
We thank Dr Rundek and her coauthors for their contribution on this very important issue. As plaque formation represents a later stage of atherosclerosis than diffuse intima-media thickening, it is likely that plaque formation is more predictive for vascular events than intima-media thickness (IMT), although formal comparisons between the 2 measurements in terms of risk relations are limited. For example, van der Meer et al indicated that plaques show a somewhat higher risk estimate than IMT, but the differences are small. In addition, one should bear in mind that in several studies, IMT is used as a marker of generalized risk and not necessarily of local atherosclerosis, and with that reasoning inclusion of thicker segments or plaques in the carotid IMT measurement is not a relevant issue. Ultrasound assessment of carotid plaque bears a number of problems, some of which are listed here.

From a pathological point of view, an atherosclerotic plaque (a Stary type III-V lesion) is defined as focal thickening of the arterial wall with protrusion into the lumen and the presence of lipid-laden macrophages, extracellular lipid accumulation, and a fibrous cap. The latter criterion is not reliably identifiable with ultrasound, despite some efforts that have been made. In studies based on high-resolution B-mode ultrasound, the definition of plaque relies on the first criterion of this definition. Unfortunately, no uniform definition of plaque assessment with the use of ultrasound has prevailed so far; the definition of a recent consensus paper has not yet widely been implemented in current studies and also uses an arbitrary definition of plaque. Naturally, the prevalence of plaque is highly dependent on the definition used. Even when uniform criteria are used, the application of the criterion of a focal lesion remains subjective to a certain degree. This is reflected in a lower reproducibility of the plaque measurements as compared with the carotid IMT measurement.

Furthermore, studies that assess carotid plaques are highly inhomogeneous in terms of the classification of subjects. Continuous parameters that reflect the plaque burden are statistically most powerful, followed by ordinal plaque scores. Plaque scores that count the number of carotid segments affected are most frequently used. However, these scores imply that the predictivity of plaques is independent of their localization, which is unlikely.

And although we do acknowledge that plaques are an important manifestation of atherosclerosis, IMT measurements are particularly relevant in areas of research where plaques have not yet developed (ie, among younger age groups).

These and further issues are highly relevant in the review of the literature on carotid plaque and clinical vascular end points, which may justify greater expenditure than just an aspect secondary to IMT. A recent review considered most of these points, but some of the resulting questions can only be answered on the basis of an individual data meta-analysis. We strongly advocate such an analysis in cooperation with all relevant study groups.

Disclosures

None.

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Response to Letter Regarding Article, "Prediction of Clinical Cardiovascular Events With Carotid Intima-Media Thickness: A Systematic Review and Meta-Analysis"
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