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THE LINK BETWEEN PREVIOUS PERCUTANEOUS CORONARY INTERVENTION AND CORONARY ARTERY BYPASS GRAFT RISK To the Editor:

We read with interest the publication by Massoudy and colleagues,¹ who observed a higher rate of in-hospital mortality and major adverse cardiac events in patients undergoing coronary artery bypass graft surgery with two or more previous percutaneous coronary interventions (PCIs). We wish to raise a few important issues that need to be considered when interpreting this study. First, multivariate analysis has limitations as a statistical tool in a context such as this, where a vastly disproportionate number of patients in each group could lead to inappropriate identification of meaningful predictors. Second, inasmuch as there is minimal clinical characterization of patients in this study, the reasons for initial multivessel PCI are likely to be important and may reflect patients undergoing PCI after being thought to be at too high a risk for initial coronary bypass surgery or being undertaken as urgent cases. Finally, another explanation for increased events in this cohort may be that these patients have declared themselves as a high-risk population, having had unsuccessful medical therapy and PCI,² and not as a direct consequence of prior stenting alone.

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Reply to the Editor:

We read with interest the remarks of Bhindi and Omerod regarding our article.¹ We agree that the design of the study inherits a number of limitations. For example, the amount of variables available in the databases was very limited. Therefore, clinical characterization of patients could not be detailed. A randomized study or prospective data acquisition would certainly reduce or abolish the limitations of the retrospective study. A prospective study is, indeed, planned, but its accomplishment raises a number of organizational and structural problems.

Questioning the reasons for initial multivessel percutaneous coronary intervention (PCI) is, indeed, very interesting. According to the American Heart Association guidelines, coronary artery bypass grafting (CABG) is the recommended therapy in 3-vessel coronary artery disease.² The increased event rate observed in the group with multiple prior PCIs thus supports published expert opinion and suggests that CABG should have

been performed earlier. We fully agree, however, that PCI is often performed in urgent cases such as acute myocardial infarction, which, indeed, represent high-risk, if not too high-risk, cases for acute CABG.

Finally, according to our multicenter data, having had unsuccessful prior single PCI and medical therapy does not render a patient high risk at subsequent CABG. Only when PCI is repeatedly applied or extended to other vessel territories does the risk at subsequent CABG increase.¹ Therefore, earlier referral of patients with unsuccessful PCI for CABG may prevent the transition of patients to a higher risk class and avoid disadvantageous results at subsequent CABG.

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A META-ANALYSIS OF CONTROLLED STUDIES OF PREOPERATIVE STATIN THERAPY FOR PREVENTION OF POSTOPERATIVE MORTALITY IN CARDIAC SURGERY

To the Editor:

We read with great interest an article by Tabata and associates,¹ because we² previously performed a meta-analysis of controlled studies of preoperative statin therapy for postoperative mortality in cardiac surgery. Tabata and

FIGURE 1. Postoperative mortality among patients undergoing cardiac surgery assigned to preoperative statin therapy versus control. SE, Standard error; IV, inverse variance; CI, confidence interval.

collaborators¹ showed that preoperative statin use was associated with lower mortality (adjusted odds ratio [OR], 0.25; 95% confidence interval [CI], 0.12–0.54; $P = .0004$) in 1389 patients without coronary artery disease who underwent cardiac surgery. Meanwhile, our previous pooled analysis of ORs from 3 randomized controlled trials and adjusted ORs from 6 observational controlled studies (representing 18,637 patients) demonstrated a statistically significant 24% reduction in postoperative mortality with preoperative statin therapy relative to control (pooled OR, 0.76; 95% CI, 0.64–0.90; $P < .01$). Because several controlled studies including the study by Tabata and colleagues¹ have been published to date since we² performed the meta-analysis, we herein updated our previous meta-analysis.

Our comprehensive search identified 4 randomized controlled trials that reported postoperative mortality and 9 observational controlled trials that stated adjusted ORs for postoperative death. We excluded observational controlled trials that reported merely crude mortality or a crude OR for death. Pooled analysis of the 13 studies (representing 24,039 patients) demonstrated a statistically significant 33% reduction in postoperative mor-

tality with preoperative statin therapy relative to control in the fixed-effects model (pooled OR, 0.67; 95% CI, 0.54–0.83; $P = .0002$) (Figure 1). There was minimal study heterogeneity ($P = .30$ by standard χ^2 tests) and accordingly little difference in the pooled result from random-effects modeling (pooled OR, 0.64; 95% CI, 0.49–0.82; $P = .0006$). Sensitivity analyses were performed to assess the contribution of each study to the pooled estimate by excluding individual studies one at a time and recalculating the pooled OR estimates for the remaining studies. In general, exclusion of any single study from the analysis did not substantively alter the overall result of our analysis. There was no evidence of significant publication bias ($P = .7143$ by an adjusted rank-correlation test). The results of our analysis suggest that preoperative statin therapy may reduce postoperative mortality by 33% over control in patients undergoing cardiac surgery, which strengthens the results of the study by Tabata and coworkers.¹

The present meta-analysis included 4 relatively small randomized controlled trials that were composed of low-risk patients because their primary end point was not mortality. Very few events (postoperative deaths) occur in

such trials, and thus the risk estimate has inadequate statistical power. Therefore, we performed a meta-analysis of not merely randomized controlled trials but also observational controlled studies. To minimize confounding effects, we carefully selected merely high-quality observational studies that reported the adjusted OR for postoperative death and included them in our meta-analysis. A large multicenter randomized controlled trial consisting of high-risk patients, however, is needed to confirm the results of the present updated meta-analysis.

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