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Risk of Stent Thrombosis Among Bare-Metal Stents, First-Generation Drug-Eluting Stents, and Second-Generation Drug-Eluting Stents

Results From a Registry of 18,334 Patients

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Objectives This study sought to compare the risk of stent thrombosis among patients treated with bare-metal stents (BMS), first-generation drug-eluting stents (G1-DES), and second-generation drug-eluting stents (G2-DES) for a period of 3 years.

Background In patients undergoing coronary stenting, there is a scarcity of long-term follow-up data on cohorts large enough to compare rates of stent thrombosis across the stent generations.

Methods A total of 18,334 patients undergoing successful coronary stent implantation from 1998 to 2011 at 2 centers in Munich, Germany, were included in this study. Patients were stratified into 3 groups according to treatment with BMS, G1-DES, and G2-DES.

Results The cumulative incidence of definite stent thrombosis at 3 years was 1.5% with BMS, 2.2% with G1-DES, and 1.0% with G2-DES. On multivariate analysis, G1-DES compared with BMS showed a significantly higher risk of stent thrombosis (odds ratio [OR]: 2.05; 95% confidence interval [CI]: 1.47 to 2.86; $p < 0.001$). G2-DES were associated with a similar risk of stent thrombosis compared with BMS (OR: 0.82; 95% CI: 0.56 to 1.19; $p = 0.30$). Beyond 1 year, the risk of stent thrombosis was significantly increased with G1-DES compared with BMS (OR: 4.72; 95% CI: 2.01 to 11.1; $p < 0.001$), but not with G2-DES compared with BMS (OR: 1.01; 95% CI: 0.32 to 3.25; $p = 0.98$).

Conclusions In a large cohort of unselected patients undergoing coronary stenting, compared with BMS, there was a significant excess risk of stent thrombosis at 3 years with G1-DES, driven by an increased risk of stent thrombosis events beyond 1 year. G2-DES were associated with a similar risk of stent thrombosis compared with BMS. (J Am Coll Cardiol Intv 2013;6:1267–74) © 2013 by the American College of Cardiology Foundation

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Stent thrombosis is a rare but frequently fatal complication of percutaneous coronary intervention (1,2). First-generation drug-eluting stents (G1-DES), compared with bare-metal stents (BMS), markedly reduce the need for reinterventions (3–6). However, the risk to be borne appears to be a small but continuous increase in the incidence of stent thrombosis in the late phase after stent implantation (7–9). Pathological samples of patients with stent thrombosis confirmed that G1-DES lead to delayed arterial healing, incomplete endothelialization, and persistent fibrin deposition compared with BMS (10). The use of durable polymer coatings, the thickness of the stent struts, and the dose of the antiproliferative drug and its release kinetics have been implicated as important contributing factors in these late adverse events (11–13). Against this background, second-generation DES (G2-DES) were developed that have improved biocompatibility, durable or biodegradable polymer coatings, thinner stent struts, and improved antiproliferative drug release kinetics. Indeed G2-DES have shown favorable safety and efficacy compared with G1-DES in a number of clinical trials and registries (14–18). To date, however, there is a scarcity of long-term follow-up data on real-world patients in cohorts large enough to compare rates of stent thrombosis with adequate statistical power across different generations of stents. The aim of this study was to compare the relative risk of stent thrombosis among 3 different stent generations, BMS, G1-DES, and G2-DES, from a dataset of 18,334 patients with coronary artery disease treated with intracoronary stents over a 13-year period.

Abbreviations and Acronyms

BMS = bare-metal stent(s)
CI = confidence interval
DES = drug-eluting stent(s)
G1-DES = first-generation drug-eluting stent(s)
G2-DES = second-generation drug-eluting stent(s)
OR = odds ratio
STEMI = ST-segment elevation myocardial infarction

Methods

Patient selection and study procedures. We analyzed clinical, angiographic, and procedural data for all consecutive patients treated with stent implantation for coronary artery disease between January 1998 and December 2011 in 2 tertiary referral centers in Munich, Germany (Deutsches Herzzentrum and 1. Medizinische Klinik, Klinikum Rechts der Isar) provided that written informed consent was obtained. Patients receiving long-term renal replacement therapy and those who had undergone previous cardiac transplantation or with stent thrombosis as an indication for intervention were excluded. BMS were the sole platforms approved for use from January 1998 to August 2002. Thereafter, DES became available. DES were arbitrarily subclassified as first or second generation. G1-DES comprised durable polymer (polyethylene-co-vinyl acetate and poly-*N*-butyl-methacrylate sirolimus-eluting stents (Cypher, Cordis, Warren, New Jersey); durable polymer (Translute) paclitaxel-eluting stents (Taxus, Boston Scientific, Natick, Massachusetts), durable polymer (phosphorylcholine) zotarolimus-eluting stents (Endeavor, Medtronic Inc., Santa Rosa, California), and polymer-free sirolimus-eluting stents (Yukon, Translumina GmbH, Hechingen, Germany); the majority of G1-DES were Cypher and Taxus stents. G2-DES were available starting in January 2006 and comprised durable fluoropolymer everolimus-eluting stents (Xience V, Abbott Vascular, Santa Clara, California), durable polymer (BioLinx) zotarolimus-eluting stents (Resolute, Medtronic Inc.), biodegradable polymer biolimus A9-eluting stents (Nobori, Terumo Corporation, Tokyo, Japan), biodegradable polymer sirolimus-eluting stents and polymer-free sirolimus and probucol-eluting stents (both Yukon; Translumina GmbH); the majority of 2G-DES were Xience and Resolute stents. The assignment to BMS or DES platforms occurred predominantly in the setting of randomized trials; typically, the same stent was implanted in a patient undergoing multilesion interventions. Antithrombotic and anticoagulant therapies reflected the changing practices during the period of observation. Until April 1999, in patients undergoing a percutaneous coronary intervention, we used the ticlopidine therapy regimen, which comprised a pre-treatment dose of 500 mg given orally 1 to several hours before the procedure followed by a 500-mg/day maintenance dose. From May to August 1999, patients received clopidogrel therapy consisting of pre-treatment with an oral dose of 300 mg given 2 to 4 h before the intervention, 150 mg/day until discharge, and a maintenance dose of 75 mg/day. Since September 1999, we initiated a high loading clopidogrel regimen with an oral dose of 600 mg of clopidogrel, 150 mg/day until discharge, and a maintenance dose of 75 mg/day. After the intervention, all patients, irrespective of treatment allocation, were prescribed 200 mg/day of aspirin indefinitely, whereas ticlopidine or clopidogrel was prescribed for a period of at least 1 month after BMS implantation and at least 6 months after DES implantation. During coronary intervention, all patients received anticoagulation with either unfractionated heparin or bivalirudin. Administration of glycoprotein IIb/IIIa inhibitors and the use of intracoronary imaging was at the discretion of the operating physician. After the intervention, patients remained in the hospital for at least 48 h. Blood samples were drawn every 8 h for the first 24 h after randomization and daily afterward for the determination of cardiac markers (creatine kinase, creatine kinase-myocardial band, troponin T or I). Daily electrocardiography was also performed until discharge. All patients were prescribed standard secondary prevention for coronary artery disease as directed by the treating physician (e.g., beta-blockers, statins, angiotensin-converting enzyme inhibitors, and other