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Angiographic Stent Thrombosis After Routine Use of Drug-Eluting Stents in ST-Segment Elevation Myocardial Infarction

The Importance of Thrombus Burden

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Objectives This study sought to investigate the impact of thrombus burden on the clinical outcome and angiographic infarct-related artery stent thrombosis (IRA-ST) in patients routinely treated with drug-eluting stent (DES) implantation for ST-segment elevation myocardial infarction (STEMI).

Background There are limited data for the safety and effectiveness of DES in STEMI.

Methods We retrospectively analyzed 812 consecutive patients treated with DES implantation for STEMI. Intracoronary thrombus burden was angiographically estimated and categorized as large thrombus burden (LTB), defined as thrombus burden ≥2 vessel diameters, and small thrombus burden (STB) to predict clinical outcomes. Major adverse cardiac events (MACE) were defined as death, repeat myocardial infarction, and IRA reintervention.

Results Mean duration of follow-up was 18.2 ± 7.8 months. Large thrombus burden was an independent predictor of mortality (hazard ratio [HR] 1.76, $p = 0.023$) and MACE (HR 1.88, $p = 0.001$). The cumulative angiographic IRA-ST was 1.1% at 30 days and 3.2% at 2 years, and continued to augment beyond 2 years. It was significantly higher in the LTB compared with the STB group (8.2% vs. 1.3% at 2 years, respectively, $p < 0.001$). Significant independent predictors for IRA-ST were LTB (HR 8.73, $p < 0.001$), stent thrombosis at presentation (HR 6.24, $p = 0.001$), bifurcation stenting (HR 4.06, $p = 0.002$), age (HR 0.55, $p = 0.003$), and rheolytic thrombectomy (HR 0.11, $p = 0.03$).

Conclusions Large thrombus burden is an independent predictor of MACE and IRA-ST in patients treated with DES for STEMI. (J Am Coll Cardiol 2007;50:573–83) © 2007 by the American College of Cardiology Foundation

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Primary percutaneous coronary intervention (PCI) with bare metal stent (BMS) implantation is established as the treatment of choice for ST-segment elevation myocardial infarction (STEMI) (1,2). There are limited data regarding the use of drug-eluting stents (DES) in a STEMI setting. Initial small registries showed superiority of sirolimus-eluting stents (SES) compared with BMS up to 1 year of follow-up (3–8). Two randomized trials confirmed these results (9,10). The findings regarding paclitaxel-eluting stents (PES) are less clear with positive small single-center reports (11,12), but a negative randomized trial (13). There are no data on the routine use of DES for STEMI with midterm outcomes.

The etiology of stent thrombosis is multifactorial, involving stent thrombogenicity and procedure-, lesion-, and patient-related factors (14). Acute coronary syndromes have been recognized as a factor of increased rates of stent thrombosis both for BMS (15–17) and DES (18–20). Limited data exist regarding the incidence and predictors of DES thrombosis during STEMI (9,10,13,18).

In patients with acute coronary syndromes, angiographic presence of thrombus increases the incidence of in-hospital major adverse cardiac events (MACE) (21,22). Mechanical treatment of thrombotic lesions, by means of thrombectomy and distal protection devices, has been proposed to prevent the complications caused by thrombus and improve clinical outcomes, but randomized trials failed to show any beneficial

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Abbreviations and Acronyms

BMS = bare-metal stent(s)
DES = drug-eluting stent(s)
IRA-ST = infarct-related artery stent thrombosis
LTB = large thrombus burden
MACE = major adverse cardiac events
MI = myocardial infarction
PES = paclitaxel-eluting stents
PCI = percutaneous coronary intervention
RT = rheolytic thrombectomy
SES = sirolimus-eluting stent(s)
STB = small thrombus burden
STEMI = ST-segment elevation myocardial infarction
TIMI = Thrombosis In Myocardial Infarction
TLR = target lesion revascularization (of the infarct-related artery)
TVR = target vessel revascularization (of the infarct-related artery)

effect of routine use in "all comers" on myocardial reperfusion or clinical outcome during STEMI (23,24). There is no angiographic thrombus classification validated to predict clinical outcomes.

In a large unselected cohort of consecutive patients with STEMI treated with PCI and DES, we propose a simple angiographic thrombus classification, and we report the 2-year clinical outcome and incidence and predictors of infarct-related artery stent thrombosis (IRA-ST).

Patients and Methods

Patients and procedure. From April 2002, when DES were introduced, until December 2004, 900 consecutive patients presented with STEMI and underwent PCI (primary or rescue) within 12 h after the onset of chest pain; 37 (4.1%) were treated with balloon angioplasty, 51 (5.7%) with BMS, and 812 (90.2%) with DES. The BMS were implanted because of unavailability of all DES sizes (length or diameter) in the initial period of their approval. This analysis focuses on patients treated exclusively with DES. All patients were pretreated with 250 mg aspirin and 300 mg clopidogrel. Preprocedural intracoronary nitrates were systematically administered. A PCI was performed according to standard clinical practice. The use of rheolytic thrombectomy (RT) (Possis Medical, Inc., Minneapolis, Minnesota), the only thrombectomy or aspiration system used, and periprocedural pharmacological treatment (e.g., glycoprotein IIb/IIIa antagonists) were at the operator's discretion. All patients received dual antiplatelet therapy: aspirin 325 mg/day indefinitely and clopidogrel 75 mg/day for 3 and 6 months after SES and PES implantation, respectively.

Clinical follow-up. Information regarding baseline clinical characteristics, procedural details, and in-hospital events was obtained from electronic databases maintained at Erasmus Medical Center. Postdischarge survival status was obtained from the Municipal Civil Registry. A questionnaire was mailed to all living patients focusing on rehospitalization and MACE. Referring cardiologists, general practitioners, and patients were contacted when necessary for additional information. All patients provided written informed consent.

Angiographic analysis. Intracoronary thrombus was angiographically identified and scored in 5 grades as previously described (25). According to this classification, in thrombus grade 0 (G0), no cineangiographic characteristics of thrombus are present; in thrombus grade 1 (G1), possible thrombus is present, with such angiography characteristics as reduced contrast density, haziness, irregular lesion contour, or a smooth convex meniscus at the site of total occlusion suggestive but not diagnostic of thrombus; in thrombus grade 2 (G2), there is definite thrombus, with greatest dimensions $\leq$1/2 the vessel diameter; in thrombus grade 3 (G3), there is definite thrombus but with greatest linear dimension $>$1/2 but $<$2 vessel diameters; in thrombus grade 4 (G4), there is definite thrombus, with the largest dimension $\geq$2 vessel diameters; and in thrombus grade 5 (G5), there is total occlusion (unable to assess thrombus burden due to total vessel occlusion).

In patients presenting with an open IRA, thrombus was scored in the preintervention angiographic sequence more clearly depicting its size. In patients presenting with an occluded IRA (G5; essentially no flow and not thrombus classification), thrombus was reclassified into one of the other categories after flow achievement with either guidewire crossing or a small (diameter 1.5 mm) deflated balloon passage or dilation. After reclassification of the G5 group, thrombus burden was stratified in 2 categories, scored as a small thrombus burden (STB) for thrombus $<$G4 and a large thrombus burden (LTB) for thrombus G4, based on clinical outcomes.

Thrombosis In Myocardial Infarction (TIMI) flow and myocardial blush were assessed as previously reported (26,27). No reflow was defined as reduced antegrade flow (TIMI flow grade $<$2) in the absence of occlusion at the treatment site or evidence of distal embolization. Distal embolization was defined as migration of a filling defect to distally occlude the infarct-related vessel or one of its branches, or a new abrupt cutoff of the distal vessel/branch.

Stent thrombosis was defined as a complete or partial occlusion within the stented segment with evidence of thrombus and reduced antegrade flow (TIMI flow grade $<$3) with a concurrent acute clinical ischemic event. The stent thrombosis cases were categorized according to the timing of occurrence into acute (from the end of the procedure up to 24 h), subacute (from 24 h up to 30 days), late (between 30 days and 6 months), and very late ($>$6 months).

All procedural parameters, including thrombus classification, were assessed by 2 experienced interventional cardiologists reviewing the angiograms together. Both reviewers were blinded to clinical outcomes. Consensus was achieved in all patients. Half of the films were randomly selected and reanalyzed by the same analysts for intraobserver variability, and by a third experienced interventional cardiologist for interobserver variability of the proposed LTB and STB classification.