The American Journal of Medicine (2006) 119, 1056-1061

ELSEVIER

THE AMERICAN JOURNAL of MEDICINE®

CLINICAL RESEARCH STUDY

Late Thrombosis of Drug-Eluting Stents: A Meta-Analysis of Randomized Clinical Trials

Anthony A. Bavry, MD, MPH,[a] Dharam J. Kumbhani, MD, SM,[b] Thomas J. Helton, DO,[a] Przemyslaw P. Borek, MD,[a] Girish R. Mood, MD,[a] Deepak L. Bhatt, MD[a]

[a]Department of Cardiovascular Medicine, Cleveland Clinic Foundation, Cleveland, Ohio; [b]Department of Internal Medicine, University of Pennsylvania, Philadelphia.

ABSTRACT

PURPOSE: Drug-eluting stents are commonly used for percutaneous coronary intervention. Despite excellent clinical efficacy, the association between drug-eluting stents and the risk for late thrombosis remains imprecisely defined.

METHODS: We performed a meta-analysis on 14 contemporary clinical trials that randomized 6675 patients to drug-eluting stents (paclitaxel or sirolimus) compared with bare metal stents. Eight of these trials have reported more than a year of clinical follow-up.

RESULTS: The incidence of very late thrombosis (>1 year after the index procedure) was 5.0 events per 1000 drug-eluting stent patients, with no events in bare metal stent patients (risk ratio [RR] = 5.02, 95% confidence interval [CI], 1.29 to 19.52, $P = .02$). Among sirolimus trials, the incidence of very late thrombosis was 3.6 events per 1000 sirolimus stent patients, with no events in bare metal stent patients (RR = 3.99, 95% CI, .45 to 35.62, $P = .22$). The median time of late sirolimus stent thrombosis was 15.5 months, whereas with bare metal stents it was 4 months. Among paclitaxel trials, the incidence of very late thrombosis was 5.9 events per 1000 paclitaxel stent patients, with no events in bare metal stent patients (RR = 5.72, 95% CI, 1.08 to 32.45, $P = .049$). The median time of late paclitaxel stent thrombosis was 18 months, whereas it was 3.5 months in bare metal stent patients.

CONCLUSIONS: Although the incidence of very late stent thrombosis more than 1 year after coronary revascularization is low, drug-eluting stents appear to increase the risk for late thrombosis. Although more of this risk was seen with paclitaxel stents, it remains possible that sirolimus stents similarly increase the risk for late thrombosis compared with bare metal stents.

KEYWORDS: Paclitaxel stents; Sirolimus stents; Stent thrombosis; Meta-analysis

Initial anecdotal experience suggested that early stent thrombosis occurred more frequently with drug-eluting stents compared with bare metal stents.[1,2] However, several reports on stent thrombosis have since been published that examined the early clinical trial experience with drug-eluting stents compared with bare metal stents.[3-7] These reports systematically showed that the risk of stent thrombosis for paclitaxel stents (Taxus, Boston Scientific, Natick, Mass) or sirolimus stents (Cypher, Cordis, Miami Lakes, Fla) is similar to bare metal stents during clinical follow-up that does not exceed 1 year.

Even though these studies demonstrated a degree of safety with the use of drug-eluting stents up to 1 year after coronary revascularization, the report by McFadden cautioned that drug-eluting stents may disproportionately be at risk for late thrombosis (around 1 year) when antiplatelet therapy is terminated.[8] Using randomized clinical trial data, we sought to quantitate the risk for drug-eluting stent thrombosis late after successful coronary intervention when clo-

This manuscript was presented at the 78th Annual American Heart Association Scientific Sessions, Dallas, Tex, November 16, 2005.

Requests for reprints should be addressed to: Deepak L. Bhatt, MD, Cardiac, Peripheral, and Carotid Intervention, Department of Cardiovascular Medicine, Cleveland Clinic Foundation, 9500 Euclid Avenue, Desk F25, Cleveland, OH 44195.

E-mail address: bhattd@ccf.org

0002-9343/$ -see front matter
doi:10.1016/j.amjmed.2006.01.023

pidogrel is no longer protocol mandated and its use may be infrequent.

METHODS

Literature Review

We searched the MEDLINE and Cochrane databases for randomized clinical trials in English language from 2000 to 2005 using the Medical Subject Heading terms "Angioplasty, Transluminal, Percutaneous Coronary", "Stents", "Paclitaxel", "Sirolimus" and "Thrombosis." We also hand-searched relevant journals, obtained recently presented data at cardiology conferences (scientificsessions.americanheart.org, www.acc.org, and www.tctmd.com), corresponded with authors and experts in the field, and used the Science Citation Index to cross-reference any articles that met our selection criteria.

CLINICAL SIGNIFICANCE

- Stent thrombosis is a serious and often fatal event.
- The association between drug-eluting stents and thrombosis remains controversial.
- Compared with bare metal stents, drug-eluting stents appear to increase slightly the risk for late thrombosis.

Selection Criteria

The main inclusion criteria were randomized clinical trials that assigned patients to paclitaxel stents versus bare metal stents or sirolimus stents versus bare metal stents. We additionally required that patients were treated with dual antiplatelet therapy, defined as aspirin and clopidogrel (or ticlopidine in lieu of clopidogrel) after percutaneous coronary intervention. Studies that used cilostazol instead of a thienopyridine were excluded. We also excluded studies that used a nonpolymeric stent platform, experimental antiproliferative agents such as everolimus (Novartis Pharma AG, Basel, Switzerland; Guidant, Indianapolis, Ind), or when paclitaxel stents were directly compared with sirolimus stents.

Endpoints/Data Abstraction

The primary endpoint was angiographic stent thrombosis. A stent thrombosis was defined as a filling defect in proximity to a previously placed stent on repeat coronary angiogram. A repeat coronary angiogram was performed either according to study protocol or due to a clinical event such as an acute coronary syndrome. A suspected stent thrombosis that resulted in complete or partial coronary occlusion was included for analysis. A clinically silent occluded index vessel discovered at the time of protocol-driven angiography was not adjudicated as a stent thrombosis. Clinical events that did not undergo angiographic evaluation, although the study investigators presumed that a stent thrombosis occurred, were adjudicated as thrombotic events. For each thrombosis, 3 independent reviewers (TJH, PPB and GRM) recorded the type of stent used and the number of days after revascularization that the event occurred. Discrepancies were resolved through a fourth reviewer (AAB). Reviewers also tabulated the duration of protocol mandated dual antiplatelet therapy and the extent of clinical follow-up in each trial. Thrombotic events were classified as early if they occurred within 30 days or late if they occurred more than 30 days after percutaneous coronary intervention. Late events were further classified as >30 days, >6 months, and >1 year.

Statistical Analysis

We calculated the risk of thrombosis for each type of stent as the number of thrombotic events that occurred during clinical follow-up divided by the number of individuals at risk for thrombosis. Risk ratios (RR) were defined as the risk of thrombosis for drug-eluting stents compared with bare metal stents. A Mantel-Haenszel model that included automatic zero-cell correction was used to calculate each summary statistic. All *P* values were 2-tailed, with statistical significance set at .05, and confidence intervals (CI) calculated at the 95% level. All analyses were performed using STATA software v8.2. (STATA Corporation, College Station, Tex).

RESULTS

Duration of Dual AntiPlatelet Therapy and Duration of Clinical Follow-Up

In all, there were 14 studies with 6675 total patients included for analysis. There were 9 sirolimus trials, largely represented by the SIRIUS and RAVEL Trials (Table 1),[9-22] and 5 paclitaxel trials represented by the TAXUS Trials (Table 2).[23-33] Most of the sirolimus trials mandated aspirin and clopidogrel for 2 to 3 months, except for the Pache et al Trial[21] and the DIABETES Trial,[20] which required 6 and 12 months of dual antiplatelet therapy, respectively (Table 1). With the exception of the C-SIRIUS Trial, which reported outcomes to 9 months, the SIRIUS and RAVEL Trials have reported 2 to 4 years of follow-up (93% to 100% complete follow-up). In contrast, the remaining sirolimus trials have not reported beyond 1 year (97% to 100% complete follow-up). All of the TAXUS Trials mandated dual antiplatelet therapy for 6 months (Table 2). With the exception of the TAXUS-V Trial, which reported outcomes to 9 months, the remaining TAXUS Trials have each reported 2 years of follow-up (94% to 99% complete follow-up).

Overall Risk of Thrombotic Events

No thrombotic events were reported in either arm of the RAVEL, DIABETES, or TAXUS-I Trials, in the bare metal stent arms of the E-SIRIUS and TAXUS–II Trials, or in the drug-eluting stent arm of the STRATEGY Trial. Each of the

Table 1 Event Data for Sirolimus versus Bare Metal Stent Studies

Trial Name	SES n = 1587	BMS n = 1575	Duration of Clopidogrel	Clinical Follow-up	Early Events	Late Events (>30 Days)
SIRIUS[9-11]	533	525	3	36	1/1	3/3
E-SIRIUS*[12,13]	175	177	2	24	2/0	1/0
C-SIRIUS[14]	50	50	2	9	1/0	0/1
RAVEL*[15-17]	120	118	2	48	0/0	0/0
SES-SMART[18]	129	128	2	8	1/1	0/3
SCANDSTENT[19]	163	159	NA	8	1/5‡	0/0
DIABETES[20]	80	80	12	9†	0/0	0/0
Pache et al[21]	250	250	6	12	1/1	1/0
STRATEGY[22]	87	88	3	8	0/2	0/0
Incidence (per 1000)					4.2/3.5	3.5/4.9

SES = sirolimus eluting stent; BMS = bare metal stent.
Duration of clopidogrel and clinical follow-up are given in months. Events are given as SES/BMS.
*Some patients received ticlopidine in lieu of clopidogrel.
†Protocol required 12 months of clopidogrel, although the interim analysis has only been reported to 9 months of follow-up.
‡These events were not included in the final analysis because it was unclear if they occurred early or late.

remaining trials reported at least 1 thrombotic event in each of their arms. The overall incidence of thrombosis from all analyzed studies was 9.3 events per 1000 drug-eluting stent patients compared with 9.0 events per 1000 bare metal stent patients (RR = 1.03, 95% CI, .63 to 1.68, $P = .91$). The chi-squared value for heterogeneity (10 degrees of freedom) was 10.63 ($P = .39$) with no evidence for publication bias $P = .45$. The overall incidence of thrombosis from 9 sirolimus trials was 7.6 events per 1000 sirolimus stent patients compared with 10.8 events per 1000 bare metal stent patients (RR = .72, 95% CI, .35 to 1.46, $P = .36$), whereas the overall incidence of thrombosis from 5 polymeric paclitaxel trials was 10.8 events per 1000 paclitaxel stent patients compared with 7.4 events per 1000 bare metal stent patients (RR = 1.45, 95% CI, .73 to 2.90, $P = .29$).

Risk of Early Thrombotic Events

The incidence of early thrombosis within 30 days from all analyzed studies was 4.4 events per 1000 drug-eluting stent patients compared with 5.0 events per 1000 bare metal stent patients (RR = .89, 95% CI, .46 to 1.75, $P = .74$). The chi-squared value for heterogeneity (9 degrees of freedom) was 4.51 ($P = .88$) with no evidence for publication bias, $P = .66$. The incidence of early thrombosis from 8 sirolimus trials was 4.2 events per 1000 sirolimus stent patients compared with 3.5 events per 1000 bare metal stent patients (RR = 1.16, 95% CI, .41 to 3.29, $P = .79$), whereas the incidence of early thrombosis from 5 paclitaxel trials was 4.6 events per 1000 paclitaxel stent patients compared with 6.3 events per 1000 bare metal stent patients (RR = .74, 95% CI, .31 to 1.80, $P = .51$).

Risk of Late Thrombotic Events

The incidence of late thrombosis more than 30 days after the procedure was 5.0 events per 1000 drug-eluting stent patients compared with 2.8 events per 1000 bare metal stent patients (RR = 1.56, 95% CI, .77 to 3.16, $P = .22$). Additionally, the incidence of thrombosis based on the type of stent was 3.5 events per 1000 sirolimus stent patients compared with 4.9 events per 1000 bare metal stent patients (RR = .77, 95% CI, .29 to 2.07, $P = .61$) and 6.3 events per 1000 paclitaxel stent patients compared with 1.1 events per 1000 bare metal stent patients (RR = 3.59, 95% CI, 1.10 to 11.72, $P = .034$) (Figure 1). The median time of late sirolimus stent thrombosis was 15.5 months (mean 14.8 ± 8.1 months) with a range of 173 to 773 days, whereas the

Table 2 Event Data for Paclitaxel versus Bare Metal Stent Trials

Trial Name	PES n = 1755	BMS n = 1758	Duration of Clopidogrel	Clinical Follow-up	Early Events	Late Events (≥30 Days)
TAXUS–I[23,24]	31	30	6	24	0/0	0/0
TAXUS–II[25,26]	266	270	6	24	1/0	5/0
TAXUS–IV[27-29]	662	652	6	24	2/4	5/1
TAXUS–V[30]	577	579	6	9	4/4	0/1
TAXUS–VI[31-33]	219	227	6	24	1/3	1/0
Incidence (per 1000 patients)					4.6/6.3	6.3/1.1

PES = paclitaxel eluting stent, BMS = bare metal stent.
Duration of clopidogrel and clinical follow-up are given in months. Events are given as PES/BMS.

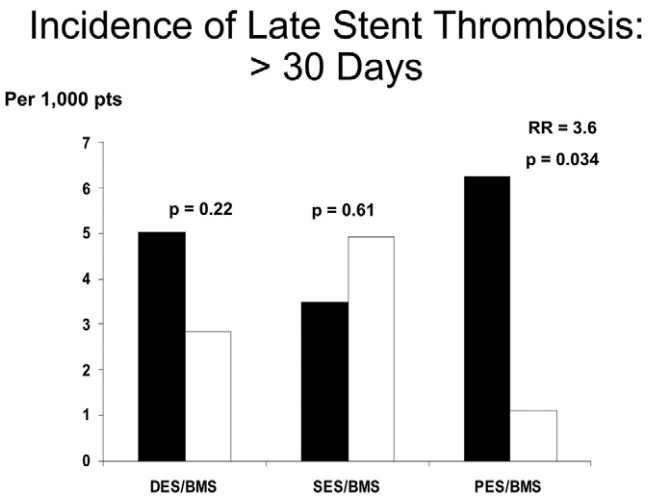

Figure 1 Incidence of late stent thrombosis: >30 days. BMS = bare metal stent; DES = drug-eluting stent; PES = paclitaxel-eluting stent; SES = sirolimus eluting stent.

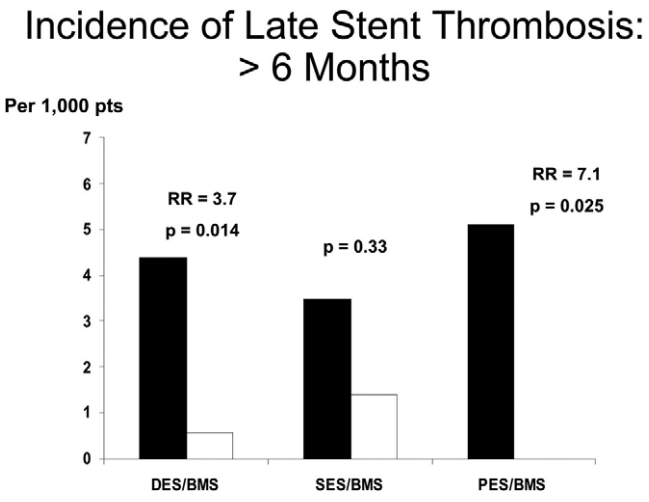

Figure 3 Incidence of late stent thrombosis: >6 months. BMS = bare metal stent; DES = drug-eluting stent; PES = paclitaxel-eluting stent; SES = sirolimus eluting stent.

median time of late bare metal stent thrombosis was 4 months (mean 4.8 ± 1.6 months) with a range of 40 to 181 days. The median time of late paclitaxel stent thrombosis was 18 months (mean 12.7 ± 6.9 months) with a range of 40 to 548 days, whereas the median time of late bare metal stent thrombosis was 3.5 months (mean 3.5 ± .08 months) with a range of 105 to 109 days (Figure 2).

The incidence of late thrombosis more than 6 months after the index procedure was 4.4 events per 1000 drug-eluting stent patients compared with .6 events per 1000 bare metal stent patients (RR = 3.67, 95% CI, 1.30 to 10.38, $P = .014$). Additionally, the incidence of late thrombosis based on the type of stent was 3.5 events per 1000 sirolimus stent patients compared with 1.4 events per 1000 bare metal stent patients (RR = 1.99, 95% CI, .50 to 7.91, $P = .33$), and 5.1 events per 1000 paclitaxel stent patients with zero events in bare metal stent patients (RR = 7.07, 95% CI, 1.28 to 39.09, $P = .025$) (Figure 3).

The incidence of very late thrombosis more than 1 year after the index procedure was 5.0 events per 1000 drug-eluting stent patients, with zero events in bare metal stent patients (RR = 5.02, 95% CI, 1.29 to 19.52, $P = .02$). Additionally, the incidence of very late thrombosis based on the type of stent was 3.6 events per 1000 sirolimus stent patients, with zero events in bare metal stent patients (RR = 3.99, 95% CI, .45 to 35.62, $P = .22$) and 5.9 events per 1000 paclitaxel stent patients with zero events in bare metal stent patients (RR = 5.72, 95% CI, 1.08 to 32.45, $P = .049$) (Figure 4).

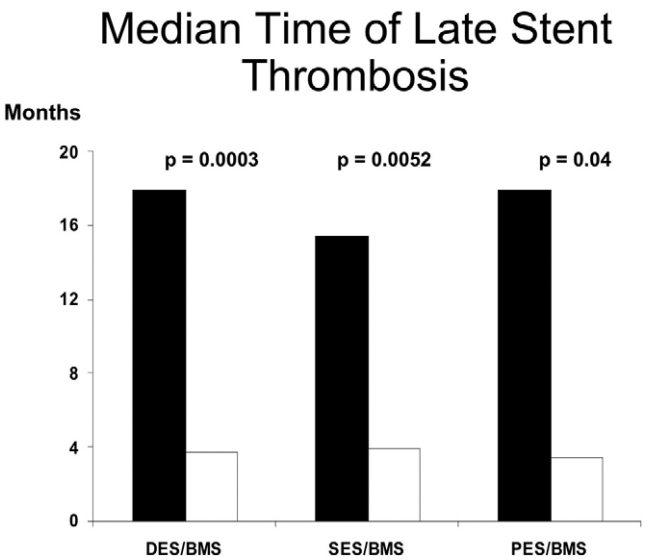

Figure 2 Median time of late stent thrombosis. BMS = bare metal stent; DES = drug-eluting stent; PES = paclitaxel-eluting stent; SES = sirolimus eluting stent.

DISCUSSION

In this analysis of 14 studies in over 6000 patients, the incidence of early thrombosis was similar between drug-eluting stents and bare metal stents. Increased risk with drug-eluting stents was suggested as early as 1 month after revascularization; however, more than 6 to 12 months after the procedure there was a 4- to 5-fold excess of drug-eluting stent thrombosis compared with bare metal stents. The time until late thrombosis was equally protracted for both sirolimus and paclitaxel stents, with a median thrombosis time of 15.5 to 18 months after coronary intervention, respectively, which was 11 to 14 months longer than late bare metal stent thrombosis.

Although analysis of sirolimus trials separately did not show an increased risk of late stent thrombosis, it was still concerning that the incidence of thrombotic events with this stent remained constant up to 4 years after coronary revascularization, while no thrombotic events were seen with bare metal stents after 1 year. Additionally, the protracted time of late thrombosis with sirolimus stents provides fur-

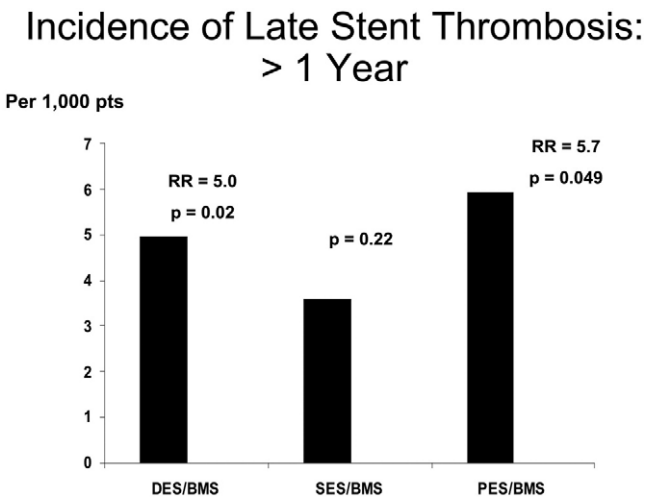

Figure 4 Incidence of late stent thrombosis: >1 year. BMS = bare metal stent; DES = drug-eluting stent; PES = paclitaxel-eluting stent; SES = sirolimus eluting stent.

ther evidence that these stents may still be at risk for late thrombosis. Insufficient power helps to explain the lack of an association, because the SIRIUS and RAVEL Trials enrolled half as many patients as the TAXUS Trials. Another explanation for the lack of association with sirolimus lies in the discrepant use of dual antiplatelet therapy between the 2 sets of trials. Among the sirolimus trials, 8 stent thromboses were seen in bare metal stent patients after 30 days, whereas in the paclitaxel trials, there were only 2 events in bare metal stent patients after 30 days. Although this disparity may have occurred by chance, it is likely that the more frequent events in the bare metal stent arms of the sirolimus studies occurred as a result of the shorter duration of dual antiplatelet therapy in this group relative to the bare metal stent arms of the paclitaxel studies. Had the sirolimus trials used a longer duration of clopidogrel (eg, 6 months), the incidence of late bare metal stent thrombosis may have been reduced, while minimally changing the incidence of late sirolimus stent thrombosis. This is supported by the fact that the median time of late bare metal stent thrombosis was less than 6 months, in contrast to more than 1 year for late drug-eluting stent thrombosis.

Most trials mandated the use of aspirin and clopidogrel for 2 to 6 months, and no trial required more than 12 months of therapy. After a protocol-mandated period of clopidogrel, the need for continued dual antiplatelet therapy was determined by individual physician preference. We assumed that the use of ongoing clopidogrel therapy would be less than universal and we had limited data on 6 of the stent thromboses to support this. Two of the sirolimus patients thrombosed their stents on days 539 and 773, although information on the use of antiplatelet therapy was unavailable. Four of the paclitaxel patients thrombosed their stents on days 500, 519, 522, and 711. In 1 patient, compliance with antiplatelet therapy was uncertain, whereas in the other 3 events, clopidogrel was not used and in one case it was discontinued because of elective surgery. Aspirin use was either uncertain or occasional in the paclitaxel events. Bias could have existed in this analysis, though, if physicians recommended a different duration of clopidogrel for drug-eluting stent patients compared with bare metal stent patients late after coronary intervention. We have no data that would support this concern, because patient treatment assignment was still blinded during clinical follow-up.

Our findings are applicable to the patient population of the 14 studies. Most of the studies shared common patient/angiographic exclusion criteria, such as severe left ventricular dysfunction, recent acute myocardial infarction, renal insufficiency, calcified or thrombus-containing vessels, bifurcation lesions, bypass graft disease, or the need for multiple stents. Accordingly, our results cannot be easily extrapolated to patients who were not well represented in these trials. This could make our findings even more concerning, because 'real life' patients would include these higher risk characteristics and could make for an even higher risk for late drug-eluting thrombosis in clinical practice.

Our findings suggest that there may not be a safe period for drug-eluting stents after which clopidogrel can safely be stopped. This analysis and others have confirmed that late bare metal stent thrombosis is very infrequent on aspirin monotherapy.[34] However, several studies have revealed that individuals with bare metal stents on chronic aspirin therapy are still at risk for late thrombotic events when total antiplatelet therapy is discontinued.[35,36] For patients who already have a drug-eluting stent implanted and need elective surgery, careful thought should be given to the relative risks of increased bleeding from remaining on antiplatelet therapy versus the hazard of precipitating stent thrombosis from discontinuing clopidogrel or aspirin. For patients whose coronary revascularization cannot be delayed until after surgery, the choice of a bare metal stent over a drug-eluting stent needs to be carefully considered.

In summary, we found that drug-eluting stents increase the risk for late thrombosis 4- to 5-fold compared with bare metal stents. Patients with drug-eluting stents may need to remain on dual antiplatelet therapy longer than the current Food and Drug Administration labeling of 6 months for paclitaxel stents and 3 months for sirolimus stents. However, the optimal duration of dual antiplatelet therapy for drug-eluting stents is unknown, although for angioplasty and bare metal stent procedures, 1 year has been demonstrated to be superior to 1 month.[37,38] Accordingly, caution should be given to interrupting long-term aspirin and clopidogrel therapy in patients who have had a drug-eluting stent implanted as long as several years previously.

References

1. FDA public health notification: Information for physicians on subacute thromboses (SAT) and hypersensitivity reactions with use of the Cordis Cypher coronary stent. Issued October 29, 2003. Available at: http://www.fda.gov/cdrh/safety/cypher.html. Accessed November 15, 2005.
2. Jeremias A, Sylvia B, Bridges J, et al. Stent thrombosis after successful sirolimus-eluting stent implantation. *Circulation*. 2004;109:1930-1932.

3. Bavry AA, Kumbhani DJ, Helton TJ, Bhatt DL. What is the risk of stent thrombosis associated with the use of paclitaxel-eluting stents for percutaneous coronary intervention? A meta-analysis. *J Am Coll Cardiol*. 2005;45:941-946.
4. Bavry AA, Kumbhani DJ, Helton TJ, Bhatt DL. Risk of thrombosis with the use of sirolimus-eluting stents for percutaneous coronary intervention (from registry and clinical trial data). *Am J Cardiol*. 2005;95:1469-1472.
5. 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.
6. Moreno R, Fernandez C, Hernandez R, et al. Drug-eluting stent thrombosis: results from a pooled analysis including 10 randomized studies. *J Am Coll Cardiol*. 2005;45:954-959.
7. Ong AT, Hoye A, Aoki J, et al. Thirty-day incidence and six-month clinical outcome of thrombotic stent occlusion after bare-metal, sirolimus, or paclitaxel stent implantation. *J Am Coll Cardiol*. 2005;45:947-953.
8. McFadden EP, Stabile E, Regar E, et al. Late thrombosis in drug-eluting coronary stents after discontinuation of antiplatelet therapy. *Lancet*. 2004;364:1519-1521.
9. Moses JW, Leon MB, Popma JJ, et al. Sirolimus-eluting stents versus standard stents in patients with stenosis in a native coronary artery. *N Engl J Med*. 2003;349:1315-1323.
10. Holmes DR Jr, Leon MB, Moses JW, et al. Analysis of 1-year clinical outcomes in the SIRIUS trial: a randomized trial of a sirolimus-eluting stent versus a standard stent in patients at high risk for coronary restenosis. *Circulation*. 2004;109:634-640.
11. SIRIUS, 3 year follow-up. Available at: http://www.tctmd.com/csportal/appmanager/tctmd/main?_nfpb=true&_pageLabel=TCTMDContent&hdCon=756655. Accessed November 15, 2005.
12. Schofer J, Schluter M, Gershlick AH, 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;362:1093-1099.
13. E-SIRIUS, 2 year follow-up. Available at: http://www.tctmd.com/csportal/appmanager/tctmd/main?_nfpb=true&_pageLabel=TCTMDContent&hdCon=814895. Accessed November 15, 2005.
14. Schampaert E, Cohen EA, Schluter M, 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;43:1110-1115.
15. Morice MC, Serruys PW, Sousa JE, et al. A randomized comparison of a sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med*. 2002;346:1773-1780.
16. RAVEL, 3 year follow-up. Available at: http://www.tctmd.com/csportal/appmanager/tctmd/main?_nfpb=true&_pageLabel=TCTMDContent&hdCon=823586. Accessed November 15, 2005.
17. RAVEL, 4 year follow-up. Available at: http://www.tctmd.com/csportal/ShowBinary/BEA%20Repository/TCTMD%20Portal/EPSlidePresPoolNew/2005/Slides_May05/RAVEL_Sousa_PCR05//pdfFile. Accessed November 15, 2005.
18. Ardissino D, Cavallini C, Bramucci E, et al. Sirolimus-eluting vs uncoated stents for prevention of restenosis in small coronary arteries: a randomized trial. *JAMA*. 2004;292:2727-2734.
19. SCANDSTENT. Available at: http://www.tctmd.com/csportal/appmanager/tctmd/main?_nfpb=true&_pageLabel=TCTMDContent&hdCon=756734. Accessed November 15, 2005.
20. DIABETES. Available at: http://www.tctmd.com/csportal/appmanager/tctmd/main?_nfpb=true&_pageLabel=TCTMDContent&hdCon=814709. Accessed November 15, 2005.
21. Pache J, Dibra A, Mehilli J, et al. Drug-eluting stents compared with thin-strut bare stents for the reduction of restenosis: a prospective, randomized trial. *Eur Heart J*. 2005;26:1262-1268.
22. Valgimigli M, Percoco G, Malagutti P, et al. Tirofiban and sirolimus-eluting stent vs abciximab and bare-metal stent for acute myocardial infarction: a randomized trial. *JAMA*. 2005;293:2109-2117.
23. Grube E, Silber S, Hauptmann KE, 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.
24. TAXUS I, 2 year follow-up. Available at: http://www.tctmd.com/csportal/appmanager/tctmd/main?_nfpb=true&_pageLabel=TCTMDContent&hdCon=880407. Accessed November 15, 2005.
25. Colombo A, Drzewiecki J, Banning A, et al. Randomized study to assess the effectiveness of slow- and moderate-release polymer-based paclitaxel-eluting stents for coronary artery lesions. *Circulation*. 2003;108:788-794.
26. TAXUS II, 2 year follow-up. Available at: http://www.tctmd.com/csportal/appmanager/tctmd/main?_nfpb=true&_pageLabel=TCTMDContent&hdCon=812016. Accessed November 15, 2005.
27. Stone GW, Ellis SG, Cox DA, et al. A polymer-based, paclitaxel-eluting stent in patients with coronary artery disease. *N Engl J Med*. 2004;350:221-231.
28. Stone GW, Ellis SG, Cox DA, et al. One-year clinical results with the slow-release, polymer-based, paclitaxel-eluting TAXUS stent: the TAXUS-IV trial. *Circulation*. 2004;109:1942-1947.
29. TAXUS IV, 2 year follow-up. Available at: http://www.tctmd.com/csportal/appmanager/tctmd/main?_nfpb=true&_pageLabel=TCTMDContent&hdCon=814047. Accessed November 15, 2005.
30. Stone GW, Ellis SG, Cannon L, et al. TAXUS V Investigators. Comparison of a polymer-based paclitaxel-eluting stent with a bare metal stent in patients with complex coronary artery disease: a randomized controlled trial. *JAMA*. 2005;294:1215-1223.
31. TAXUS VI, 30 day follow-up. Available at: http://www.tctmd.com/csportal/appmanager/tctmd/main?_nfpb=true&_pageLabel=TCTMDContent&hdCon=880460. Accessed November 15, 2005.
32. TAXUS VI, 9 month follow-up. Available at: http://www.tctmd.com/csportal/appmanager/tctmd/descoe?_nfpb=true&_pageLabel=DESCenterContent&hdCon=958541. Accessed November 15, 2005.
33. TAXUS VI, 2 year follow-up. Available at: http://www.tctmd.com/csportal/appmanager/tctmd/main?_nfpb=true&_pageLabel=TCTMDContent&hdCon=1256014. Accessed November 15, 2005.
34. Bhatt DL, Bertrand ME, Berger PB, et al. Meta-analysis of randomized and registry comparisons of ticlopidine with clopidogrel after stenting. *J Am Coll Cardiol*. 2002;39:9-14.
35. Ferrari E, Benhamou M, Cerboni P, Marcel B. Coronary syndromes following aspirin withdrawal: a special risk for late stent thrombosis. *J Am Coll Cardiol*. 2005;45:456-459.
36. Collet JP, Montalescot G, Blanchet B, et al. Impact of prior use or recent withdrawal of oral antiplatelet agents on acute coronary syndromes. *Circulation*. 2004;110:2361-2367.
37. Mehta SR, Yusuf S, Peters RJ, et al. Effects of pretreatment with clopidogrel and aspirin followed by long-term therapy in patients undergoing percutaneous coronary intervention: the PCI-CURE study. *Lancet*. 2001;358:527-533.
38. Steinhubl SR, Berger PB, Mann JT 3rd, et al. Early and sustained dual oral antiplatelet therapy following percutaneous coronary intervention: a randomized controlled trial. *JAMA*. 2002;288:2411-2420.