Repeat Coronary Revascularization Procedures after Successful Bare-Metal or Drug-Eluting Stent Implantation

Cynthia A. Yock, MS, J. Michael Isbill, MS, Spencer B. King III, MD, Mark A. Hlatky, MD

ABSTRACT: Background. The goal of this study was to assess the rate and anatomical targets of repeat revascularization procedures in routine clinical practice after either bare-metal stent (BMS) or drug-eluting stent (DES) implantation. Randomized trials provide a reference standard for comparing outcomes after BMS or DES, but the rates of repeat revascularization procedures in clinical trials do not necessarily represent the rates in routine practice. **Methods.** Baseline and 1-year follow-up angiographic data from a cardiac catheterization laboratory data registry with 32 participating hospitals were analyzed. **Results.** In 17 hospitals 14,459 eligible patients had a BMS implanted between 1998 and 2003, and in 20 hospitals 9,575 eligible patients had a DES implanted in 2005. DES patients had more multivessel disease and diabetes than BMS patients, but fewer DES patients had all diseased vessels stented. Over the subsequent year, there were significantly fewer repeat procedures in the initially stented region after DES than BMS (4.7% vs. 8.1%), but significantly more procedures in previously unstented remote segments (7.8% vs. 4.3%). Consequently, the overall rate of additional percutaneous coronary intervention admissions was not reduced by DES (12.5% vs. 12.3%; $p > 0.7$). **Conclusions.** In this sample of routine clinical practice DES reduced repeat intervention of the stented segment to a lesser extent than has been reported in randomized trials. For our cohort, the reduction in restensosis was offset by increased use of additional interventional procedures to treat remote segments, predominantly within the first 2 months after initial stenting.

J INVASIVE CARDIOL 2010;22:XXX–XXX

Drug-eluting stents (DES) rapidly replaced bare-metal stents (BMS) based on the results of randomized trials that demonstrated a dramatic reduction of in-stent restenosis. Initial cost-effectiveness studies based on the randomized trials outcomes were generally favorable to DES, but subsequent cost-effectiveness studies have been less supportive.[1–4] The European Society of Cardiology and the National Institute for Health and Clinical Excellence recommend DES for selected patients with defined clinical characteristics associated with a higher rate of in-stent restenosis.[4,5]

Several large longitudinal population studies suggest that there is a more modest clinical burden of BMS restenosis in practice than was observed in the randomized trials.[6,7] The repeat revascularization rate in the BMS arm of one sirolimus-eluting stent cost-effectiveness study based on randomized trials results was 26.9% and the authors used an absolute reduction in revascularization events with DES of 19.4 events per 100 patients to estimate the effectiveness of DES.[2] Similarly, the estimate for revascularization events averted with DES use was 12.7 per 100 patients in the paclitaxel-eluting stent cost-effectiveness study.[1] In contrast, in 12,492 consecutive BMS patients, one registry found clinically evident restenosis in 6.0% of the patients between 30 days and 1 year of stenting, and another registry of 13,738 BMS patients reported a 5.9% restenosis rate over a 3-year follow-up period.[8,9] The 1-year stented region reintervention rate was 7.1% in another longitudinal study of 17,102 BMS patients.[10] Factors related to the design of the randomized trials affect the use of repeat interventional procedures, and may have amplified the clinical burden of BMS restenosis. The trials compared DES stents to a prior generation of stents with the same physical structure but without the cell proliferation-limiting drugs, and not to the newest generation BMS which are associated with substantially better outcomes than earlier BMS device designs. The angiographic follow up required by randomized trials protocol is associated with higher reintervention rates, and further amplifies the differences in DES and BMS follow up events.[11]

DES did not affect the rate of death and myocardial infarction compared with BMS in the randomized trials, but subsequent large-population studies raised concerns about increased mortality stemming from late DES thrombosis.[12–15] More recently, a large study of Medicare patients reported that, when compared with BMS, DES was associated with reduced rates of myocardial infarction and all-cause mortality.[16] If there are differences in serious late-term complications between BMS and DES the rates are small and modifications to follow up clinical care have the potential to reduce the differences further.

The randomized DES trials results describe effects of DES on reintervention related to restenosis, but did not study reintervention for other reasons related to therapeutic strategies or disease progression. Lagervist reported that 14.5% of the BMS patients underwent further coronary revascularization during the subsequent 3 years, but fewer than half (5.9%) experienced in-stent restenosis.[9] In another longitudinal study of 17,102 BMS patients, the authors reported that 6.1% of the patients returned within the first year of follow up for a

From the Department of Health Policy, Stanford University School of Medicine, Stanford California, VHA Inc, Norcross, Georgia, St. Joseph's Heart and Vascular Institute, Atlanta, Georgia.

The authors report no conflicts of interest regarding the content herein.

Manuscript submitted August 6, 2009, provisional acceptance given September 14, 2009, final version accepted September 15, 2009.

Address for correspondence: Cynthia A Yock, MS, Research Associate, Department of Health Policy, Stanford Health Policy, 117 Encina Commons, Stanford CA 94305-6019. E-mail: Cynthia.Yock@stanford.edu

Table 1. Baseline characteristics and admission outcomes.

	Full Cohort		Common Site Subset		Stable Patients§	
	BMS	**DES**	**BMS**	**DES**	**BMS**	**DES**
24,034 n	14,459	9,575	2,815	2,978	5,829	4,308
Age (mean years ± SD)	64.2 ± 12.2	62.9 ± 11.9	63.5 ± 12.0	63.0 ± 12.0	64.0 ± 12.0	63.2 ± 11.5
%						
Male	63.8*	64.2*	62.3	64.6	65.2	63.6
Diabetes	24.6	30.4	26.4	28.9	23.7	31.5
Hypercholesterolemia†	40.8	62.3	36.7	60.3	39.3	63.9
Hypertension	63.8	71.7	68.2	71.9	63.3	73.9
Smoker or tobacco use‡	23.7	27.4	24.9	27.2	23.9	24.7
Prior myocardial infarction	11.0	16.8	9.0	13.8	9.2	15.1
Prior PCI	25.4	27.8	23.3	27.2	22.8	28.5
Prior CABG	17.9	16.3	18.2	16.1	15.7	17.1
Unstable angina on admission	53.3	46.7	47.4	45.3*	excluded	
AMI on admission	9.0	14.8	9.9	16.0	excluded	

BMS = bare-metal stent; DES = drug-eluting stent; PCI = percutaneous coronary intervention; CABG = coronary artery bypass surgery; SD = standard deviation
** prob chi-square (categorical variables) or probability \|z\| (continuous variables) > 0.05*
† Includes patients on statin therapy regardless of lipid levels.
‡ The definition of smoking was expanded to include use of any tobacco products.
§ The stable patient subset excludes those with unstable angina or acute myocardial infarction at admission.

repeat PCI in a site remote from the initially stented segment.[10] The benefit of DES in reducing reintervention rates overall may be diminished by the need to treat progressive coronary disease.

Consequently, we examined the angiographic follow-up records of a large series of unselected BMS and DES patients to answer: How has patient selection changed with DES use? How great is the reduction in subsequent revascularization due to restenosis suppression with DES? What is the net readmission effect of DES restenosis suppression once the effects of disease progression and shifts in practice are factored in?

Methods

This study used data from cardiac catheterization procedures collected by hospitals using CathSource Enterprise™ software (*VHA Inc., Norcross, Georgia*). These data analyses were conducted with approval from the Stanford University Panel for Human Subjects in Medical Research, in compliance with the Privacy Rule contained in the Health Insurance Portability and Accountability Act of 1996.

Patients undergoing BMS implantation at 17 clinical sites were identified between December 1, 1998 and March 31, 2003; patients undergoing DES implantations at 20 clinical sites were identified between January 1, 2005 and December 31, 2005. The BMS study period was chosen to end before market release of DES in April of 2003, and the DES study period was chosen to start in 2005 to minimize any confounding due to device selection, as by then DES were used in more than 90% of all stent procedures.[17]

The initial PCI record was linked to all subsequent catheterization procedures for the same patient in the databank by means of an encrypted and unique patient identifier. Procedural complications that occurred in the catheterization laboratory were captured in the database, but data on complications or admissions outside the catheterization laboratory were not collected.

Coronary anatomy and procedural details were recorded using the standardized data definitions of the American College of Cardiology's National Cardiovascular Data Registry.[18] The internal diameters of vessels and lesions were estimated visually, as were lesion lengths. Significant coronary stenosis was defined as > 70% lumenal diameter reduction of a native vessel.[17] We compared the angiographic data from the initial PCI to those from subsequent catheterization admissions to determine whether subsequent PCI was performed within the target lesion or initially stented segment (SS) or other segments (OS). As a sensitivity analysis, and to accommodate variation in arterial segment coding that can arise during interpretation of sequential angiograms, we reanalyzed the angiographic data using an expanded definition of the stented region. The stented region was defined as the stented segment and all immediately adjacent segments in the same vessel or ostia of adjacent branches.[10] Remote segments are anatomy not included in the stented region.

Data analyses were performed using JMP, Version 7 (*SAS Institute, Cary, North Carolina*). We compared categorical variables with chi-square tests, and continuous variables with Wilcoxon signed rank tests or analysis of variance: $p < 0.05$ was considered statistically significant. We used logistic regression analysis to examine the relationship between each patient, lesion and procedural trait (apart from cost) listed in Tables I and II, and three outcomes of interest: any repeat PCI, any stented segment reintervention, and remote segment reintervention only. To build the regression models we excluded patient, lesion

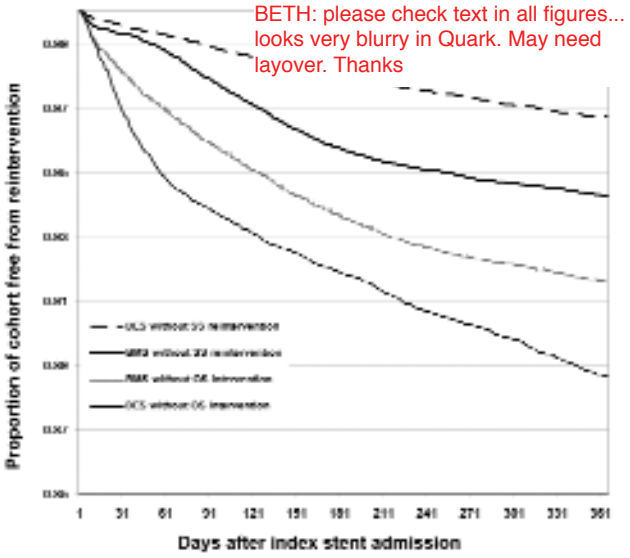

Figure 1. *Freedom from reintervention. Freedom from repeat revascularization procedures over follow-up period among patients treated with a drug-eluting stent or a bare-metal stent in the stented segment (SS) or other segments (OS).*

and procedural variables with statistically insignificant relationships to the outcomes, and examined the remaining variables for collinearity and correlations. We used the resulting regression equations to calculate crude and adjusted odds ratios (OR) for the three outcomes of interest in DES patients compared to the BMS cohort.

In a secondary analysis, we used data only from sites that contributed patients in both time periods to assess any differences in practice or outcomes related to the clinical site. The definition of unstable angina was expanded prior to the time frame of the DES subset, and clinical guidelines recommend staged intervention of the non-infarct artery for multivessel disease patients who receive urgent intervention in the context of acute myocardial infarction (AMI).[17] We excluded patients with unstable angina or AMI at admission and repeated the analyses to observe the different traits and outcomes of stable patients who underwent elective stenting.

Results

The study included 26,954 patients who underwent implantation of at least one intracoronary stent. We subsequently excluded 23 patients who also underwent atherectomy or brachytherapy, 366 patients who received both types of stent at the index admission, 264 patients who underwent emergent bypass surgery and 206 who died during the index admission. Additionally, 2,059 patients were excluded due to incomplete data describing the location and dimensions of the stented segment. The study group consists of 24,034 patients, stented at one of 31 participating hospitals. In 17 hospitals 14,459 eligible patients had a BMS implant between 1998 and 2003, and in 20 hospitals 9,575 eligible patients had a DES implant in 2005. Six hospitals contributed data to the registry in both time periods, which included 2,815 patients in the BMS group and 2,978 patients in the DES group, and all analyses were repeated in this subset.

Baseline characteristics. The clinical characteristics of patients undergoing DES implantation were generally similar to those of the patients undergoing BMS implantation (Table 1), although some small differences were statistically significant in this large population. The DES patients were a year younger on average and more likely to have a history of diabetes, hypertension and prior MI. The DES patients were more likely to have been admitted for AMI, but less likely to have been admitted with unstable angina or to have had prior CABG.

Multivessel disease was more common in the DES patients (36.8%) than in BMS patients (30.7%), but multivessel stenting

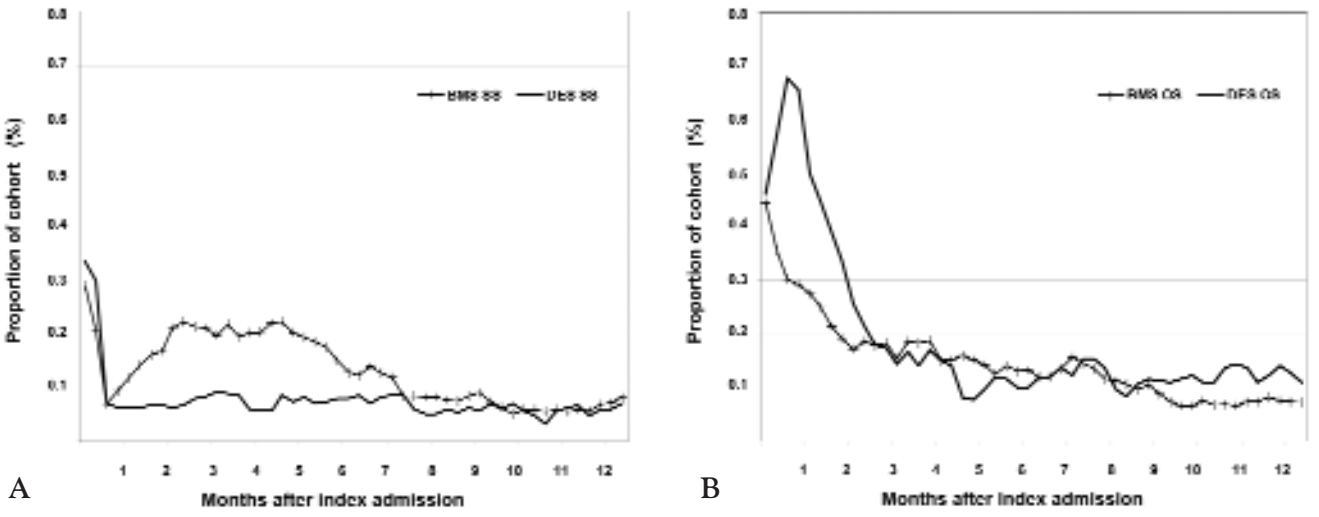

Figure 2. (A) *Stented segment reintervention. The running weekly average rate of patients undergoing repeat percutaneous coronary intervention (PCI) procedures in the stented segment (SS) among drug-eluting stents (DES) and bare-metal stents (BMS) patients.* **(B)** *Non-stented segment reintervention. The running weekly average rate of patients undergoing additional PCI procedures limited to segments other (OS) than the initially stented segment among DES and BMS patients.*

Table 2. Extent of disease and stenting.

	Full Cohort		Common Site Subset		Stable Patients§	
	BMS	DES	BMS	DES	BMS	DES
% n	14,459	9,575	2,815	2,978	5,829	4,308
Multi-segment disease	48.5	51.9	50.0	45.9	48.4	47.3
Multi-vessel disease	30.7	36.8	33.8	30.4	29.9	34.5
Multi-segment stenting	22.9	25.5	22.0	21.8	23.1	24.5
Multi-vessel stenting	10.7	11.0*	9.1	9.6*	10.8	10.1
All segments ≥ 70% LDR stented	65.4	59.2	63.5	61.8	65.9	48.8
All vessels ≥ 70% LDR stented	76.7	70.3	76.2	71.3	77.7	60.7
Segments stented n	17,505	12,539	3,299	3,750	7,063	5,660
% of all segments stented						
Left main	1.0	0.8*	0.7	0.7*	0.7	1.0
Left anterior descending	30.5	32.8	30.1	32.6	30.6	33.2
Left anterior descending branch	6.1	6.4	5.3	6.8	5.9	6.3
Left circumflex	15.2	14.3	15.9	14.5	15.4	14.4
Left circumflex branch	9.1	8.8*	9.3	9.1*	8.7	8.4*
Right coronary artery	35.0	33.5	36.4	32.6	35.7	33.2
Right coronary artery branch	3.0	3.4	2.2	3.8	3.1	3.5
Denovo lesion	94.3	96.0	92.9	97.1	95.6	97.8
mean, standard deviation						
Pre stent lumen diameter reduction (%)	87.3 ± 15.0	85.9 ± 12.2	86.2 ± 10.7	85.3 ± 11.5	85.2 ± 10.2	81.5 ± 13.5
Reference vessel diameter (mm)	3.15 ± 0.69	3.06 ± 0.65	3.16 ± 0.58	3.00 ± 0.48	3.11 ± 0.64	3.09 ± 0.58
Stent diameter (mm)	3.13 ± 0.50	2.97 ± 0.42	3.16 ± 0.54	2.93 ± 0.42	3.1 ± 0.50	2.96 ± 0.39
Stent length (mm)	15.64 ± 5.60	18.61 ± 6.98	15.45 ± 5.35	17.67 ± 6.39	15.26 ± 5.48	18.49 ± 9.67
Device acquisition costs† ($)	3,741 ± 1,698	5,719 ± 3,741	3,824 ± 1,782	5,769 ± 2,579	3,698 ± 1,655	5,693 ± 2,542

BMS: bare metal stent; DES: drug eluting stent; PCI: percutaneous coronary intervention; CABG: coronary artery bypass surgery; LDR: luminal diameter reduction
** prob ChiSquare (categorical variables) or probability |z| (continuous variables) >0.05*
† device aquisition costs ($ 2009) include stents, catheters, guidewires, vascular access and closure devices, antiplatelet drugs

was performed at a similar rate in both groups (11.0% vs. 10.7%). Patients who received DES had more segments stented (1.33 ± 0.59) than patients who received BMS (1.27 ± 0.53), and overall had more stents implanted (1.55 in the DES group, 1.40 in the BMS group). Mean reference vessel and stent diameters were slightly smaller in the patients receiving DES than in patients receiving BMS (Table 2). Consistent with clinical guidelines, coronary stenosis was defined as > 70% luminal diameter reduction: nearly all BMS-stented segments (99.2%) satisfied this definition while only 93.5% of DES-stented segments did.[17]

Clinical Outcomes. Mortality related to the initial procedure did not differ significantly between the DES (0.8%) and BMS (0.7%) patient groups, but there was significantly less coronary bypass surgery during the initial admission in the DES group (0.3%) than in the BMS group (1.4%). The percentage of patients readmitted for diagnostic catheterization over the following 12 months was slightly higher among patients treated with a DES (21.5%) than with a BMS (21.1%), although fewer DES patients (0.6%) were referred to CABG in follow-up than BMS patients (1.4%). In all patients, and in the subset of patients with stable symptoms, the percentage of patients who had subsequent PCI admissions was slightly higher among patients treated with DES (12.5%) than with BMS (12.3%). The overall patterns seen in the data from all sites were evident in the data collected only from the six clinical sites that contributed both BMS and DES patients (Table 3). Likewise, the results were essentially unchanged when we excluded patients who had prior PCI or CABG. The unadjusted OR for any repeat PCI after DES compared with BMS was 0.99 (CI 0.91–1.07), and after adjustment for patient clinical characteristics, including diabetes, was 1.08 (CI 0.98–1.18).

Reintervention of the stented segment (target lesion) was significantly less frequent among DES patients (3.2%) than among BMS patients (6.2%), as was reintervention of the stented segment plus the surrounding anatomy (stented region) (4.7% vs. 8.1%) (Table 3). The difference in stented segment reintervention occurred mostly between 2 and 7 months after the initial procedure (Figure 1 and Figure 2A). There was no significant difference in the rate of stented-segment reintervention between patients who received sirolimus-coated versus paclitaxel-coated stents. The stented region reintervention rate in diabetic patients was 9.4% in the BMS cohort and 5.3% in the DES group. Age > 65 years, male gender and AMI at time of admission significantly increased the likelihood of stent region reintervention in both DES and BMS cohorts. Diabetes was significantly associated with stent region reintervention for BMS patients, but not for DES patients. The unadjusted OR for reintervention in the stented region after DES compared with BMS was 0.56 (CI 0.36–0.77), and after adjustment for differences in patient traits, including diabetes, was 0.51 (CI 0.23–0.78).

Table 3. Clinical outcomes.

	Full Cohort		Common Site Subset		Stable Patients§	
Follow-up Outcomes	**BMS**	**DES**	**BMS**	**DES**	**BMS**	**DES**
% n	14,459	9,575	2,815	2,978	2,815	2,978
Subsequent diagnostic catheterization	21.1	21.5	20.2	20.6	20.7	20.9
CABG recommendation in any diagnostic record	1.4	0.6	1.2	0.9	1.3	0.7
Readmitted for further PCI within one year	12.3	12.5	11.0	10.9	11.0	12.0
Stented segment reintervention (any)	6.2	3.2	4.3	2.6	5.7	3.5
Stented segment reintervention as the only repeat in follow-up	3.6	1.8	2.4	1.5	3.1	2.0
Other segment intervention (only)	6.2	9.3	6.6	8.4	5.2	8.6
Stented region reintervention (any)	8.1	4.7	5.6	3.8	7.4	4.8
Remote segment intervention (only)	4.3	7.8	5.3	7.2	3.6	7.2
Number of PCI readmissions						
0	87.7	87.5	89.0	89.0	89.0	88.0
1	10.4	11.0	9.1	9.7	9.1	10.4
2	1.5	1.2	1.4	1.0	1.5	1.5
3	0.4	0.2	0.5	0.2	0.4	0.2

BMS = bare-metal stent; DES = drug-eluting stent; PCI = percutaneous coronary intervention; CABG = coronary artery bypass graft surgery
** probability chi-square (categorical variables) or probability |z| (continuous variables) > 0.05*
§ The stable patient subset excludes those with unstable angina or acute myocardial infarction at admission

In contrast to the results in the stented segment, subsequent intervention limited to unstented arterial segments was significantly higher after DES (9.3%) than after BMS (6.2%) (Figure 2B). Not counting segments adjacent to the initially stented segment, reintervention in remote segments was also significantly higher among patients undergoing DES (7.8%) than in patients undergoing BMS implantation (4.3%), with most of the difference due to readmissions within 60 days of the index stent procedure. This finding was essentially unchanged after exclusion of patients with AMI or unstable angina (Table 3). For patients with two- and three-vessel disease, the remote segment reintervention rate after DES was nearly double that of BMS patients (Table 4). The unadjusted OR for remote segment PCI after DES compared with BMS was 1.90 (CI 1.78–2.02), and the adjusted OR was 1.80 (CI 1.74–1.86).

Readmission rates for diabetic patients were higher than those for nondiabetic patients in both cohorts, however once we adjusted the OR to control for other factors, the effect of diabetes on the three outcomes of interest was statistically significant only in the BMS cohort. Adjusted for the effects of other clinical factors, diabetes was associated with higher readmission for PCI after BMS (OR 1.19; $p = 0.003$) but not after DES (OR 1.08; $p = 0.27$). Similarly, the OR for stented region reintervention in diabetics compared with nondiabetics was 1.15 ($p = 0.05$) in the BMS group and 1.01 ($p = 0.94$) for DES patients. The OR for remote intervention was 1.23 ($p = 0.03$) for diabetics in the BMS group and 1.12 ($p = 0.18$) in the DES cohort.

Catheterization laboratory device acquisition costs include stents, catheters, guidewires, vascular access and closure devices, and antiplatelet and thrombolytic drugs used during the index admission, and these costs do not include personnel, professional or facility costs. DES procedure device acquisition costs averaged $1,973 more than BMS procedures, with all costs adjusted for inflation to 2009 dollars at 2.8% per year after the index procedure date.

Discussion

In this real world registry we found that PCI patients who had implantation of a DES were more likely to have multi-vessel coronary disease and diabetes than patients who received BMS. Despite a somewhat higher patient risk profile for restenosis, use of DES reduced the rate of repeat PCI in the stented region by 2–3% in absolute terms.

The reduction in repeat PCI procedures in the stented region among DES patients was counterbalanced by an increase in repeat procedures in remote segments, so that the overall rate of PCI readmission was not reduced in patients receiving DES compared with patients who received BMS. This surprising finding appears to be due, in part, to an increase in the prevalence of multivessel disease (from 31–38%) in the DES group that was not matched by an increase in the use of multi-vessel stenting during the initial procedure. The difference in remote reintervention held true in patients with both stable and unstable clinical presentations and especially in patients with multivessel disease identified at the time of the index admission. The remote segment reintervention rate after DES was nearly double that of BMS patients for patients with two- and three-vessel disease, which implies a shift in treatment planning for multivessel disease patients treated by DES. It is possible that many of the repeat PCIs in patients with multivessel disease were intentionally staged procedures, suggested by of the pattern of remote-segment reintervention within the first 60 days

Table 4. Extent of Disease and readmissions for percutaneous coronary intervention.

	Extent of Disease		Any Additional PCI		Any Stent Region		Remote Segment Only	
%	BMS	DES	BMS	DES	BMS	DES	BMS	DES
Full Cohort								
1-vessel disease	69.3%	63.2%	10.7%	10.1%	7.4%	4.5%	3.2%	5.5%
2-vessel disease	19.9%	24.7%	15.7%	16.9%	9.3%	4.9%	6.4%	12.0%
≥ 3-vessel disease	10.8%	12.1%	16.9%	16.4%	9.8%	5.4%	7.1%	11.0%
Stable Patients*								
1-vessel disease	70.1%	64.7%	9.7%	10.3%	6.7%	4.9%	2.9%	5.3%
2-vessel disease	20.1%	23.8%	14.3%	15.0%	9.2%	4.5%	5.0%	10.5%
≥ 3-vessel disease	9.8%	11.5%	13.4%	16.0%	8.4%	4.9%	5.1%	11.1%

BMS = bare-metal stent; DES = drug-eluting stent; PCI = percutaneous coronary intervention
** The stable patient subset excludes those with unstable angina or acute myocardial infarction at admission.*

of the index procedure, peaking at 4 weeks. However, rapid clinical progression of moderate lesions or a more aggressive approach to stenting moderate lesions in follow up may contribute a portion of those reinterventions.

DES patients were less likely to be referred for CABG than BMS patients, either during the initial admission or after follow-up diagnostic angiography. These findings suggest a possible shift away from CABG to sequential PCI for patients with multivessel disease. The implications of this shift in practice are uncertain and present an opportunity for further study.

This study has several limitations that may affect our results. BMS patients were drawn from 17 clinical sites and the DES patients from 20 clinical sites. The two cohorts had six clinical sites in common, however, and it is reassuring that the results were similar when we restricted the analyses to only those sites that contributed data to both groups. We are unable to observe important outcomes and complications that did not result in readmission to catheterization laboratories that used the VHA data collection software. We do not have any reason to suspect a difference in the frequency of readmissions outside the VHA system between the two time periods, but this effect cannot be ruled out. We do not have access to pharmaceutical records, so we are unable to document the role that changes in clinical practice, such as dual-antiplatelet therapy or expanded use of lipid-lowering therapy in the DES cohort may have had on clinical outcomes. Nor do we have access to data that would reveal the clinical decision-making process regarding staged treatment of multivessel disease, or to the results of functional tests or the symptoms reported by patients prior to readmission for additional PCI. By constraining the time periods of patient selection, we attempted to reduce the effect of device selection bias, however, we do report important shifts in patient traits — for example, a higher proportion of patients with multivessel disease —that may have affected outcomes.

These findings highlight the difficulty in relying solely on randomized trials to assess new medical technology. Randomized trials are a well-accepted standard for assessing comparative effectiveness and the results are often used to generate secondary evidence, such as meta analyses and cost effectiveness studies. In addition, trials are important for regulatory purposes, such as approval by Food and Drug Administration. However, trials conducted prior to, or soon after, the introduction of a new technology do not reflect ongoing evolution and refinements in clinical practice and outcomes that occur as a result of clinical experience or broadened clinical applications and patient selection in the months after adoption. Nor can the structure of randomized trials account for a wide range of external factors that logically influence the costs and application of new medical technologies. For these reasons, comparative effectiveness studies should consider, in addition to trials data, evidence drawn from longitudinal studies that reflect general clinical practice and real-world outcomes.

Conclusion

In conclusion, the effect of DES on repeat PCI procedures in routine clinical practice is more complex than suggested by pivotal randomized trials. More patients with multivessel disease have undergone PCI since DES came available and readmissions for PCI in previously unstented anatomy have grown. To some degree, in-stent restenosis procedure "savings" have been counterbalanced by changes in patient selection and clinical strategy that contribute to an increase in subsequent procedures to treat disease in non-stented segments. The net effect of these opposing trends is that the overall rate of repeat procedures one year after initial PCI was relatively unchanged as these centers shifted from BMS to DES. Research efforts to examine the safety of stenting continue, as do development efforts to improve stent devices and further reduce in-stent restenosis. Our study suggests that better understanding of the clinical indications and outcomes related to multi-admission PCI revascularization strategies could lead to further efficiencies in coronary revascularization services.

References

1. Bakhai, A, Stone, GW, Mahoney, E, et al. Cost effectiveness of paclitaxel-eluting stents for patients undergoing percutaneous coronary revascularization: Results from the TAXUS-IV Trial. *J Am Coll Cardiol* 2006;48:253–261.
2. Cohen, DJ, Bakhai, A, Shi, C, et al. Cost-effectiveness of sirolimus-eluting stents for treatment of complex coronary stenoses: Results from the Sirolimus-Eluting Balloon Expandable Stent in the Treatment of Patients With De Novo Native Coronary Artery

Lesions (SIRIUS) trial. *Circulation* 2004;110:508–514.
3. Filion, KB, Roy, AM, Baboushkin, T, et al. Cost-effectiveness of drug-eluting stents including the economic impact of late stent thrombosis. *Am J Cardiol* 2009;103:338–3-44.
4. Neyt, M, Van Brabandt, H, Devriese, S, et al. Cost-effectiveness analyses of drug eluting stents versus bare metal stents: A systematic review of the literature. *Health Policy* 2009.
5. Daemen, J, Simoons, ML, Wijns, W, et al. ESC Forum on Drug-Eluting Stents European Heart House, Nice, 27–28 September 2007. *Eur Heart J* 2009;30:152–161.
6. James, SK, Stenestrand, U, Lindback, J, et al. Long-term safety and efficacy of drug-eluting versus bare-metal stents in Sweden. *N Engl J Med* 2009;360:1933–1945.
7. Tu, JV, Bowen, J, Chiu, M, et al. Effectiveness and safety of drug-eluting stents in Ontario. *N Engl J Med* 2007;357:1393–1402.
8. Bainey, KR, Norris, CM, Graham, MM, et al. Clinical in-stent restenosis with bare metal stents: Is it truly a benign phenomenon? *Int J Cardiol* 2008;128:378–382.
9. Lagerqvist, B, James, SK, Stenestrand, U, et al. Long-term outcomes with drug-eluting stents versus bare-metal stents in Sweden. *N Engl J Med* 2007;356:1009–1019.
10. Yock, C, Isbill, J, King, S. Bare-metal stent outcomes in an unselected patient population. *Clinical Cardiology* 2006;29:352–356.
11. Tung, R, Kaul, S, Diamond, GA, et al. Narrative review: Drug-eluting stents for the management of restenosis: A critical appraisal of the evidence. *Ann Intern Med* 2006;144:913–919.
12. Babapulle, MN, Joseph, L, Belisle, P, et al. A hierarchical Bayesian meta-analysis of randomised clinical trials of drug-eluting stents. *Lancet* 2004;364:583–591.
13. Chen, JP, Crisco, LV, Jabara, R, et al. Late angiographic stent thrombosis: The LAST straw for drug-eluting stents? *Angiology* 2008;59:667–675.
14. Daemen J, Boersma, E, Flather, M, et al. Long-term safety and efficacy of percutaneous coronary intervention with stenting and coronary artery bypass surgery for multivessel coronary artery disease: A meta-analysis with 5-year patient-level data from the ARTS, ERACI-II, MASS-II, and SoS trials. *Circulation* 2008;118:1146–1154.
15. Jensen LO, Maeng M, Kaltoft A, et al. Stent thrombosis, myocardial infarction, and death after drug-eluting and bare-metal stent coronary interventions. *J Am Coll Cardiol* 2007;50:463–470.
16. Douglas PS, Brennan JM, Anstrom KJ, et al. Clinical effectiveness of coronary stents in elderly persons: Results from 262,700 Medicare patients in the American College of Cardiology-National Cardiovascular Data Registry. *J Am Coll Cardiol* 2009;53:1629–1641.
17. Smith SC Jr, FeldmanTE, Hirshfeld JW Jr, et al. ACC/AHA/SCAI 2005 guideline update for percutaneous coronary intervention: A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (ACC/AHA/SCAI Writing Committee to Update the 2001 Guidelines for Percutaneous Coronary Intervention). *J Am Coll Cardiol* 2006;47:e1–e121.
18. Scanlon PJ, Faxon DP, Audet AM, et al. ACC/AHA guidelines for coronary angiography. A report of the American College of Cardiology/American Heart Association Task Force on practice guidelines (Committee on Coronary Angiography). Developed in collaboration with the Society for Cardiac Angiography and Interventions. *J Am Coll Cardiol* 1999;33:1756–1824.