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**Statins and Antioxidant Vitamins: Should Co-Administration Be Avoided?**

Dimitris Tousoulis, Charalambos Antoniades, and Christodoulos Stefanadis  
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size measurement is well-established (4) on the basis of multiple lines of scientific evidence. We agree that myocardium at risk is highly variable and a major determinant of infarct size in both animal models and humans. The absence of measurement of myocardium at risk will reduce power (i.e., increase the likelihood of a type II [beta] statistical error). However, the estimates reported in our paper of a type I (alpha) statistical error for infarct size remain valid. In the AMISTAD I study (5), myocardium at risk was measured in a subset of patients. In anterior infarcts, adenosine showed similar benefit using either myocardial salvage index ( $p = 0.015$ ) or infarct size ( $p = 0.014$ ). Other randomized trials that have measured myocardium at risk and infarct size (6,7) have reported similar significant differences using either infarct size or salvage index as an end point.

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## Statins and Antioxidant Vitamins: Should Co-Administration Be Avoided?

In the interesting study by Arad et al. (1), co-administration of atorvastatin (20 mg/day) and high-dose antioxidant vitamins C (1 g/day) and E (1,000 IU/day) failed to decrease the progression of coronary calcification, whereas a borderline decrease of cardiovas-

cular events was observed. Based on the fact that previous studies have shown that statins do decrease both the progression of coronary artery calcification and cardiovascular events (2), the investigators proposed that the atorvastatin dosage they used was low, and they suggested that their population was not large enough to detect any differences. However, another possibility might be considered: The results of the present study may reflect a negative effect of antioxidant vitamins (especially vitamins C and E), which could interfere with lipoprotein metabolism, preventing the statin-induced increase of high-density lipoprotein (HDL)-2 subfraction, as has been proposed in the past (3). Indeed, in a study by Brown et al. (4), it was shown that co-administration of statin and antioxidant vitamins C and E partly prevents the beneficial effects of statins on cardiovascular outcome. Additionally, we (5) have recently demonstrated that, although low-dose atorvastatin treatment (10 mg/day) improves endothelial function in patients with ischemic heart disease, this effect is abolished when vitamin E (400 IU/day) is co-administered. Therefore, further studies examining the effect of atorvastatin 10 to 20 mg/day alone on the progression of coronary artery calcification and clinical events rate are required before any conclusion is made.

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## REPLY

As Dr. Tousoulis and colleagues point out, the design of the St. Francis Heart Study Randomized Clinical Trial (two cells of a  $2 \times 2$  factorial) does not permit a definitive conclusion as to whether statins alone retard the progression of coronary calcification. However, there are other reasons to believe that statins do not reduce the rate of coronary calcification, or, if they do, that said

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