Editorial

Atherosclerotic Plaque Composition Is Still an Almost Unrecognized Factor of Risk Stratification in Patients with Carotid Artery Disease

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Stroke represents the third leading cause of death and the leading cause of disability in developed countries. Atherosclerosis of the carotid arteries is common in the adult and elderly population, and is a major risk factor of cerebral ischemia. Therefore, carotid artery revascularization seems to be an important therapeutic method with a potentially large impact on the incidence of cerebrovascular events and related mortality.

Several randomized and nonrandomized studies dealing with the optimal therapeutic approach to severe atherosclerotic disease of carotid arteries were published in the last two decades. We have learned that safely performed carotid endarterectomy can improve the long-term outcome, and carotid artery stenting can be comparable to endarterectomy in selected patients.^{1–3} However, all these largely discussed and often justifiably criticized studies have been based on the angiographic, ultrasound, and/or computed tomographic measurement of the severity of atherosclerotic disease resulting in a simple assessment of diameter stenosis. Thus, atherosclerotic plaque composition, which might be the main factor of lesion-related vulnerability, has not been recognized. Since “the Devil is in the details,” I believe that future studies should avoid the persistent simplification in carotid diagnostics and focus their attention much more on plaque composition.

Of course, carotid plaque composition has been investigated as a means of therapeutic stratification in a few studies.^{4–7} It has been presumed that plaques that are more vulnerable have a large lipid and necrotic core size, which may subsequently lead to distal embolization. Therefore, we began speculating that better determination of plaque morphology and composition could predict the future embolic potential and help in selecting the best therapeutic approach. Several invasive and noninvasive methods have been used to determine plaque composition, but still, there is an ongoing debate as to which produces the most relevant results.

One of the invasive imaging methods that were associated with promising expectations was virtual histology–intravascular ultrasound (VH–IVUS). This examination uses

spectral analysis of radiofrequency ultrasound backscatter signals from the IVUS images to define the four components of atherosclerotic plaque—fibrous, fibrofatty, calcified, and necrotic core. Unfortunately, carotid plaque composition determined by VH–IVUS only weakly correlated with the degree of cerebral embolization during or immediately after carotid artery stenting.⁶ In addition, it has been suggested that a necrotic core, as defined by VH–IVUS, was not definitely associated with subclinical cerebral embolization after carotid artery stenting under embolic protection.⁶

Another invasive diagnostic technique is the near-infrared spectroscopy (NIRS), which has been developed for the identification of a lipid core within an atherosclerotic lesion. This is achieved by determination of the lesion's chemical composition based on the different absorbencies of the near-infrared spectra.⁸ The catheters incorporate both NIRS and IVUS, which provide us with structural and compositional information in a single examination. This suggests a great potential of this modality for identification of high-risk, lipid-rich carotid plaques. However, only the first pieces of information have been presented regarding the potential significance of NIRS–IVUS in carotid disease.^{9,10}

Recently, several studies have demonstrated that magnetic resonance imaging (MRI) techniques can characterize specific components of carotid plaque compared with histopathological specimens.^{4,5} A systematic review and meta-analysis of studies dealing with carotid plaque MRI suggested that intraplaque hemorrhage, a lipid-rich necrotic core, and thinning/rupture of the fibrous cap might be associated with the hazard ratio of an ipsilateral cerebrovascular event ranging between three and six.⁵ Despite several limitations of thus far performed studies with MRI, there seems to be sufficient evidence that characterization of the specific plaque elements can provide additional measures of future stroke risk not provided by a simple assessment of luminal stenosis.

Computed tomography angiography (CTA) is widely used for the examination of patients with peripheral

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atherosclerotic disease and quantification of luminal diameter stenosis. Unfortunately, concordance between CTA and histology in the detection of lipid issues in carotid plaque is low.⁷ Thus, with the exception of the quantification of the amount of calcium, the use of CTA for the assessment of plaque composition is extremely limited. Similarly, the duplex ultrasound description of plaque echogenicity has been studied. Findings vary from echolucent (dark) plaques to hyperechogenic, calcified (bright) plaques. It has been demonstrated that echolucent plaques are associated with a higher risk of future cerebrovascular accidents. Unfortunately, the evidence describing the association between plaque compositions assessed by the duplex ultrasound is not strong enough to affect decision-making processes in clinical practice.

Recent data from imaging methods suggest that this field progresses rapidly, and multimodal imaging might represent the next step in the investigation of carotid atherosclerosis. Yet, most studies in the field have been statistically underpowered and currently available data have limited clinical consequences. Therefore, we can expect that many teams of investigators will focus on this topic in the near future, which, subsequently, could influence our therapeutic strategies.

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