RESPONSE TO COMMENT ON STEGMAN ET AL.

High-Intensity Statin Therapy Alters the Natural History of Diabetic Coronary Atherosclerosis: Insights From SATURN. Diabetes Care 2014;37:3114–3120

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We appreciate interest of Drs. Huang and Chen (1) in our article (2). We agree that the diabetic population is heterogeneous in terms of cardiovascular risk, with varying comorbidities and duration and severity of diabetes per se. However, we disagree with the notion of the Study of Coronary Atheroma by Intravascular Ultrasound: Effect of Rosuvastatin Versus Atorvastatin (SATURN) cohort representing a purely low-risk population, as study inclusion required the presence of symptomatic coronary artery disease. Furthermore, 30% of the SATURN population was enrolled following an acute coronary syndrome (ACS) and 23% had a history of previous myocardial infarction. With regard to the relative low frequency of insulin use, while insulin dependency has previously been associated with greater atheroma burden (3), we observed no difference in the degree of atheroma regression (as measured by change in percent atheroma volume [$P = 0.91$] or total atheroma volume [$P = 0.81$]) when comparing insulin-treated with non-insulin−treated diabetic patients.

With regard to patients suffering an ACS, we felt it difficult to draw comparisons with the Integrated Biomarkers and Imaging Study-4 (IBIS-4) given that this study contained a mere nine diabetic patients (4). However, we did perform further analysis of the SATURN population and found that diabetic patients enrolled following an ACS demonstrated significantly less percent atheroma volume regression when compared with nondiabetic ACS patients (-0.44 ± 0.23 vs. $-1.54 \pm 0.22\%$, $P < 0.001$). These findings are consistent with those from the Japan Assessment of Pitavastatin and Atorvastatin in Acute Coronary Syndrome (JAPAN-ACS) trial (5), suggesting a possible attenuation of the net plaque regressive effects of high-intensity statin therapy in diabetic patients suffering an ACS. It is important to note that this high-risk patient subset still demonstrated significant atheroma regression from baseline, underscoring the importance of intensive statin therapies in high-risk populations.

With regard to evaluating plaque composition, serial radiofrequency intravascular ultrasound was obtained only in a subset of the overall SATURN population (6). Thus, we are unable to comment on potential differential changes in plaque composition in patients with and without diabetes treated with high-intensity statins. Despite the known limitations of serial radiofrequency intravascular ultrasound imaging (7), the effects of high-intensity statins on coronary atheroma composition require further evaluation.

Last, we agree that glycemic control is an important component of managing patients with diabetes, especially for preventing microvascular events. However, prospective data demonstrating significant reductions in cardiovascular events following strict glycemic control are still lacking (8). While high-intensity statins are yet to be specifically tested in a randomized clinic trial of diabetic patients, current data strongly suggest significant reductions in cardiovascular event rates following intensive LDL cholesterol lowering with potent statins (9). Overall, the current data are in accordance with the recent American College of Cardiology and American Heart Association guidelines (10) that recommend high-intensity statin therapy for diabetic patients deemed to be at high risk or cardiovascular risk.

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