis rate unchanged with a policy of selective DES implantation? First, were DES failing to prevent restenosis? Probably not, because in group 2, the clinical restenosis rate in DES was 1.3 per 100 stents (3/237) versus 3.2 per 100 stents (18/559) in BMS ($p = 0.15$), despite the DES being deployed in smaller arteries and longer lesions, which would be expected to produce a higher rather than lower restenosis rate. Second, was a 30% DES implantation rate inadequate to make any impact, even when targeted to lesions judged to be at high risk for restenosis? In the 21 patients in group 2 who experienced clinical restenosis, 18 had received BMS. Of these, seven should have received a DES according to our guidelines (and did not, either through imperfect judgment or for reasons of deliverability), but the remaining 11 received a BMS “appropriately”, suggesting that the selective policy “failed” because a certain small percentage of lesions outside any set of width/length guidelines will still undergo restenosis. Third, did DES encourage us to undertake PCI in more complex patients and lesions, thereby diluting their beneficial effect? Possibly, because the number of patients was identical in both groups, but 796 stents were implanted in group 2 compared with 696 in group 1, a 14% increase and the stents in group 2 were longer and narrower than in group 1. In these circumstances, limiting clinical restenosis to 4.3% might be regarded as a positive achievement. Fourth, could traditional, lesion-based, risk factors for restenosis have assumed undue significance as the basis of our policy? This is unlikely as confirmed by a recent publication suggesting that vessel size and stent type are the most important predictors of clinical and angiographic restenosis.⁵

The main weakness of this study was that the endpoint was repeat revascularisation at our hospital. It is possible that some patients re-presented to other hospitals or were not referred back to us. Our referral base in North Trent is, however, well defined, and patients tend to be sent back to us for re-investigation and treatment. Our database captures all patients who have re-catheterisation, re-PCI or coronary artery bypass graft. There is no reason why this pattern should have changed in the period in question.

CONCLUSION

A policy of limited (30%) DES implantation seems to make no difference to clinical restenosis in the “real world” setting. An extreme interpretation of our findings would be that one should implant DES in every lesion to make any real impact

Abbreviations: BMS, bare metal stents; DES, drug eluting stents; PCI, percutaneous coronary intervention; TVR, target vessel revascularisation

Table 1 Results of implanting only BMS (group 1) versus limited DES implantation at a single centre

	Pre-DES (group 1)	Post-DES (group 2)	p Value
Patients (n)	485	485	
Mean age (years)	60.05	61.23	0.07
Males (n)	341	334	0.68
Elective cases (n)	283	277	0.75
Patients receiving stents (n)	420	452	<0.01
Stents (n)	696	796	
Stents/patient	1.66	1.76	0.07
BMS (n)	696	559	
DES (n)	0	237	
Mean stent length (mm)	15.16	16.53	<0.01
Mean stent width (mm)	3.15	3.07	<0.01
Clinical restenosis (n)	22	21	
Clinical restenosis (% all patients)	4.5	4.3	1
Clinical restenosis (% stented patients)	5.2	4.7	0.76
Re-PCI	15	15	
CABG	6	5	
Medical treatment	1	1	

BMS, bare metal stents; CABG, coronary artery bypass graft; DES, drug eluting stents; PCI, percutaneous coronary intervention.

upon restenosis. A contrary view (equally supported by our data) might be that this is unlikely to be cost-effective (because of the low absolute reduction in restenosis) and a clinical restenosis rate of 4.5% with modern generation BMS makes a policy of universal BMS implantation tenable. A compromise position might be to continue selective DES implantation but make stricter our implementation of the implantation protocol,

perhaps using quantitative angiography to measure lesion length and vessel size. Randomised studies of these approaches would be interesting, but may be unworkable if DES become universal (and cheap).

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Competing interests: Drs Gunn and Morton have accepted sponsorship from Boston Scientific Corporation, manufacturers of the Taxus stent, for attendance at scientific meetings.

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Accepted 23 June 2006

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