Hyperintense carotid plaque on T1-weighted turbo-field echo MRI in symptomatic patients with low-grade carotid stenosis and carotid occlusion

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Hyperintense Carotid Plaque on $T_1$-Weighted Turbo-Field Echo MRI in Symptomatic Patients with Low-Grade Carotid Stenosis and Carotid Occlusion

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Key Words
Atherosclerosis • Carotid arteries • Carotid stenosis • Carotid occlusion • Magnetic resonance imaging • Vulnerable plaque

Abstract
Background: In addition to stenosis grading, magnetic resonance imaging (MRI) may provide valuable information about plaque 'status', e.g. hyperintense vulnerable carotid plaque, associated with higher morbidity and mortality. In the present study, we investigated the prevalence, clinical and radiological correlates of hyperintense carotid plaques on $T_1$-weighted turbo-field echo ($T_1$w-TFE) MRI in patients with ischemic symptoms. Methods: A total of 153 patients presenting with transient ischemic attack or ischemic infarct, studied with contrast-enhanced magnetic resonance angiography (CEMRA), were retrospectively examined. Stenosis grade was obtained from CEMRA images, presence or absence of hyperintense carotid plaque from $T_1$w-TFE MRI. Stenosis grade and baseline characteristics were compared between patients with and without a hyperintense plaque. Results: Twenty-eight patients (18%) showed one or more hyperintense internal carotid (ICA) plaques. Hyperintense plaques were found in patients with <50% stenosis (6 of 158 ICAs), 50–70% stenosis (4 of 11), >70% stenosis (14 of 74) and carotid occlusion (4 of 28). Presence of hyperintense plaque was associated with older age (70 vs. 62 years; $p < 0.05$), higher prevalence of cardiac disease (61 vs. 28%; $p < 0.01$), ischemic infarct as presenting symptom (37 vs. 14%; $p < 0.01$), ischemic cerebral lesions on MRI (63 vs. 32%; $p < 0.01$), and the ICA on the patients’ symptomatic side (70 vs. 42%; $p < 0.01$). Conclusions: More than one third of patients with 50–70% stenosis present with a hyperintense plaque. This subgroup of patients could in the future possibly benefit from more aggressive medicinal therapy or revascularization.

Introduction

Ischemic stroke is one of the leading causes of morbidity and mortality worldwide. Most cerebral ischemic events result from rupture or erosion of atherosclerotic plaque, frequently around the carotid bifurcation, leading to acute occlusion of the carotid artery by thrombus.
formation, propagation of the thrombus more distally, or embolization [1–3]. Management of patients with these ischemic events is based on the degree of carotid stenosis, where 70–99% stenosis indicates surgery [4–6]. In the last decade, there has been increasing evidence of the existence of the so-called ‘vulnerable plaque’, described by the American Heart Association (AHA) as an AHA type VI lesion causing higher morbidity and mortality compared to noncomplicated plaques [3]. The detection of this vulnerable plaque could be important in patients with lower degrees of carotid stenosis (0–70%) because in these patients, the large randomized trials concerning management of carotid stenosis did not show a clear beneficial effect of surgery [4, 5]. Imaging of the carotid plaque may potentially define a subgroup of patients with <70% carotid stenosis but a high risk of recurrent ischemia, which might subsequently benefit from a more aggressive medicinal approach or even revascularization [1, 7, 8].

Several studies have shown the ability of carotid plaque magnetic resonance imaging (MRI) to detect a vulnerable plaque based on certain imaging characteristics in patients with various grades of carotid stenosis. An important characteristic in this regard is a hyperintense signal of the carotid plaque on T1-weighted gradient-echo images, which is thought to represent lipid-rich necrotic core and/or intraplaque hemorrhage [9–18]. These studies have also provided evidence as to the role of the hyperintense (vulnerable) plaque on T1-weighted gradient-echo images in predicting subsequent plaque progression and morbidity [19–24], specifically the relationship between hyperintense plaque and the occurrence of recurrent ischemic infarct [20]. However, it remains unclear how many patients with a hyperintense plaque are present within a cohort with low (<50%) to mild (50–70%) degree of carotid stenosis relative to the group of patients with a severe (>70%) carotid stenosis. Similarly, it is unknown how often a hyperintense plaque can be found in patients with an occlusion of the carotid artery, which might be an indication that the occlusion is acute and not chronic. Acute occlusions are known to recanalize occasionally, with subsequent risk of ischemic infarct [25–27].

The aim of the present study was to investigate the absolute and relative prevalence of the hyperintense (vulnerable) carotid plaque in patients with expected varying degrees of carotid stenosis and occlusion in a general survey of patients evaluated for ischemic symptoms using magnetic resonance (MR) angiography. In addition, we assessed the relationship between the hyperintense plaque, ipsilateral (symptomatic) carotid artery, general vascular risk factors, and the presence of cardiac disease.

**Materials and Methods**

**Study Population**

This study was approved by the Institutional Review Board of the University Medical Center Utrecht, the Netherlands. In this retrospective study, we collected baseline characteristics and imaging information of consecutive sampled patients in our institution between August 2006 and January 2009 who presented with cerebral ischemic symptoms, and who subsequently underwent contrast-enhanced magnetic resonance angiography (CEMRA) of the neck vessels combined with T1-weighted turbo-field echo (T1w-TFE) MRI to assess the cause of these symptoms. Baseline characteristics were retrieved from patient records and included age, gender, general vascular risk factors (hypertension, hypercholesterolemia, diabetes mellitus, previous or current smoking), presence of atherosclerotic disease in other vascular beds (cardiac disease, e.g. angina pectoris, coronary artery bypass graft, myocardial infarction; peripheral arterial disease, e.g. claudication, aortic prosthesis), and the type of presenting cerebral ischemic symptom (amaurosis fugax, transient ischemic attack, ischemic infarct).

**Conventional MRI and CEMRA**

All patients were imaged at the University Medical Center Utrecht in a 1.5-tesla MRI scanner (Philips Achieva XR, release 2.5) using a SENSE 16-element NeuroVascular coil (NV16, Philips). For basic clinical brain imaging, sagittal T1- and transversal 2.5) using a SENSE 16-element NeuroVascular coil (NV16, Philips).

**Magnetic Resonance Carotid Plaque Imaging**

Plaque imaging was performed before contrast administration. To visualize the common, external and internal carotid arteries, a T1w-TFE MRI sequence was acquired of the area around

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van der Kolk/de Borst/den Hartog/Kooi/Mali/Hendrikse
the carotid bifurcation in the transversal plane, a technique previously described by Cappendijk et al. [18] and used for identification of hyperintense plaque. A sagittal phase contrast survey image showing the carotid bifurcation was used as a scout image to manually orient the field of view (120 × 95.6 × 27 mm) around the bifurcation; care was taken to involve the bifurcation on both sides. Imaging parameters were inversion prepulse, TR/TI/TE 10/900/4.2 ms, shot interval time 3,000 ms, flip angle 15°, TFE factor 163, matrix size 256 × 163 mm, slice thickness 3 mm, number of slices 9, acquisition time 3.35 min. Assessment of the images involved reading of axial source data, executed independently by A.G.K. and J.H. who were blinded for baseline characteristics and CEMRA-derived stenosis results. A hyperintense (vulnerable) plaque was diagnosed if a hyperintense signal (brighter than the adjacent muscle) was seen within the wall or lumen of the ICA in the scanned region around the carotid bifurcation. The presence or absence of hyperintense signal was recorded for the ICA on both sides. Both observers needed to positively identify a hyperintense plaque for it to be designated definite. In case of discrepancy between the 2 observers – which occurred in 30 of 308 arteries – the plaque was scored as not being hyperintense.

Data Analysis
All analyses were carried out using the Statistical Package for Social Sciences program, version 15.0 for Windows. Continuous baseline variables are given as mean and standard deviation. Baseline characteristics and imaging results were associated with the presence or absence of hyperintense ICA plaque on T1w-TFE MRI using Pearson’s χ² test and, in case of small sample size or continuous variables, the Fisher exact test or the independent-sample t test, respectively. Multivariate logistic regression was used for significant differences in baseline characteristics between patients with and without hyperintense plaques, with variables corrected for age and gender. For analysis of associations between presenting symptoms, ipsilateral (symptomatic) artery (based on side of presenting symptoms), ischemia on MRI and stenosis grade, and hyperintense plaque, single arteries instead of single patients were designated as separate cases to correct for variable side (right or left), and χ² and p were calculated. p < 0.05 was considered to be statistically significant.

Results
Patient Population
Between August 2006 and January 2009, 187 patients presented with cerebral ischemic symptoms, and had undergone CEMRA of the neck vessels combined with T1w-TFE MRI. In 33 patients, the initial diagnosis was adjust-
ed around the time of presentation, which resulted in exclusion from our study. One other patient was excluded from analysis because of an ineligible T₁w-TFE scan. Therefore, baseline characteristics for 153 patients were collected (table 1). Patients were divided into 2 groups by the presence or absence of hyperintense plaque signal in one or both ICAs on T₁w-TFE MR imaging.

**Baseline Characteristics**

Baseline characteristics are presented in table 1. In 28 (18.3%) patients, a hyperintense plaque was identified. Two patients were found with bilateral hyperintense plaques (fig. 1). Of all hyperintense plaques, 70% were associated with the symptomatic ICA of the patient (fig. 2); 15.6% of all symptomatic ICAs showed a hyperintense plaque (p = 0.004). This correlation also remained statistically significant after correction for age and gender (p = 0.007). Of all general vascular risk factors, only age showed a statistically significant relationship with hyperintense plaque (p = 0.013). The presence of cardiac disease was positively correlated with a hyperintense plaque, with p = 0.003, which remained statistically significant after correction for age and gender (p = 0.019). There was also a significant positive correlation between hyperintense plaque and ischemic infarct as a presenting symptom, and ischemic cerebral lesions as seen on brain MRI, with p = 0.002 and p = 0.001, respectively.

**Hyperintense ICA Plaque versus Stenosis**

Information on stenosis grade was available for 271 ICAs (88.6%); in 35 ICAs stenosis grade could not be measured. Most ICAs were assigned to the <50% stenosis group (58.3%), followed by >70% (27.3%, fig. 3), occlusion (10.3%) and 50–70% (4.1%). When the presence of hyperintense plaque was correlated with stenosis grade (table 2), there were 6 (3.8%) hyperintense plaques

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![Fig. 1. Bilateral plaque formation in a 63-year-old man presenting with a right-sided cerebral transient ischemic attack: the T₁w-TFE MRI (middle frame) shows hyperintense plaque in both right and left ICA (arrows), with corresponding maximum intensity projection of CEMRA (left frame = right carotid) with a <50% stenosis of the right and 50–70% stenosis of the left ICA.](image)
seen in arteries with 0–50% stenosis, 4 (36.4%) in arteries with 50–70% stenosis (fig. 4), 14 (18.9%) in arteries with >70% stenosis, and 4 (14.3%) in arteries with occlusion (fig. 5).

Discussion

In the present study, we retrospectively investigated the prevalence, clinical and radiological correlates of hyperintense carotid plaques on T1w-TFE MRI in symptomatic patients with any ICA stenosis grade. Our main results show that, although only a small portion (1 of 7) of all symptomatic patients showed hyperintensity on MR plaque imaging, in the 50–70% carotid stenosis group, a striking amount of more than a third of all arteries showed a hyperintense plaque. These results differ from those of Albuquerque et al. [17], who found no correlation between a high signal on MRI and stenosis grade, but are in concordance with the results from Saam et al. [15], Gao et al. [21] and Altaf et al. [24] who found a substantial amount of hyperintense plaques in arteries with <70% stenosis [15, 24]. Our study expands the results of the aforementioned studies, since these studies often used only a specific stenosis subgroup of symptomatic (or asymptomatic) patients, and measured stenosis grade with duplex ultrasound instead of (CE)MRA.

The primary conclusion that can be drawn from our results is that more than a third of arteries with 50–70% stenosis show hyperintensity on MR plaque imaging. Although stenosis grade still remains the parameter on which management of symptomatic carotid artery atherosclerosis is based, the hyperintense plaque on gradient-echo MR images also has been shown to play an important role in progression of and subsequent morbidity and mortality from carotid atherosclerosis [19–24, 28]. Our aforementioned group of patients with 50–70% stenosis and hyperintense plaque, currently ineligible for revascularization, has a larger risk of morbidity and mortality despite their moderate stenosis grade, and therefore, would hypothetically be likely candidates

<table>
<thead>
<tr>
<th>Stenosis grade</th>
<th>Hyperintense carotid plaque, n (%)</th>
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<tbody>
<tr>
<td></td>
<td>present</td>
</tr>
<tr>
<td>0–50%</td>
<td>6 (3.8)</td>
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<tr>
<td>50–70%</td>
<td>4 (36.4)</td>
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<tr>
<td>&gt;70%</td>
<td>14 (18.9)</td>
</tr>
<tr>
<td>100% (occlusion)</td>
<td>4 (14.3)</td>
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Percentages are given for number of arteries with or without hyperintense plaque for each stenosis grade.

Fig. 2. Contralateral (asymptomatic) hyperintense plaque: a 75-year-old man presented with a left-sided cerebral transient ischemic attack; the T1w-TFE MRI (right frame) shows a substantial hyperintense plaque in the asymptomatic right ICA with narrowing of the vessel lumen (arrows), with >70% stenosis on the maximum intensity projection image of CEMRA (left frame).
for revascularization because of their high percentage of hyperintense plaques.

To our knowledge, there has been no previous specific report of a hyperintense plaque in patients with a carotid occlusion. Theoretically, this hyperintense plaque could represent acute intraplaque hemorrhage, or acute thrombus caused by rupture of a vulnerable plaque, two often named causes of acute carotid occlusion [25–27, 29]. Differentiating acute carotid occlusion from chronic occlusion is important because acute occlusions have a tendency to recanalize by disappearance of swelling from intraplaque hemorrhage or lysis of the acute thrombus [25, 26], in which case an underlying stenosis often becomes visible which may possibly require surgery because of high risk of ischemic infarct [26, 27]. Therefore, our new finding could hypothetically be a way to distinguish acute carotid occlusion with a risk of recanalization from chronic occlusion in symptomatic patients and have consequences for future clinical management. On the other hand, we feel that – in light of our small sample size – more information is needed regarding the nature of the hyperintense plaque in the occluded carotid artery before clinical implementation can be considered. Still, in symptomatic patients with an occlusion of the carotid artery in addition to a contralateral stenosis, the information on the acuteness of the occlusion may be important in the decision to operate or not in operative decisions of the contralateral stenosis.

Analysis of the baseline characteristics showed that presence of a hyperintense plaque was associated with a significantly higher prevalence of cardiac disease (61 vs. 28%), ischemic infarct as presenting symptom (37 vs. 14%) and ischemic cerebral lesions on MRI (63 vs. 32%). These results have, to our knowledge, not been reported previously for carotid hyperintense plaques [17, 22–24]. The high prevalence of cardiac disease in patients with a hyperintense carotid plaque may be related to the more generalized atherosclerotic disease in these patients. This is in line with the concept of the ‘vulnerable patient’ in patients with more generalized atherosclerotic disease instead of a single vulnerable plaque [30, 31].

Our study has some limitations. Because of our retrospective format, baseline characteristics and imaging information could not be found for a significant number of patients. Subsequently, some of our data did not have great statistical power. Second, we used a 1.5-tesla MRI

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**Fig. 3.** Patient with >70% ICA stenosis: an 82-year-old man presented with right-sided cerebral transient ischemic attack; the T₁w-TFE MRI (6 panels on the right) shows a hyperintense plaque (arrows) ranging over a wide trajectory from below the right-sided bifurcation into the ICA, with substantial lumen narrowing conform maximum intensity projection image of CEMRA (shown on the left).
scanner to obtain images for assessment; a 3.0-tesla scanner could probably produce images with better resolution and would perhaps identify hyperintense plaques not seen with lower resolution. On the other hand, scan time would be longer with this higher resolution, making the 3.0-tesla scanner less suitable for clinical practice. Another limitation of the present study may be the use of a multi-channel head-neck coil instead of a dedicated carotid coil for carotid plaque imaging and the subgroup of patients in which the stenosis grade could not be measured with high confidence on CEMRA [32]. Still, the strong hyperintensity of a carotid plaque could easily be distinguished. Furthermore, in daily clinical practice, the use of a head-neck coil is very practical be-
cause no change of coils or additional (surface) coils are needed, which increases patient throughput. Scan time for plaque imaging was held at a minimum (3.35 min) to make it suitable for daily clinical practice by using only a single sequence protocol (T1w-TFE). A previous study found that T1w-TFE MRI is a reproducible, accurate and fast way to quantify lipid-rich necrotic core including intraplaque hemorrhage – associated with hyperintensity on plaque imaging – in carotid atherosclerotic plaques, and that it showed the same sensitivity to detect lipid-rich necrotic core including intraplaque hemorrhage compared to a multisequence MRI approach [18]. In addition to MR plaque studies, future studies may show the importance of cofactors such as surface characteristics with instability of the plaque not assessed in this study.

Based on our results, 50% of all hyperintense ICA plaques occur in symptomatic patients presenting with either <70% stenosis or an ICA occlusion. Furthermore, a striking amount of more than a third of patients with 50–70% stenosis presented with a hyperintense plaque. Patients in this stenosis group with a hyperintense plaque have a relatively higher risk of subsequent ischemic events and could possibly benefit from aggressive medicinal therapy or revascularization. Our new finding of hyperintense plaque in carotid occlusion may hypothetically distinguish acute occlusion from chronic occlusion, and may possibly have consequences for future clinical management.

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