Journal of Geriatric Cardiology (2013) 10: 330–335

Research Article · **Open Access** ·

Long-term clinical outcomes of drug-eluting stents *vs.* bare-metal stents in Chinese geriatric patients

Pak-Hei Chan[1], Sha-Sha Liu[1], Hung-Fat Tse[1], Wing-Hing Chow[2], Man-Hong Jim[2], Hee-Hwa HO[2], Chung Wah Siu[1]

[1]*Department of Medicine, Li Ka Shing Faculty of Medicine, The University of Hong Kong, 102 Pokfulam Rd., Hong Kong, China*
[2]*Cardiac Medical Unit, Grantham Hospital, 125 Wong Chuk Hang Rd., Aberdeen, Hong Kong, China*

Abstract

Background & objective Little is known about the relative efficacies of percutaneous coronary intervention (PCI) with drug-eluting stents (DES) and bare-metal stents (BMS) in elderly patients. The objective of this study was to evaluate the clinical outcome for geriatric patients who received either DES or BMS. **Methods** From January 2002 to October 2005, 199 consecutive Chinese geriatric patients (≥ 75 years old) underwent PCI with coronary DES or BMS implantation at our institution. We analyzed the major clinical end points that included all-cause mortality, cardiovascular death, myocardial infarction, target lesion revascularization (TLR), stent thrombosis, and bleeding complications. **Results** The three-year cumulative rates of all-cause mortality, cardiovascular death, and myocardial infarction were significantly lower in the DES group (6.3%, 3.6%, 5.4%) compared with the BMS group (16.2%, 11.5%, 14.9%; $P < 0.05$). No significant differences were found in the three-year cumulative rate for target lesion revascularization (6.3% *vs.* 4.6%, $P = 0.61$) or stent thrombosis (3.6% *vs.* 2.3%, $P = 0.70$). Likewise, there were no statistically significant differences in the cumulative rate for intracranial hemorrhage, or major and minor hemorrhage at three years. **Conclusions** DES-based PCI was associated with a significant reduction in the three-year cumulative rate of all-cause mortality, cardiovascular death, and myocardial infarction compared with BMS, without increased risk of TLR, stent thrombosis, or bleeding complications at three years in this group of Chinese geriatric patients.

J Geriatr Cardiol 2013; 10: 330–335. doi: 10.3969/j.issn.1671-5411.2013.04.003

Keywords: Percutaneous coronary intervention; Geriatric patients; Drug-eluting stents; Bare-metal stents

1 Introduction

With the ageing population, increasing numbers of elderly patients who require treatment for coronary artery disease are observed. These elderly patients who have symptoms of angina, or who present with acute coronary syndrome very often need treatment for symptom relief and improved prognosis.

The outcome for elderly patients who undergo percutaneous coronary intervention (PCI) remains under-presented in published literature, particularly with regard to the clinical outcome of drug-eluting stents (DES) *versus* bare-metal stents (BMS). Previously published trials have demonstrated the clinical superiority of DES in reducing the need for repeat revascularization.[1–6] Despite such clinical benefit, BMS usage remains high in this population due to the inability to tolerate prolonged dual anti-platelet therapy. Though recent published data demonstrate the feasibility of shortened dual anti-platelet therapy,[7,8] the use of BMS remains the treatment of choice for elderly patients at high risk of bleeding and who require surgery following PCI.

This retrospective study aimed to evaluate the clinical outcome for geriatric patients who received either DES or BMS. The primary clinical endpoints included all-cause mortality, cardiovascular death, myocardial infarction, target lesion revascularization (TLR), stent thrombosis, and bleeding complications.

2 Methods

2.1 Study population

From January 2002 to October 2005, a total of 1,236 consecutive Chinese patients with obstructive coronary artery disease underwent elective or early percutaneous coronary intervention (PCI) at the Grantham Hospital, Hong

Correspondence to: Chung-Wah Siu, MD, Department of Medicine, University of Hong Kong, Queen Mary Hospital, Hong Kong, China.
E-mail: cwdsiu@hkucc.hku.hk
Telephone: +852-2255-4694 **Fax:** +852-2818-6304
Received: September 11, 2013 **Revised:** November 8, 2013
Accepted: November 9, 2013 **Published online:** December 20, 2013

Kong, a major tertiary referral center specializing in comprehensive medical treatment for adult heart and lung diseases. Of these patients, 199 aged 75 years or older were recruited for analysis (mean age, 78.4 ± 3.4 years; male sex, 64.8%). Patients were assigned to either DES or BMS group according to the stent used during the index procedure. A total of 562 patients who received BMS and 674 patients who received a DES (317 patients with sirolimus-eluting stents（SES; Cypher, Cordis Corp., Johnson & Johnson, Warren, NJ, USA), and 357 patients with paclitaxel-eluting stents (PES; TAXUS Express, Boston Scientific, Natick, MA, USA)) were recruited to the study.

2.2 Study design

This was a single-center registry based on the three-year clinical outcome for Chinese geriatric patients with obstructive coronary artery disease undergoing elective or early PCI at the Grantham Hospital, Hong Kong, using a DES or BMS.

PCI procedures were performed as described as following. Patient's demographic characteristics and procedural data were entered into the Grantham Hospital Cardiovascular Interventional Services Database upon discharge. All patients were followed up in the cardiac clinic at four weeks, 12 weeks, and every three months thereafter. For the present study, clinical data concerning major adverse cardiovascular events during any subsequent hospitalization within the three-year follow-up period were retrieved from the medical records and discharge summaries of our hospital as well as other institutions. Patients who were lost to follow-up within the three-year period were contacted by phone.

2.3 Interventional procedure

All PCIs were performed using a standard technique and according to current practice guidelines. All patients were prescribed aspirin (80 to 300 mg daily) prior to the procedure and indefinitely thereafter. Patients also received clopidogrel (an oral loading dose of 300 mg followed by 75 mg daily) before the procedure, continued for a minimum of 1 month in patients who received BMS, 3 months in those who received SES, and 6 months in those who received PES. Further clopidogrel treatment was at the discretion of the attending physician.

2.4 Outcomes and definitions

The major clinical outcomes in this study included death from any cause, cardiovascular death, myocardial infarction, need for target lesion revascularization (TLR), and stent thrombosis. Information about the circumstances of all deaths was obtained from the available sources. Death from a cardiovascular cause included death due to acute myocardial infarction, cardiac perforation or tamponade, arrhythmia, a complication of the PCI procedure, or any death in which a cardiovascular cause could not be excluded. Death from a non-cardiovascular cause was noted. Myocardial infarction (MI) was defined according to the latest consensus on MI definition.[9] Target lesion revascularization was defined as any repeat revascularization (percutaneous or surgical) required due to a stenosis > 50% within the stent or within 5 mm proximal or distal to the stented segment. Stent thrombosis was defined according to the Academic Research Consortium criteria.[10] Major bleeding was defined as any bleeding, not due to intracranial hemorrhage, which required hospitalization and/or blood transfusion and/or caused a > 2 g/L decrease in hemoglobin level. Intracranial hemorrhage was diagnosed in the presence of new onset neurological symptoms with radiological confirmation (computerized axial tomography scan or magnetic resonance imaging), and classified as intra-cerebral, subarachnoid or subdural hemorrhage.

2.5 Statistical analysis

Continuous variables are expressed as mean ± SD. Dichotomous variables are expressed as counts and percentages. Statistical comparisons were performed using the Student *t* test or Fisher's exact test, as appropriate. We used Kaplan-Meier time-to-event analysis with log-rank test to assess the cumulative incidence of events over time and to evaluate differences between the two groups. Cox regression analysis was used to evaluate independent predictors of cardiovascular death at three years. Calculations were performed using SPSS software (version 12.0; SPSS, Inc., Chicago, IL). All P values were 2-sided and $P < 0.05$ was considered statistically significant.

3 Results

During the study period, 1,236 consecutive Chinese patients with obstructive coronary artery disease underwent PCI at the Grantham hospital. Of these, 199 patients aged 75 years or older were included in this analysis. Table 1 summarizes the clinical characteristics of the study population. The mean age was 78.4 ± 3.4 years with a male preponderance (64.8%). One hundred and twelve patients received a DES and the remaining 87, a BMS. There were no significant differences in age, sex, or cardiovascular risk factors between the two groups, except those who received a DES had a higher prevalence of hypertension (80.4% *vs.* 60.4%, $P = 0.01$). Concerning the index PCI, there was no significant difference between the two groups in location of target vessels or number of stents deployed (Table 2).

Table 1. Baseline clinical characteristics of patients undergoing PCI with DES and BMS.

	DES (*n* = 112)	BMS (*n* = 87)	*P*-value
Age, yrs	78.4 ± 3.5	78.4 ± 3.4	0.92
Male	73 (65.2)	57 (65.5)	0.96
Smoker	49 (43.8)	45 (51.7)	0.26
Diabetes mellitus	49 (43.8)	41 (47.1)	0.64
Hypertension	90 (80.4)	56 (64.4)	0.01
Hyperlipidemia	51 (45.5)	35 (40.2)	0.45
Renal failure	4 (3.6)	1 (1.1)	0.39
Previous myocardial infarct	12 (10.7)	16 (18.4)	0.12
Previous PCI	49 (43.8)	27 (31.0)	0.07
Previous CABG	21 (18.8)	10 (11.5)	0.16
Duration of clopidgrel, ds	230.5 ± 241.6	58.3 ± 78.6	< 0.01

Data are presented as mean ± SD and *n* (%). BMS: bare-metal stent; CABG: coronary artery bypass graft; DES: drug-eluting stent; PCI: Percutaneous coronary intervention.

Table 2. Procedural characteristics of patients undergoing PCI with DES and BMS.

	DES (*n* = 112)	BMS (*n* = 87)	*P*-value
Target vessel			
LMCA	3 (2.7)	1 (1.1)	0.63
LAD	41 (36.6)	33 (37.9)	0.85
LCx	35 (31.3)	23 (26.4)	0.46
RCA	45 (40.2)	41 (47.1)	0.33
Vein graft	7 (6.3)	5 (5.7)	0.88
Number of stents per patient	1.8 ± 0.8	1.6 ± 0.9	0.17

Data are presented as mean ± SD and *n* (%). BMS: bare-metal stent; DES: drug-eluting stent; LAD: left anterior descending artery; LCx: left circumflex artery; LMCA: left main coronary artery; RCA: right coronary artery.

During the three-year period, no patients were lost on follow-up. As expected, patients who received a DES were prescribed a longer mean duration of clopidogrel compared with those who received a BMS (230.5 ± 241.6 days *vs*. 58.3 ± 78.6 days, $P < 0.01$). Table 3 summarizes the cumulative three-year rates of major clinical outcomes for patients who received DES and BMS.

3.1 Death, cardiovascular death and myocardial infarction

Patients who received a DES had a lower cumulative three-year rate of all-cause death (6.3% *vs*. 16.2%, $P = 0.03$; Figure 1A), cardiovascular death (3.6% *vs*. 11.5%, $P = 0.03$; Figure 1B), and MI (5.4% *vs*. 14.9%, $P = 0.02$; Figure 1C) than those who received a BMS. The higher rate of all-cause death in the BMS group was mainly driven by a higher rate of cardiovascular death. The rate of non-cardiovascular deaths was similar for each group (2.6% *vs*. 4.6%, $P = 0.70$). Cox regression analysis, nonetheless, failed to identify any independent predictor of cardiovascular death at the three-year follow-up.

Table 3. Three-year clinical outcomes.

	DES (*n* = 112)	BMS (*n* = 87)	*P*-value
All-cause death	7 (6.3)	14 (16.2)	0.03
Cardiovascular death	4 (3.6)	10 (11.5)	0.03
Myocardial infarction	6 (5.4)	13 (14.9)	0.02
TLR	7 (6.3)	4 (4.6)	0.61
Stent thrombosis	4 (3.6)	2 (2.3)	0.70
Intracranial hemorrhage	3 (2.7)	0 (0)	0.26
Major bleeding	5 (4.5)	6 (6.9)	0.46
Minor bleeding	19 (17.0)	16 (18.4)	0.79

Data are presented as *n* (%). BMS: Bare-metal stent; DES: Drug-eluting stent; TLR: Target lesion revascularization.

3.2 Stent thrombosis and revascularization

The cumulative three-year rate for stent thrombosis for patients who received DES did not differ significantly to that for patients who received BMS (3.6% *vs*. 2.3%, $P = 0.7$; Figure 1D). Likewise, the cumulative three-year rate for TLR was similar (6.3% DES *vs*. 4.6% BMS, $P = 0.61$; Figure 1E).

3.3 Bleeding complications

There were 36 instances of bleeding complications (18.1%) during this three-year period: three intracranial hemorrhages (2.7%), 11 major hemorrhages (5.5%), and 22 minor hemorrhages (11.1%). No intracranial hemorrhage, 4 out of 11 (36.4%) major hemorrhages, and 13 out of 35 minor hemorrhages occurred while the patient was taking dual anti-platelet agents. There was no statistically significant difference in the cumulative risk of intracranial hemorrhage, major hemorrhage, or overall event-free survival between patients who received DES and BMS (Figure 1F to H).

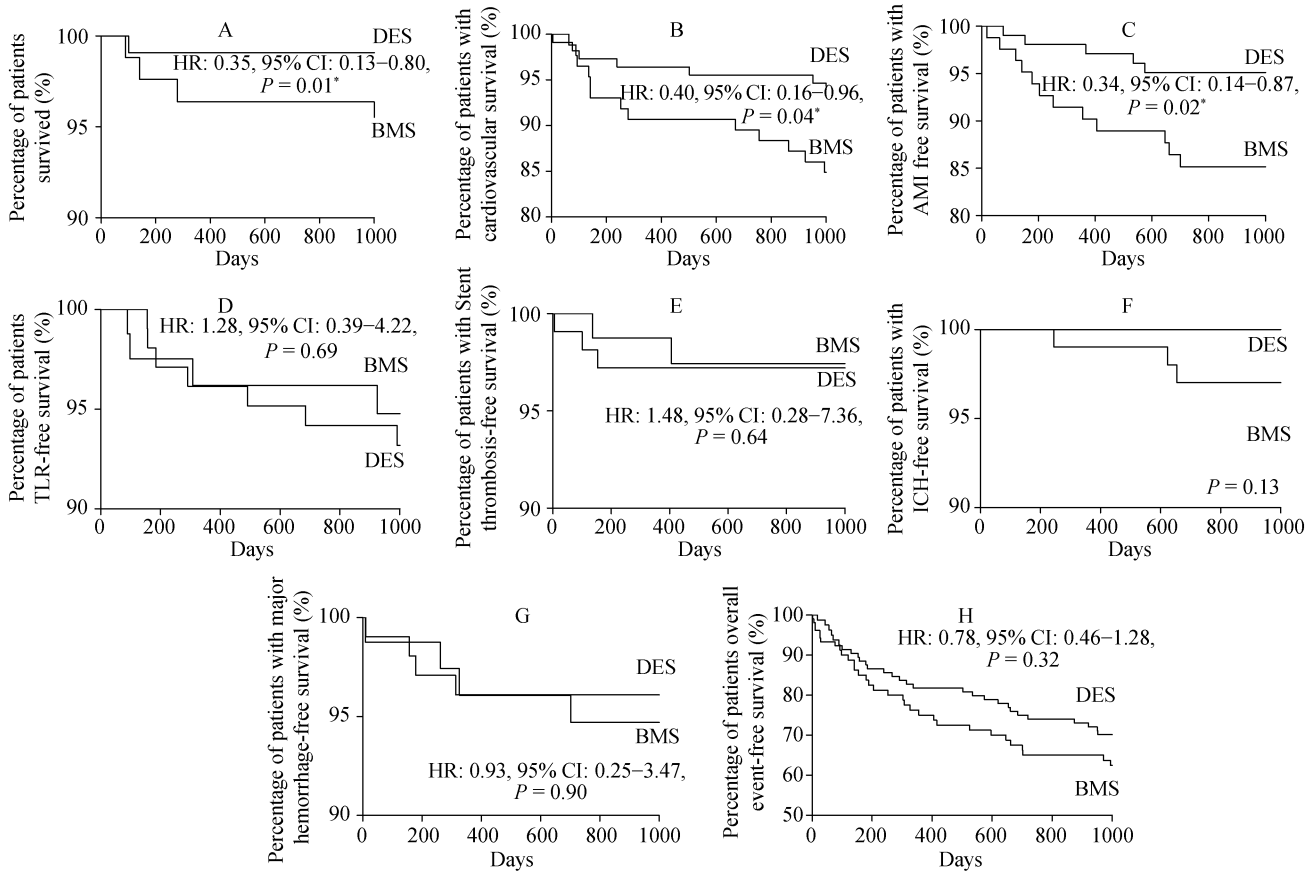

Figure 1. Kaplan-Meier estimate of percentage of (A) Overall survival; (B) Cardiovascular survival; (C) AMI-free survival; (D) TLR-free survival; (E) Stent thrombosis-free survival; (F) ICH-free survival; (G) Major hemorrhage-free survival; (H) Overall event-free survival in the three year study period. AMI: acute myocardial infarction; BMS: bare-metal stents; DES: drug-eluting stents; ICH: intracranial hemorrhage; TLR: target lesion revascularization.

4 Discussion

Landmark trials of DES have demonstrated their superiority over BMS in reducing the need for repeat revascularization.[1–6] Nonetheless, most of these clinical trials focused on patients of younger age, and elderly patients were very often under-represented. Randomized trials with elderly patients, particularly those aged 75 or above, are largely lacking and thus not representative of every-day clinical practice. Thus, the choice between DES and BMS for such patients is very often at the discretion of the surgeon. Whether use of a DES would confer more clinical benefit remains uncertain.

This retrospective review focuses on the clinical outcome of patients who underwent PCI in a non-acute setting utilizing either a DES or a BMS. While there was no difference in terms of non-cardiovascular death, or need for repeat revascularization, all-cause mortality was less in those who received a DES compared with BMS (6.3% *vs.* 16.2%, P = 0.03). This enhanced clinical outcome was largely driven by fewer cardiovascular deaths in the DES group (3.6% *vs.* 11.5%, P = 0.03) and a lower incidence of myocardial infarction compared with the BMS group (5.4% *vs.* 14.9%, P = 0.02). In this study, use of DES did not lead to a lower revascularization rate, thus dispelling the belief that DES had an anti-stenotic effect. This observation may be due to the more conservative approach in managing elderly patients, particularly in this Chinese population. In addition, some events may not have been observed as routine angiographic follow-up was not performed and the need for TLR was symptom-driven only. Nevertheless, DES implantation did benefit patients at lower risk of MI and associated cardiovascular morbidities and mortalities. In several previously published observational studies,[11–14] use of DES in elderly patients has been associated with lower risk of mortality and MI.

Bleeding tendency, particularly in elderly patients, has always been a major concern that influences choice of DES or BMS in a particular patient. No statistically significant difference in the incidence of bleeding complications was observed between the two study groups despite the difference in duration of anti-platelet therapy. This is not surpris-

ing given the observational nature of this study and the fact that very often, patients at higher bleeding risk and unable to tolerate a longer duration of anti-platelet therapy were treated with BMS and vice versa. The absence of randomization in stent selection might also have affected the bleeding complication result.

In our study, first generation DESs, namely Cypher and Taxus stents, were used. The incidence of definite stent thrombosis in first generation DES is approximately 0.9% and 1.3% at one and two years, respectively.[15] Late and very late stent thrombosis is a known phenomenon with these first generation devices with an annual increment in incidence of around 0.4%.[16–18] The comparable one and two year incidence in BMS has been reported to be around 1.2% and 1.4%.[15] Our reported data were similar and at three years, the rate of definite stent thrombosis was 3.6% and 2.3% in the DES and BMS (P = 0.7) groups, respectively. The trend towards a higher rate of stent thrombosis in the DES group may be due to the use of first generation DES (these have a slightly higher rate of stent thrombosis compared with the second generation DES device that are currently our preferred DES).

4.1 Study limitations

The major limitation of the present study was its observational nature and patients were recruited from a single center, even though our center serves as a high-volume tertiary referral center for treatment of coronary artery disease. Though no patient was lost on follow up, the relatively small number of patients recruited may have prevented identification of predictors for cardiovascular death. The study was also not sufficiently powered to compare rates of infrequent clinical events in either group, such as bleeding complications and stent thrombosis. First generation DESs were in use at the time of patient recruitment, but have since been replaced by second generation DES with a lower incidence of stent thrombosis and a requirement for shorter dual anti-platelet therapy.

4.2 Conclusions

This single-center registry has demonstrated in Chinese geriatric patients, utilizing DES in PCI was associated with a significant reduction in the three-year cumulative rates of all-cause mortality, largely driven by lower cardiovascular death and rate of myocardial infarction compared with BMS. Over the three years, there was no statistical difference in the risk of TLR, stent thrombosis or bleeding complications as shown in this study.

References

1 Morice MC, Serruys PW, Sousa JE, *et al*. A randomized comparison of sirolimus-eluting stent with a standard stent for coronary revascularization. *N Engl J Med* 2002; 346: 1773–1780.

2 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.

3 Grube E, Silber S, Huptmann 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.

4 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.

5 Park SJ, Shin WH, Ho DS, *et al*. A paclitaxel-eluting stent for the prevention of coronary restenosis. *N Engl J Med* 2003; 348: 1537–1545.

6 Kastrati A, Mehilli J, Pache J, *et al*. Analysis of 14 trials comparing sirolimus-eluting stents with bare-metal stents. *N Engl J Med* 2007; 356: 1030-1039.

7 Palmerini T. Pooled data of 10,615 patients from four real-world trials–XIENCE V USA, SPIRIT V, SPIRIT Women SAS and XIENCE V India. Presented at EuroPCR 2012, Paris, France, 15-18 May 2012.

8 Manoharan G. Pooled analysis of clinical events from prospective trials of the Resolute zotarolimus-eluting stent: three year outcomes of 5130 patients. Presented at ACC. 13, San Francisco, USA, 9-11 March 2012.

9 Thygesen K, Alpert JS, Jaffe AS, *et al*. Third universal definition of myocardial infarction. *J Am Coll Cardiol* 2012; 60: 1581–1598.

10 Cutlip DE, Windecker S, Mehran R, *et al*. Clinical end points in coronary stent trials: a case for standardized definitions. *Circulation* 2007; 115: 2344–2351.

11 Wang TY, Masoudi FA, Messenger JC, *et al*. Percutaneous coronary intervention and drug-eluting stent use among patients ≥ 85 years of age in the United States. *J Am Coll Cardiol* 2012; 59: 105–112.

12 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.

13 Groeneveld PW, Matta MA, Greenhut AP, *et al*. Drug-eluting compared with bare-metal coronary stents among elderly patients. *J Am Coll Cardiol* 2008; 51: 2017–2024.

14 Anstrom KJ, Kong DF, Shaw LK, *et al*. Long-term clinical outcomes following coronary stenting. *Arch Intern Med* 2008; 168: 1647–1655.

15 Sarno G, Lagerqvist B, Fröbert O, *et al*. Lower risk of stent

thrombosis and restenosis with unrestricted use of 'new-generation' drug-eluting stents: a report from the nationwide Swedish Coronary Angiography and Angioplasty Registry (SCAAR). *Eur Heart J* 2012; 33: 606–613.

16 Simsek C, Magro M, Boersma E, *et al*. The unrestricted use of sirolimus- and paclitaxel-eluting stents results in better clinical outcomes during 6-year follow-up than bare-metal stents: An analysis of the RESEARCH (Rapamycin-Eluting Stent Evaluated At Rotterdam Cardiology Hospital) and T-SEARCH (Taxus-Stent Evaluated At Rotterdam Cardiology Hospital) registries. *JACC Cardiovasc Interv* 2010; 3: 1051–1058.

17 Wenaweser P, Daemen J, Zwahlen M, *et al*. Incidence and correlates of drug-eluting stent thrombosis in routine clinical practice. 4-year results from a large 2-institutional cohort study. *J Am Coll Cardiol* 2008; 52: 1134–1140.

18 de la Torre-Hernandez JM, Alfonso F, Hernandez F, *et al*. Drug-eluting stent thrombosis: Results from the multicenter Spanish registry ESTROFA (Estudio ESpanol sobre TROmbosis de stents FArmacoactivos). *J Am Coll Cardiol* 2008; 51: 986–990.