Letters to the Editor

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Fibrous Cap Thickness and Rupture in Carotid Atheromata: Still Hunting in the Dark?

To the Editor:

Redgrave et al1 are to be congratulated for their superb and cumbersome work. We had been waiting for a large well-designed histopathologic study focusing exclusively on the critical cap thickness of carotid atheromata, and we are grateful for this important contribution. Hitherto, data extrapolation from coronary pathology to the carotids had left to vascular neurologists the bitter taste of hunting in the dark. We had published 3 years ago the first in vivo study of cap thickness measurement in carotid atheromata2 and had proposed a threshold of 650 μm for the mean cap thickness for the differentiation between symptomatic and asymptomatic plaques. The currently proposed threshold of 500 μm for representative cap thickness, in my view, lies in full accordance with our results, if one considers the fundamental methodological differences between the 2 studies.1,2

First, the concept of “representative” cap thickness, defined as “the part with a thickness considered to be most representative of the cap as a whole” looks to me at least as (if not more) “operator-dependent” as ultrasound. Was this part at the point of maximal stenosis or not, over the midportion of the plaque or over its shoulders? The authors provide modest inter- and intrarater agreement treating cap thickness as a categorical variable (Cohen κ for detection <500 μm and <200 μm). Ideally, cap thickness should have been treated as a continuous variable with Bland-Altman graphs (intraclass correlation coefficient). Because the representative cap thickness is the only variable potentially applicable in imaging studies (given the currently relatively low resolution of MRI and ultrasound), it would seem crucial to validate optimally the method of its measurement. Second, the proposed thresholds in our study were meant to differentiate symptomatic from asymptomatic plaques while the current study pertained exclusively to ruptured from unruptured symptomatic plaques. This constitutes a major difference. It would seem logical to assume that if the 650 μm limit is critical for interclass (symptomatic versus asymptomatic) discrimination, the limit for intraclass (symptomatic ruptured versus symptomatic unruptured) discrimination would lie even lower; hence, the 500 μm threshold would perfectly fit! It would be more than interesting if the authors could compare their results in symptomatic patients with a group of asymptomatic ones.

But beyond cap thresholds, the great surprise (and challenge) of this beautiful study is the finding that 40% of symptomatic carotid atheromata had no rupture at all! That is, in 40% of patients with symptomatic moderate-to-high grade carotid stenosis, plaque rupture is not the presumed etiology of stroke. To put it differently, by definition high-risk or vulnerable plaques have a high risk or vulnerability to rupture (and cause symptoms). Have I the right (or the perversity) to think that in 40% of decant symptomatic plaques our (a priori) definition is flawed? I would not be eager to attribute this great paradox, at least not the major part of it, to limitations such as selection bias (inclusion of patients with carotid disease having other or coexisting causes of stroke or hemodynamic stroke), technical flaws missing ruptures or healed ruptures due to time delay from the index event. A detailed review of the medical records of this dynamic minority of patients could reveal whether in fact a large number of stenoses were misclassified as to their clinical status or degree of severity. In my view, this is crucial given the modest discriminatory capacity of the representative but even of the minimum cap thickness (both had sensitivity and specificity <80%). If a major methodological flaw does not bias the results, it would seem that there is more than cap rupture in the clinical phenomenology of a carotid atheroma. I know the questions but I certainly do not know the answers: should we start looking not at the cap itself but at the cap-blood interaction? Do unruptured thrombogenic caps exist and if yes how can we detect them? The study by Redgrave et al certainly shed a glimmer of light showing that the labyrinth has still many dark turns. People who go hunting for minotaurs in the dark should always expect the unexpected.

Disclosures

None.

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