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Letters

TO THE EDITOR

Does Current Evidence Favor Drug-Eluting Stents Over Bare-Metal Stents for Saphenous Venous Graft Interventions?

Insights From an Updated Meta-Analysis of Randomized Controlled Trials

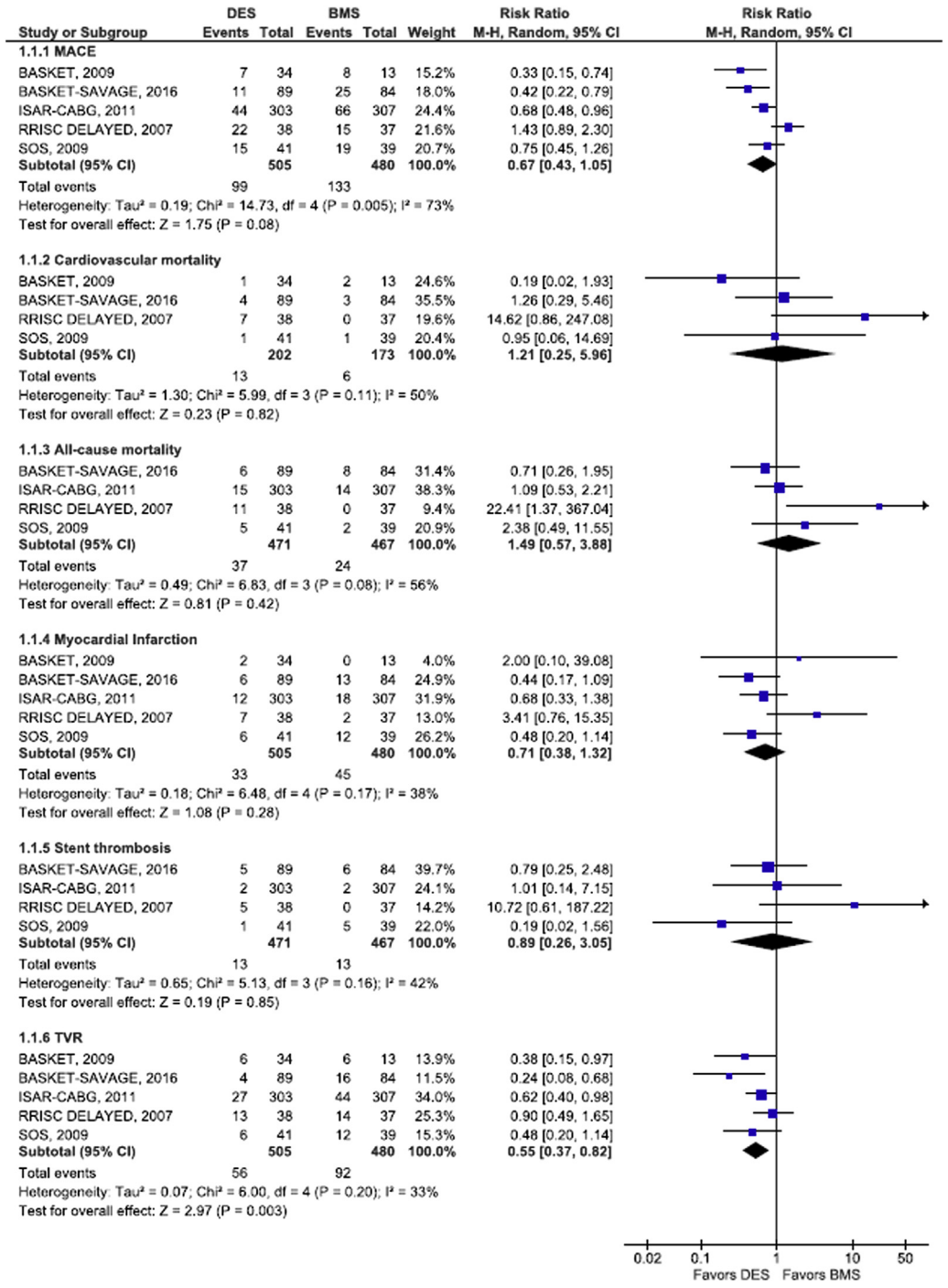
Percutaneous interventions of saphenous venous grafts (SVGs) are associated with higher early and late complications and worse outcomes compared with native coronary artery interventions (1). Late complications are driven by a high rate of restenosis at the target lesion or progressive disease in the target vessel. Drug-eluting stents (DES) have been shown to have enhanced safety and efficacy compared with bare-metal stents (BMS) in native coronary arteries (2). However, the superiority of DES over BMS in SVG interventions has not been clearly established. Prior meta-analysis involving observational studies and randomized controlled trials have yielded conflicting results (3-5). Earlier this month, the outcomes from BASKET-SAVAGE (Basel Stent Kosten Effektivitäts Trial—Saphenous Venous Graft Angioplasty Using Glycoprotein IIb/IIIa Receptor Inhibitors and Drug-Eluting Stents) were presented at the annual scientific sessions of the European Society of Cardiology (6). Hence, we performed an updated meta-analysis to systematically review the available data on the efficacy and safety of DES versus BMS in SVG interventions.

We performed a systematic search of PubMed, Scopus, the Cochrane Collaboration Central Register of Controlled Trials, and Embase, from inception to September 10, 2016. We used the following key words and Medical Subject Headings: "drug eluting stent," "DES," "bare metal stent," "BMS," "stent," "saphenous venous graft," "SVG," "saphenous graft," "randomized controlled trials," and "clinical trials." A manual search of reference lists of the original retrieved studies and conference abstracts was also performed. Studies were included if they 1) evaluated the efficacy and safety of DES versus BMS for SVG interventions; and 2) had follow-up duration of at least 1 year. Two physician reviewers (C.B. and S.C.) independently reviewed originally identified titles and abstracts. The quality of each study was assessed using the domains suggested by the Cochrane Collaboration. We evaluated the following outcomes: 1) major adverse cardiac events; 2) cardiovascular and all-cause mortality; 3) myocardial infarction; 4) target vessel revascularization (TVR); and 5) stent thrombosis, at the longest reported follow-up. The trial-specific definitions for each outcome were used. Analysis was performed on an intention-to-treat basis. Considering that the heterogeneity of the included trials might influence the treatment effects, we used a random-effects model to estimate aggregate relative risks and confidence intervals from the included studies.

Five randomized controlled trials (6-10) were included. Of 985 total randomized patients, 505 were randomized to DES and 480 to BMS. The mean follow-up duration for the overall analysis was 18 ± 8 months. All 5 trials compared BMS with first-generation DES (paclitaxel-eluting stents or sirolimus-eluting stents). All studies were of low bias risk. Compared with BMS, patients undergoing DES implantation had significantly lower TVR (relative risk: 0.55; 95% confidence interval: 0.37 to 0.82; $p = 0.003$) and showed a trend toward reduction in major adverse cardiac events (relative risk: 0.67; 95% confidence interval: 0.43 to 1.05; $p = 0.08$). There were no significant differences between the stents in cardiovascular mortality, all-cause mortality, myocardial infarction, or stent thrombosis (**Figure 1**). Moderate heterogeneity was found in all the analysis ($I^2 = 33\%$ to 73%).

This meta-analysis of 5 randomized trials demonstrated that first-generation DES were associated with a significant reduction of TVR in SVG lesions at a mean follow-up time of 1.5 years. A trend toward a reduction in major adverse cardiac events with DES was also present, driven by lower TVR and numerically fewer myocardial infarctions. No significant differences were present in stent thrombosis, myocardial infarction, or death. However, these trials were limited by small sample sizes and use of first-generation DES. Data on contemporary DES in SVG lesions are lacking. Newer DES have better efficacy and safety outcomes than first-generation DES and

FIGURE 1 Forest Plots of Efficacy and Safety Outcomes in Trials Comparing Bare-Metal Versus Drug-Eluting Stents in Saphenous Vein Graft Interventions



Squares represent the risk ratios of the individual studies; **horizontal lines** represent the 95% confidence intervals (CIs) of the risk ratio. The size of the **square** reflects the weight the corresponding study exerts in the meta-analysis. The **diamond** represents the pooled risk ratio or the overall effect. BASKET = Basel Stent Cost Effectiveness Trial; BASKET-SAVAGE = Basel Stent Kosten Effektivitäts Trial—Saphenous Venous Graft Angioplasty Using Glycoprotein IIb/IIIa Receptor Inhibitors and Drug-Eluting Stents; BMS = bare-metal stent; DELAYED RRISC = Death and Events at Long-Term Follow-Up Analysis: Extended Duration of the Reduction of Restenosis in Saphenous Vein Grafts With Cypher Stent; DES = drug-eluting stent; ISAR-CABG = Drug-Eluting-Stenting Associated With Improved Results in Coronary Artery Bypass Grafts?; MACE = major adverse cardiac event(s); M-H = Mantel-Haenszel; SOS = Stenting of Saphenous Vein Grafts; SVG = saphenous venous grafts.

BMS in native coronary arteries (2), and their use in SVG lesions could further reduce device-related events. The ongoing DIVA (Drug-Eluting Stents vs. Bare Metal Stents in Saphenous Vein Graft Angioplasty) trial (NCT01121224) is using contemporary DES and should provide further information in this regard.

Chirag Bavishi, MD, MPH
Saurav Chatterjee, MD
***Gregg W. Stone, MD**

*Columbia University Medical Center
New York Presbyterian Hospital
1700 Broadway, 8th Floor
New York, New York 10019
E-mail: gs2184@columbia.edu

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Effect of Pre-Procedural Beta-Blocker in Patients Undergoing Percutaneous Coronary Intervention

We read with interest the article by Motivala et al. (1) that described the predictors and trends regarding beta-blocker prescriptions for stable angina using the data from National Cardiovascular Data Registry (NCDR) CathPCI registry. The authors noted that beta-blocker use at the time of discharge (despite strong recommendation for its use in clinical practice guidelines) (2) was not associated with a reduction in mortality, revascularization, or readmission related to myocardial infarction, or stroke at the 30-day and 3-year follow-ups.

We would like to suggest that the use of pre-procedural beta-blockers might have confounded the interpretation of the findings. Our premise is based on the following findings.

First, despite unknown prognostic implications, a significant percentage of patients with stable coronary artery disease receive de novo administration of beta-blockers prior to revascularization procedures (30% for bypass surgery and 8.5% in elective percutaneous coronary intervention, according to our own series) (3). Classically, beta-blockers are known to exert their effects by decreasing the heart rate, systolic blood pressure, and myocardial contractility, which results in reduced myocardial oxygen consumption. Patients who are administered beta-blockers pre-procedurally may benefit from its use during their hospitalization, particularly immediately after the procedure. In fact, based on data from our own registry (the Japan Cardiovascular Database-Keio interhospital Cardiovascular Studies [JCD-KiCS], whose recorded variables is similar to that of the NCDR CathPCI), the incidence of the composite endpoint of new onset heart failure, cardiogenic shock, and death was lower in patients receiving de novo administration of beta-blockers than that in controls (in 1,556 propensity-matched patients from among 9,425 PCI patients, 1.2% vs. 2.8%; $p = 0.018$). Hence, the lack of consideration in pre-procedural use of beta-blockers could lead to a significant underestimation in the long-term effects of beta-blockers.

Second, there are concerns regarding the bias owing to patients for whom beta-blockers were withdrawn during or immediately after the procedure. The decision to withdraw beta-blockers could be related to a number of factors, and it is also associated