Eur J Vasc Endovasc Surg (2015) 50, 563–572

REVIEW

Non-invasive Carotid Artery Imaging to Identify the Vulnerable Plaque: Current Status and Future Goals

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WHAT THIS PAPER ADDS

Characteristics of the carotid plaque in patients with carotid stensosis can identify those patients with relatively higher risk for stroke and help select patients who may benefit from intervention over medical treatment alone or vice versa. This review discusses the current role of two-dimensional and three-dimensional ultrasound, computed tomography, magnetic resonance imaging, and positron emission tomography in defining carotid plaque characteristics and in informing clinical practice. Most of these non-invasive imaging techniques have been discussed as single entity techniques. This paper puts the relative strengths and weaknesses of the different technical options in perspective in relation to clinical applicability.

Background: The current clinical practise to determine if a patient should undergo carotid intervention to prevent stroke is to determine the clinical features combined with degree of carotid stenosis. However, this does not accurately determine the individual patient's risk for future stroke. A thin fibrous cap, a large lipid core, high macrophage count, and intraplaque haemorrhage have all been identified as markers of the so-called "vulnerable" plaque being related to a higher stroke risk. There is a need to assess the accuracy of in vivo imaging to identify vulnerable plaque characteristics, thereby enabling in vivo risk stratification to guide clinical decision-making.

Methods: The aim of this topical review is to assess the roles of currently available imaging modalities that are applied in clinical practice and those experimental techniques that are close to clinical translation in defining carotid plaque characteristics and in informing clinical practice.

Results: Ultrasound is a low cost and ready available low-risk tool, but it lacks the accuracy to reliably detect individual plaque components and characteristics. Computed tomography is considered to be the best imaging technique to identify calcification in the carotid plaque. Magnetic resonance imaging (MRI) can identify most described plaque characteristics with moderate to good agreement. Positron emission tomography allows assessment of specific metabolic functions with tracers labelled with positron emitting radio-isotopes, but limited spatial resolution makes anatomic precision imprecise.

Conclusion: MRI has demonstrated the most potential, with good sensitivity and specificity for most plaque characteristics. However, currently there is no single imaging modality that can reliably identify the vulnerable plaque in relation to development of future stroke.

Article history: Received 4 March 2015, Accepted 19 June 2015, Available online 19 August 2015

Keywords: Carotid artery, Non-invasive imaging, Vulnerable plaque

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http://dx.doi.org/10.1016/j.ejvs.2015.06.113

INTRODUCTION

Cerebral embolism from atherosclerotic carotid plaque remains an important pathophysiological mechanism of ipsilateral stroke, and carotid endarterectomy (CEA) in recently

symptomatic patients with a high-grade carotid artery stenosis significantly reduces the (recurrent) stroke risk.

The principle indication for carotid revascularisation is based on symptomatic status, timing, and degree of ipsilateral carotid artery stenosis. In symptomatic patients, with for example a single ocular symptom and smooth 70% carotid stenosis, the risk for recurrent stroke may be very low, and in these patients the benefit of revascularisation may be marginal. Alternatively, in asymptomatic patients the indication for revascularisation still remains a matter of debate, and current UK guidelines generally advocate a conservative approach in these patients, unless part of a clinical trial.[1] Overall in asymptomatic males, younger than 75 years, CEA compared with best medical treatment (BMT) significantly reduces the 10-year stroke risk.[2] However, based on clinical patient characteristics, selected subgroups of patients with asymptomatic carotid stenosis may benefit from carotid revascularisation. Increased systolic blood pressure, raised serum creatinine, smoking history, and a history of contralateral transient ischaemic attacks have been associated with an increased natural risk of ipsilateral cerebrovascular or retinal ischemic events.[3] However, these parameters are insufficient to fully balance the natural risk with procedural risk and additional anatomical and vessel wall-specific parameters are needed to ultimately assess the individual patient risk for future stroke and related benefit of revascularisation.

Research in carotid imaging has focused on identifying characteristics that determine the "vulnerable" or unstable carotid plaque making the patient at "high risk for future ipsilateral stroke".[4,5] Several structural plaque characteristics are proposed that distinguish the "vulnerable" from the "non-vulnerable" plaque, which includes plaque ulceration, intraplaque haemorrhage (IPH), thin or ruptured fibrous cap (FC), lipid-rich necrotic core, and the presence of calcification.[6] Inflammation may also play a role in the development and progression of disease as well as identifying the vulnerable plaque.[7] A limitation of these studies on histological validation is the basis on post-endarterectomy specimens, and that they are mostly derived from symptomatic patients, with a relative long time interval between index event and CEA.[8]

Identifying features of the vulnerable plaque in vivo may help select patients who benefit from intervention over medical treatment alone or vice versa. A variety of conventional and advanced in vivo imaging modalities including two-dimensional (2D) or three-dimensional (3D) ultrasound (US), computed tomography (CT), high-resolution magnetic resonance imaging (HRMRI), and nuclear imaging techniques such as positron emission tomography (PET) have been applied to identify plaque characteristics. Each technique and modality has been applied in observational studies to identify features of the carotid plaque, but it is unclear whether these newer techniques can be translated to, and impact on, daily clinical care, leading ultimately to patient benefit.

This paper overviews the literature on currently available non-invasive imaging techniques to characterise the vulnerable carotid plaque with histology as the gold standard, and summarises the challenges and needs for the development of next-generation imaging tools to be of help in future clinical decision-making (Tables 1 and 2).

ULTRASOUND

Current state

US is the modality of choice for initial evaluation and confirmation of carotid artery disease. US is used with high-resolution B-mode imaging alone or in combination with colour Doppler flow. US is a widely available, low cost and low-risk tool, which is well tolerated by patients and thus ideal for screening for the presence of the atherosclerotic plaque. A disadvantage is that it relies on the operator's ability, and systemic haemodynamic and local anatomic factors, such as calcification and tortuosity of the carotid artery. Variable levels of interobserver agreement for Internal Carotid Artery Peak Systolic Velocity (ICA PSV) ranging from −25% to 43% between experienced technologists have been reported.[9] However, in the UK the Society of Vascular Technologists promote internal audit with duplicate scanning between technicians to standardise reporting.

The use of the grey-scale median (GSM), a computerised measurement of plaque echogenicity, aims to differentiate echogenic carotid plaques (associated with a fibrocalcified content [stable appearance]) from echolucent plaques (with a thin FC, a higher lipid or haemorrhagic content [unstable appearance]). Although a low GSM, reflecting an echolucent (unstable) lesion, has been associated with an increased risk of cerebrovascular events,[10] the use of different software and different applications for GSM measurement between research groups has resulted in a wide range of cut-off values for the definition of vulnerable plaque with no clear consensus or standardisation for routine practise.[11]

Ulceration

A focal depression, causing an irregular surface, suggests plaque ulceration. The most widely used criteria to define plaque ulceration are the presence of a recess of at least 2 mm deep and 2 mm long, a well-defined wall at its base and an area of reversed flow at the level of the recess.[12] Ultrasound may vary significantly in sensitivity (33—75%) and specificity (33—92%) for determining plaque ulceration

Table 1. Non-invasive carotid imaging techniques and relevant needs for the future.

Techniques	Relevant needs for the future
Ultrasound (US)	3D ultrasound Contrast-enhanced ultrasound (CEUS)
Computed tomography (CT)	Automated removal of bone pixels Thin slice reconstructions 3D lumen geometry and shear stress
Magnetic resonance imaging (MRI)	3D SNAP protocol 7-Tesla MRI Automated segmentation techniques
Position emission tomography (PET)	Development of new tracers Coregistration PET/CT and PET/MRI