The 5-Year Clinical Outcomes After a Randomized Comparison of Sirolimus-Eluting Versus Bare-Metal Stent Implantation in Patients With ST-Segment Elevation Myocardial Infarction

To the Editor: Because patients with acute ST-segment elevation myocardial infarction (STEMI) were excluded from early randomized trials, only relatively short-term data from large multicenter studies comparing drug-eluting stents (DES) with bare-metal stents (BMS) are currently available. Unambiguous ascertainment of long-term compliance with thienopyridines is problematic in STEMI, which is a matter of serious concern (1,2), and one observational registry suggested higher late (>6 months) unadjusted and adjusted mortality rates in STEMI patients with a DES compared with those with a BMS (3). Thus, the use of a DES in STEMI patients still remains highly controversial.

The design of the study and outcomes at 8- and 24-month follow-up were previously reported (4,5). Since then, all eligible patients underwent routine clinical follow-up at 6-month intervals for 5 years after index intervention. All events up to 5 years were adjudicated by an independent clinical event committee that was blinded to the treatment assignments.

All analyses were conducted according to the intent-to-treat principle. Event-free survival curves were generated using the Kaplan-Meier method, and survival between groups was compared using the log-rank test. Hazard ratios (HRs) with 95% confidence intervals (CIs) were calculated using the Cox proportional hazards model.

The cumulative duration of dual antiplatelet treatment trended longer in the tirofiban–sirolimus-eluting stent (SES) arm (182 ± 92 days vs. 155 ± 105 days in the abciximab + BMS group; p = 0.073); however, 80% and 100% of patients in both groups discontinued thienopyridines after 250 days and 360 days, respectively. Overall, use of medications did not differ between study groups at any time point during follow-up. Complete follow-up information for as long as 1,800 days was available for all patients.

At 5 years, the cumulative incidence of major adverse cardiac events (MACE) (death, myocardial infarction [MI], or target vessel revascularization) trended lower in the tirofiban–SES group (29.9% vs. 43.2%; HR: 0.63 [95% CI: 0.39 to 1.03]; p = 0.067) (Fig. 1A). All-cause mortality (18.4%; 95% CI: 12% to 28%) (Fig. 1A) and the composite of death or MI (21.8%; 95% CI: 14% to 32%) (Fig. 1B) were similar in the tirofiban–SES versus the abciximab–BMS group (15.9%; 95% CI: 10% to 25%, p = 0.70 and 25.0%; 95% CI: 17% to 35%, p = 0.58, respectively), whereas the need for target vessel revascularization remained markedly reduced (10.3% vs. 26.1%; HR: 0.37 [95% CI: 0.17 to 0.79]; p = 0.007) in the tirofiban–SES group (Fig. 1C).

The cumulative incidence of definite, probable, or possible stent thrombosis was 6.9% versus 7.9% in the tirofiban–SES group and abciximab–BMS group, respectively (HR: 0.86 [95% CI: 0.29 to 2.6]; p = 0.78 (Fig. 1B). The cumulative incidence of definite and definite or probable stent thrombosis also did not differ between the 2 groups.

Among patients who were alive at 12 months, the cumulative incidence of death or nonfatal MI at 5 years was 11.2% in the tirofiban–SES group and 10% in the abciximab–BMS group (p = 0.80 at log-rank test). Finally, excluding patients who underwent target vessel revascularization between 30 days and 1 year after the index procedure, the cumulative incidence of death or nonfatal MI at 5 years was 21.5% in the tirofiban–SES and 24.7% in the abciximab–BMS group (p = 0.78 at log-rank test), whereas the incidence of death or nonfatal MI at 5 years in patients who survived the first year follow-up free from target vessel revascularization was 9.7% in the tirofiban–SES group and 9.2% in the abciximab–BMS group (p = 0.88; log-rank test).

Although it was open label and single center, our study is the first randomized controlled investigation of DES versus BMS implantation in the setting of STEMI patients undergoing mechanical intervention.

A maintained clinical benefit for 24 months in terms of reintervention in the previously instrumented artery with no excess of subacute or late stent thrombosis was previously reported (5,6). The current report extends these findings to 5-year follow-up.

Although results from randomized controlled trials are still pending (7), expert consensus recommends prolonging treatment with aspirin and thienopyridines for at least 1 year after DES placement. Importantly, our study was conceived and conducted well before unambiguous safety issues for DES use were raised. As a consequence, only relatively short duration of dual antiplatelet treatment (i.e., a minimum of 3 months) was protocol mandated. Accordingly, approximately one-half of the patients discontinued thienopyridines by 6 months after intervention and nearly all discontinued dual antiplatelet treatment at 1 year. Thus, long-term follow-up of this study is critical to shed light on the safety profile of SES implantation followed by a relatively short combined antiplatelet regimen in unselected patients undergoing intervention for STEMI, a currently off-label indication.

At 5-year follow-up, the cumulative incidence of death or nonfatal MI remained similar in the 2 study groups, and this held true at landmark analysis of patients alive at 12-month follow-up. Based on a broad clinical definition of stent thrombosis, namely, the Academic Research Consortium classification, we likewise failed to observe an excess of late events in those patients assigned to receive SES implantation, whereas the benefit in terms of reintervention persisted almost unchanged after 1,800 days without evidence of a late catch-up phenomenon. This is in keeping with the long-term results of the landmark randomized studies that led to DES approval, whereas it contrasts with recent data from observational studies on acute MI patients that questioned the long-term durability of DES benefit in this patient/lesion subset (3,8).
Importantly, it remains possible that our reassuring observations may have a type II error due to the small sample size. Therefore, while reassuring, our results cannot lend support to unrestricted use of SES in STEMI patients, because a probably small yet potentially sizable risk of late adverse events in patients treated with SES cannot be excluded.

We conclude that at 5-year follow-up, a strategy of SES implantation in patients undergoing treatment for STEMI remained superior in terms of re-intervention in the infarcted artery compared with traditional BMS with no safety concerns.

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REFERENCES