a relatively high cumulative event rate at follow-up in multidetector computed tomography coronary angiographic (MDCT-CA) obstructive coronary artery disease compared with other studies, which may be due to characteristics of patients who had chest pain and positive stress tests in 43% and 29% of cases, respectively. However, the CONFIRM registry demonstrated that MDCT-CA has the best prognostic value in this patient subset, whereas its value in asymptomatic patients is quite limited (2). We agree that including patients with acute coronary syndromes (ACS) may lead to an overestimation of MDCT-CA prognostic capability. Accordingly, we excluded patients in whom ACS was confirmed by cardiac enzyme or electrocardiographic changes. The discrepancy between hypercholesterolemia rate and statin use in our patients is in agreement with the suboptimal therapy adherence reported in a substantial proportion of European patients (3). Medical therapy reported in our patients was administered before MDCT-CA. Indeed, 26% of them were taking aspirin, not for CAD but for other indications. We agree that the European Heart Score would have been more appropriate than Framingham cardiovascular risk estimation. However, the former has been challenged because it is not mathematically consistent and unfit to estimate cardiovascular mortality (4). In the first version of our paper, revascularizations were defined "early" if performed within 2 months after MDCT-CA. However, a reviewer criticized this definition. Indeed, using a 2-month cutoff, only 6 patients were excluded despite 295 patients having MDCT-CA stenosis ≥70%. This indicates that many revascularizations occurring later than 60 days were probably driven by MDCT-CA. We agree that the 6-month cutoff may have led to an underestimation of obstructive CAD prognostic value. However, this limitation did not affect hard cardiac events survival analysis. Finally, we believe that assigning 1 coronary plaque per coronary segment and classifying a plaque as calcific in cases in which a coronary segment contained calcific and noncalcific plaques was correct, as previously reported (5). Indeed, in the presence of small plaques, those calcific plaques are the easiest to detect with MDCT-CA, and most prognostic data are based on simple coronary plaque scores, regardless of plaque composition (3).

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Ultrasonographic Measure of Carotid Plaque Burden

In their excellent paper, Sillesen et al. (1) omitted mention of the original work on measurement of carotid plaque burden. Spence et al. (2) first measured carotid total plaque area (TPA) in 1990, and developed it for patient management and genetic research, and 3-dimensional methods for evaluation of new therapies. They showed that TPA and progression of TPA strongly predicted the 5-year risk of stroke, death, or myocardial infarction after adjusting for coronary risk factors.

Sillesen et al. (1) stated that the prevalence of plaque they observed (78%) was 2-fold higher than previously reported. However, in the NOMAS (Northern Manhattan Study) study, a population-based study of individuals free of stroke at similar ages, plaque prevalence was 58% on 2-dimensional ultrasound imaging and it was greater by age and among certain race-ethnic groups (3). Prevalence of plaque depends on age and how it is defined. If defined as a focal thickening >1 mm, in vascular patients it increases from 75% of patients at age 35 to 45 years to 99% by age 65 to 75 years, and 100% over age 75 years (2).

Besides plaque burden, other ultrasonographic characteristics of plaque morphology such as plaque surface irregularity, ulceration, texture, and plaque density may be even more important predictors of stroke and cardiovascular disease.

The Tromsø study showed that TPA was a stronger predictor of myocardial infarction and stroke (4) than intima-media thickness, and this was confirmed in a meta-analysis (5). Three-dimensional plaque volume is highly correlated with TPA, and is much more sensitive to change with therapy than intima-media thickness or TPA, so it is the best way to assess effects of new therapies (2). There is little doubt that carotid plaque burden will be a stronger predictor of cardiovascular events in the High Risk Plaque Bioimaging Study than any of the other imaging modalities measured, with the possible exception of coronary calcium.

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Please note: Dr. Spence holds an interest in Vascularis.com.

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REPLY

We appreciate the comments provided by Drs. Rundek and Spence and recognize their important contribution to this area, documented by the cited references. We would, however, like to stress that our data (1) were obtained in an asymptomatic population without known cardiovascular disease, not only stroke-free as in the Northern Manhattan Study (2), and neither "vascular patients" with premature atherosclerosis or cerebrovascular disease as those studied by Dr. Spence (3). As previously reported (4), we agree that ultrasonographic characteristics other than plaque size or plaque burden may provide additional prognostic information, such as plaque echolucency, heterogeneity, and surface irregularity and ulceration. We also agree that the Tromsø study is important and did refer to it.

The High Risk Plaque BioImage study is the first large population-based study with a cross-sectional evaluation of subclinical arterial disease in 4 different arteries at the same baseline examination (5), including quantitative assessment of carotid plaque burden as described in our paper. We look forward to presenting clinical outcomes and their predictability by baseline findings in the near future.

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