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## Reply

We appreciate the comments from Drs. Bode and Simpson regarding our report on simvastatin's effect on skeletal muscle.

We agree that a crossover design would be a more optimal approach. However, we did find that the case patients and control individuals were appropriately and close to optimally matched when the present design was applied.

The inherent "clinical" differences between case and control individuals as Drs. Bode and Simpson suggested are possible but in our minds unlikely. In support for their contention, they cited a paper for finding alterations in coenzyme Q10 concentrations in patients with diabetes, but unfortunately the essential information of whether these patients were being treated with statins is lacking (1).

We do not claim to have proven that a decrease in coenzyme Q10 content is instrumental in the myalgia. Rather, we wrote that the impaired oxidative phosphorylation capacity was a plausible mechanistic explanation for the muscle pain.

A study conducted in mice showed that treatment with a lipophilic statin (atorvastatin) impaired mitochondrial activity (NADH oxidase activity) as well as ubiquinone content without an effect on mitochondrial density, compared with control mice (2). This was reversed with coenzyme Q10 supplementation (2). This study confirmed that the statin treatment itself had the negative effect on skeletal muscle (2), as we reported in our study (3). However, overall reports on the effects of coenzyme Q10 supplementation on myalgia are ambiguous (4,5), but none of these studies investigated coenzyme Q10 content in human skeletal muscle.

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# Issues Needing Clarification Regarding Population Characteristics in the Analysis From the National Cardiovascular Data Registry

We read with interest the paper by Baklanov et al. (1), but we think that some issues need to be clarified regarding the population characteristics of the Prevalence and Outcomes of Transradial Percutaneous Coronary Intervention for ST-Segment Elevation Myocardial Infarction: Analysis From the National Cardiovascular Data Registry (2007 to 2011).

First, there is no information about sheath sizes used in the study groups. One of the endpoints was bleeding, and overt access site bleeding and retroperitoneal hemorrhage within 72 h of percutaneous coronary intervention (PCI) were included in the definition of bleeding. Doyle et al. (2) reported that using sheath sizes >6-F was identified as a strong independent predictor of major femoral bleeding. Trimarchi et al. (3) reported that adopting a sheath size of 8-F or larger was independently related to independent predictors of retroperitoneal hematoma after PCI.

Second, the incidence of high-risk C-type coronary lesions was significantly greater in the femoral access group compared with the radial access group. Barbash et al. (4) concluded that a type-C coronary lesion was an angiographic predictor of PCI failure for ST-segment elevation myocardial infarction. In addition, Wilensky et al. (5) reported that PCI for complex lesions was associated with increased in-hospital mortality. When considering that PCI success and mortality were defined as primary endpoints of the study, results may be affected because of this difference between groups.

Finally, patients with renal failure receiving hemodialysis were significantly more common in the femoral access group. It is well-known that patients with renal failure have bleeding disorders due to uremic platelet dysfunction (6). Skin bleeding time is used for the evaluation of platelet dysfunction (7). Dialysis may partially correct these defects, but cannot totally eliminate them. The hemodialysis process itself may in fact contribute to bleeding. Baklanov et al. (1) did not clarify whether they evaluated bleeding disorders using skin bleeding time and excluded this type of patient from the study population. They used propensity score (PS) matching in the study. Even though the PS can balance observed baseline covariates between groups, they do nothing to balance unmeasured characteristics and confounders. PS analyses have the limitation that remaining unmeasured confounding may still be present. According to their paper, the PS did not include skin bleeding time or any different method to identify the presence of a bleeding disorder. Therefore, this situation may have affected the results of the study.

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## Reply

The letter by Dr. Yarlioglues and colleagues reflects the challenges associated with interpreting analyses of large data registries, such as the CathPCI Registry (1). From the very beginning of the information era in cardiology, the greatest challenges of data analysis were the frequency of changing treatments, confusing terminology, and nonstandard definitions. Recognizing these challenges, the American College of Cardiology in 1987 set out to standardize percutaneous coronary intervention (PCI)–related information (2). Data pertaining to >100,000 PCI procedures are uploaded to the CathPCI Registry every quarter, which underscores the importance of selective approach to this process.

None of the variables that interest Dr. Yarliogues and colleagues were included in the propensity scores because they are not collected nor validated in the National Cardiovascular Data Registry bleeding and mortality models. Because the information regarding sheath size and "skin bleeding time" is not included on CathPCI Registry data collection forms, we cannot comment on the association between these variables and patient outcomes. Importantly, renal failure, a marker for platelet dysfunction, was reported and adjusted for in our analysis.

Differences between clinical and procedural characteristics are quite common when comparison groups are formed retrospectively. Dr. Yarliogues and colleagues noted a 64% versus 66% difference between C-type lesions in the radial and femoral access groups. Clinically, this difference is not important. Similar differences are present in the proportion of patients with peripheral vascular disease, a family history of coronary artery disease, and other characteristics, all of which reach nominal statistical significance due to the size of the registry.

Our study accurately describes the prevalence of transradial PCI in ST-segment elevation myocardial infarction and its association with the outcomes. Moreover, the results of our study are consistent with those of the recently published randomized trials showing transradial primary PCI to be superior with respect to bleeding and clinical outcomes (3). Therefore, although we appreciate the thoughtful comments by Dr. Yarlioglues and colleagues we believe that the data in our paper are robust and supported by other studies.

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