ASYMPTOMATIC CAROTID STENOSIS: ARE THE CURRENT TOOLS SUFFICIENT TO IDENTIFY THE VULNERABLE PLAQUE? NO

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Introduction: In the recent years the "instable or vulnerable carotid plaque" has received attention as a diagnostic clue to identify high risk patients.
The benefit of carotid endarterectomy in high-grade stenosis has been proven with recent trials; however, the benefits of endarterectomy in patients with intermediate grade stenosis is still questionable. The identification of instable plaques could have a role in the selection of therapy for patients with non-significant carotid stenosis. Plaque instability means the susceptibility of a plaque to rupture, resulting in clinical symptoms.
Observations: The extensive research of the recent years focused on histological abnormalities, biomarkers and imaging findings. Most primary studies were of cross-sectional comparing potential features of instable plaque (e.g. imaging before CEA and histology from postsurgical specimens). These studies examined the expression of molecules or cells within the plaque tissue. As for the carotid samples (carotid endarterectomy species):macrophage infiltration was the most commonly evaluated feature of vulnerability while other studies investigated matrix metalloproteinase and endothelial growth factor etc.. Only relatively small number of longitudinal studies evaluated the natural history of plaques for example, plaque characterization by imaging methods and subsequent risk for cerebrovascular events).
The most longitudinal studies have used magnetic resonance imaging for the characterization of carotid lesions. The presence of vulnerability features at baseline was associated with occurrence
of cerebrovascular events or with development of new lesions with vulnerability features. In studies that used carotid artery ultrasonography, plaque echolucency (lipid core) seems to be a sensitive marker.
2.1. Biomarkers: numerous substances were investigated:C-reactive protein, matrix metalloproteinases, and pregnancy-associated plasma protein A, apolipoprotein (apo) B–apo A-I ratio, insulin-like growth factors etc.. These markers were compared with clinical outcomes, histopathology features, and imaging findings. The majority of studies evaluating the association between biomarkers and vulnerability features of plaques or clinical outcomes were also cross-sectional in design and provided weak information on the predictive value of biomarkers for future events.
2.2.Imaging
Studies that focused on imaging of carotid artery plaque were dominantly also cross-sectional. More than ten imaging methods were used, but carotid ultrasonography CT and magnetic resonance imaging were the most commonly used.
Utrasonography: plaque echolucency on ultrasonography, presence of intraplaque hemorrhage, and ulceration complexity of the lesion were the most commonly examined features. The ultrasound provides information about plaque components as lipid core, intraplaque hemorrhage, inflammation, and vasa vasorum neovascularization . The necrotic core and macrophage infiltration (a heterogenous plaque), which is echolucent, can be detected by ultrasound with good sensitivity and specificity; Neither MRI nor multi-slice CT will replace ultrasound as a screening tool.
Multislice CT: can demonstrate significant differences in densities for calcifications, fibrous tissue, and the lipid core, however, with substantial overlap. It accurately detect calcified plaques, the soft tissue contrast is low. The exposure to ionization radiation limits its use.MRI: accurately detects intraplaque hemorrhage, the lipid core (sensitivity and calcifications and accurate detection of the fibrous cap. The long scan times result in a high number of motion artifacts. Each of the 3 noninvasive imaging techniques has its advantages and disadvantages. The use of ultrasound has a high spatial and temporal resolution, safe and cheap. Plaque characterization using CT is currently limited by a poor soft tissue contrast and moderate spatial resolution. MRI shows the best discrimination in soft plaque components, but this technique has a relatively low spatial resolution and is contraindicated in patients with severe claustrophobia and implanted electronic devices. The importance of imaging studies is limited by the diverse nature of above mentioned imaging methods.

Discussion: Not not all rupturing plaques result in a cerebrovascular vascular event. Some plaques would rupture and then become „silent" without causing a stroke and vice versa not all acute vascular events are the result of plaque rupture (emboli from the heart, hemodynamic stroke etc.) All these observation limit the importance the vulnerable plaque as a predictor of a future event. Questionable if features of plaque vulnerability are interchangeable among vascular beds. A major problem with the instable plaque theory is that majority of important observation has been carried out in patients who have already had an event. In addition, most studies were cross-sectional (including histopathologic, biomarker, imaging studies and studies) with relatively small sample sizes. Large, prospective studies including patients without previous cerebrovascular events and follow-up are required for validation. In the present literature practically none of the prospective imaging studies that followed patients for clinical outcomes documented that the vulnerable plaque was the one responsible for the clinical event during follow-up. The plaque progression (stable or instable plaque) is influenced not only systemic effects but also local circumstances (geometry of carotid bifurcation, shear stress etc.) that are very different from individual to individual.

Once it is prospectively validated that certain plaque features are independently predictive of a future cardiovascular event, demonstrating the incremental utility of such a concept will be required. In applying the concept in persons who are not considered high risk by current criteria (typical of a primary prevention The presence of an instable plaque does not determine the occurrence of an event at present but rather a higher risk for such occurrence in the future relative to a stable or less instable plaque. The validated plaque vulnerability characteristics should be able to provide better predictive value on top of currently available methods of risk stratification, If the features of a vulnerable plaque are established, we have have to also demonstrate that pharmacological treatments in patients who would otherwise not have been candidates for a preventive intervention will improve outcomes. The cost-effectiveness of such intervention should be also proven.Would diagnosis of instable plaques modify the therapeutic intervention for recurrent events?
Should local vascular reconstruction intervention applied or should conservative secondary prevention intervention followed after detection of instable plaques? Such questions will need to be answered before the instable plaque becomes a cornerstone routinely used in the prevention and treatment of carotid disease. The current technologies for carotid imaging like ultrasound, MRI and MSCT need to be carried out in a large cohort of asymptomatic individuals with noncritical stenosis with the goal of identifying high-risk plaques with systematic follow-up