Review article

The role of imaging for identifying unstable carotid plaque

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Abstract
Stroke is one of the major causes of morbidity and mortality worldwide and approximately 15 million strokes occur every year. The risk of stroke depends not only on the grade of carotid artery stenosis but also on plaque characteristics that make them unstable. The features of unstable plaques include thin fibrous cap, large lipid core, inflammation, neovascularization and intraplaque hemorrhage. The present review summarizes existing data on the role of imaging in the identification of vulnerable carotid plaque.

Keywords: stroke, stenosis, unstable carotid plaques, imaging techniques

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Introduction
Stroke is the third leading cause of death worldwide and is a major cause of long-term disability (Campbell and Khatri, 2020; GBD 2019 Diseases and Injuries Collaborators, 2020). Approximately 30% of all ischemic strokes are due to thromboembolism from carotid arteries due to atherosclerosis (Campbell and Khatri, 2020). Even though the grade of carotid artery stenosis is strongly related to stroke risk, unstable plaque is also an independent risk factor for ischemic stroke (Campbell and Khatri, 2020; Thammongkolchai et al., 2017). Features of unstable carotid plaque include intra-plaque hemorrhage, neovascularization, large lipid core, inflammation and thin cap (Salem et al., 2013, 2014). Imaging is the most frequently used modality for identifying unstable carotid plaque. In the present review, we summarize the role of imaging in the detection of vulnerable carotid plaque.

Ultrasonography
Ultrasonography is a noninvasive, low-cost and safe imaging modality that provides real-time information about blood flow and vessel wall movement (Cires-Drouet et al., 2017). Using B-mode imaging, carotid plaques are categorized into 4 types: hypoechoic (type I), hypoechoic with small hyperechoic areas (type II), hyperechoic with small hypoechoic areas (type III) and hyperechoic (type IV)(Cires-Drouet et al., 2017). According to Gray-Weale, patients with type I and type II plaques are at higher risk for stroke (Cires-Drouet et al., 2017). Three-dimensional ultrasonography can evaluate the surface of the plaque with more accuracy compared with two-dimensional ultrasonography (Cires-Drouet et al., 2017). Contrast-enhanced ultrasound (CEUS) is based on B-mode imaging with the simultaneous intravenous administration of a contrast agent (Cires-Drouet et al., 2017). This contrast agent, consisting of gas microbubbles, is not toxic to the kidneys and seldom causes allergies (Cires-Drouet et al., 2017; Partovi et al., 2012). On the other hand, it can cause headache, paresthesias, burning and pain at the site of injection (Cires-Drouet et al., 2017). Finally, elastography or strain imaging can identify the deformity that carotid plaques sustain in response to shear stress (Cires-Drouet et al., 2017).
Several studies evaluated the role of CEUS in detecting unstable carotid plaques. Luo et al evaluated carotid plaques of 62 symptomatic and 54 asymptomatic patients with CEUS (Luo et al., 2019). Patients with acute cerebral infraction showed a larger area of neovascularization (Luo et al., 2019). Schmidt et al also reported that neovessels identified by CEUS was more prominent in cartotid plaques of symptomatic patients (Schmidt et al., 2017). Neovessels are fragile, more prone to rupture and have a larger concentration of inflammatory cells, including T-lymphocytes and macrophages (Schmidt et al., 2017). Motoyama et al suggested that the concomitant use of CEUS and magnetic resonance imaging (MRI) can identify unstable plaques with better reliability (Motoyama et al., 2019). The former is
more sensitive in detecting neovascularization whereas MRI is more accurate in identifying intraplaque hemorrhage (Motoyama et al., 2019). Recently, Zamani et al applied superb microvascular imaging for detecting vulnerable carotid plaque in 31 patients who underwent endarterectomy (Zamani et al., 2019). SMI is an ultrasound imaging technique able to detect neovessels and intraplaque microvascular flow (IMVF) signals without using intravenous contrast agent (Zamani et al., 2019). Patients also underwent CEUS, B-mode ultrasound and histological examination of the plaques (Zamani et al., 2019). Plaques with higher degrees of inflammation, lipids and granulation tissue at histological analysis had low echogenicity on B-mode ultrasound, higher IMVF on SMI and higher absorption on CEUS (Zamani et al., 2019).

Various forms of elastography also appear to be useful in the detection of unstable carotid plaque. Hansen et al used compound ultrasound strain imaging (CUSI) to measure carotid plaque strains in 34 patients with carotid stenosis > 70% and observed that plaque regions with higher strain showed morphological characteristics of instability (Hansen et al., 2016). Khan et al also demonstrated that patients with high strain scores had higher risk for plaque rupture (Khan et al., 2017). Ramnarine et al suggested that shear wave elastography (SWE), an ultrasound-based imaging technique that can distinguish normal from abnormal tissue by measuring tissue elasticity is a promising modality for differentiating stable from unstable plaques (Ramnarine et al., 2014). Finally, Roy Cardinal et al, using MRI as reference examination, demonstrated that ultrasound-based, noninvasive vascular elastography (NIVE) can differentiate vulnerable from stable plaques (Roy Cardinal et al., 2017).

**Magnetic Resonance Imaging**

Magnetic resonance imaging (MRI) is frequently used for evaluating the severity of carotid stenosis and has also been implemented for detecting plaque instability. Lee et al performed MRI in 15 patients and reported that 66.7% of patients with intraplaque hemorrhage (IPH) developed a cerebrovascular event during follow-up even though they had only mild stenosis (Lee et al., 2017). Millon et al showed that fibrous cap rupture (FCR), gadolinium enhancement (GE) and intraplaque hemorrhage (IPH) are more frequent in symptomatic patients than in asymptomatic patients in MRI (Millon et al., 2013). Moreover, high-resolution MRI (HR-MRI) was able to distinguish with greater accuracy the features of unstable plaques, particularly thin fibrous cap and lipid-rich cores; notably, even though these characteristics are more prevalent in patients with more severe carotid artery stenosis, they are also present in some patients with mild stenosis (Sun et al., 2020; Trivedi et al., 2004). Finally, dynamic contrast-enhanced (DCE)-MRI can identify microvasculature, which is another key characteristic of vulnerable plaques (van Hoof et al., 2016).
Computed Tomography
Computed tomography (CT) has also been evaluated as a tool for detecting unstable carotid plaque. Wintermark et al performed CT angiography (CTA) in combination with histological evaluation of carotid plaques in patients who underwent endarterectomy and reported that CTA can identify calcification, ulceration, fibrous cap thickness, lipid cores and intraplaque hemorrhages with a good correlation with histological examination (Wintermark et al., 2008). Zhou et al compared CT with MRI in a large study (n = 264) and showed that CT could better recognize calcification compared with MRI but that MRI was superior in recognizing stenosis and plaque hemorrhage; the 2 imaging modalities has similar accuracy in identifying unstable fibrous cap (Zhou et al., 2019).

Gupta et al also reported that the combination of CTA and MRA might be more sensitive in detecting carotid plaques at high risk for causing stroke than either method alone (Gupta et al., 2015).

Conclusions
Ultrasonography, MRI and CT appear to be useful tools for identifying unstable carotid plaques. However, few studies compared the 3 methods in a sizable population and therefore it is unclear which is the most accurate in detecting vulnerable plaques. Accordingly, the choice of imaging in patients with carotid stenosis should be determined based on local availability and expertise.

Disclosure statement
There are no conflicts of interest to declare.

References


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