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Embolic complications after carotid artery stenting or carotid endarterectomy are associated with tissue characteristics of carotid plaques evaluated by magnetic resonance imaging

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ABSTRACT

Background: Unstable carotid plaques are associated with an increased incidence of embolic complications after carotid artery stenting (CAS) or carotid endarterectomy (CEA). The aim of this study was to elucidate the relationship between the tissue components of carotid plaques and the incidence of new ipsilateral silent ischemic lesions (NISIL) after CAS or CEA.
Methods: We performed CAS in 56 patients and CEA in 25 patients. We also performed quantitative analyses of carotid plaque characteristics before treatment using T1 weighted black-blood magnetic resonance imaging (BB-MRI). The signal intensity ratio (SIR) was defined as the ratio of signal intensity evaluated by BB-MRI in carotid plaques to that of sternocleidomastoid muscle. According to criteria that we and other investigators previously reported, an SIR $\geq$ 1.25 was defined as "high". NISIL were evaluated by diffusion-weighted imaging of MRI before and after CAS or CEA.
Results: In the high SIR group, the incidence of NISIL was significantly greater after CAS than after CEA (61% vs 13%, respectively, $p = 0.006$), whereas there were no significant difference in NISIL after the two procedures when the SIR was <1.25 (21% vs 0%). In multivariate regression analysis, the independent predictors of NISIL were CAS ($p = 0.002$), symptomatic stenosis ($p = 0.036$) and the SIR ($p = 0.049$).
Conclusions: Noninvasive quantitative tissue characterization of carotid plaques using BB-MRI is useful to determine the indication for CAS.

1. Introduction

Carotid artery stenosis is one of the major causes of cerebral infarction, and carotid endarterectomy (CEA) is the gold standard treatment for stroke prevention. However, carotid artery stenting (CAS) has recently emerged as a potential alternative to CEA, because it is less invasive and requires a shorter duration of hospitalization. A randomized controlled trial, SAPPHIRE showed that CAS and CEA had similar efficacy in high-risk patients [1]. Moreover, a recent randomized controlled trial, CREST, showed that the risk of the composite primary outcome of stroke, myocardial infarction or death did not differ significantly between CAS and CEA in both patients with symptomatic and asymptomatic carotid stenosis (2). Although several advantages of CAS have been reported, one of its disadvantages is a high incidence of distal emboli, even when the emboli cause asymptomatic or silent ischemia that can be detected by diffusion-weighted imaging of magnetic resonance imaging (DWI-MRI). Several studies indicated that analysis of carotid plaques using black-blood MRI (BB-MRI) can identify the histological components of carotid plaques [3,4], and there is an association between unstable plaque and an increased number of emboli after CEA or CAS (5–8). However, there is no quantitative information on the timing of the diagnosis of unstable plaque or the relative risk of newly appearing ipsilateral silent ischemic lesions (NISIL) detected by DWI-MRI after CAS or CEA. Thus, the aim of this study was to elucidate the relationship between plaque tissue components and the incidence of NISIL after these two procedures.

2. Methods

2.1. Study protocol

This study was a single center prospective study. Between June 2007 and April 2010, 81 consecutive patients (72 men and 9

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women) with high grade carotid stenosis (symptomatic carotid stenosis of more than 50% and asymptomatic carotid stenosis of more than 80% assessed with angiography), as suggested by the North American Symptomatic Carotid Endarterectomy Trial collaborators [9] were treated with CAS or CEA. CAS was performed in those patients who were high risk for CEA according to the SAPPHIRE trial (1) (8 patients: ≥80 years old, 12 patients: clinically significant cardiac diseases, 2 patients: severe pulmonary diseases). In addition, 34 patients had a preference for CAS based on the results of the CREST trial [2]. There were no patients who underwent CAS against the exclusion criteria of the SAPPHIRE trial. Assessments of NISIL were performed before and after a total of 81 procedures (56 CAS and 25 CEA). NISIL were counted by comparing the DWI-MRI before and after treatment. Quantitative analysis of plaque characteristics was performed just before treatment in all patients using BB-MRI. The experimental protocol was approved by the institutional ethics committee and informed consent was obtained from all patients.

2.2. MRI black-blood imaging

BB-MRI was performed using a 1.5-T system (Intera Achieva Nova Dual, Philips Medical Systems, Best, The Netherlands) equipped with standard neck array coils. Fat suppression was used to reduce signal from subcutaneous tissues, and a zero-filled interpolation technique was used to reduce pixel size and minimize partial-volume artifacts. Plaque imaging was performed in the oblique section at three parts including the minimal lumen area. The parameters for T1 weighted images (T1WI) were: cardiac gated, double inversion recovery two-dimensional (2D) turbo spin-echo (TSE) under spectral pre-saturation with inversion recovery (TSE factor: 7, echo time [TE]: 10 ms, repetition time [TR]: 1 × R–R interval (duration of the interval from the center of one R wave to the center of the following R wave on an electrocardiogram), 256 × 80% (recon 512) matrix; and a scan time of 1 min 13 s. The signal intensity of plaques was compared with that of the adjacent sternocleidomastoid muscle (SCM) by one radiologist who was blinded to all clinical information of patients. We calculated the ratio of the signal intensity of plaques to that of the SCM.

It has been reported that lipid-rich necrotic cores were identified as areas of high signal intensity in T1WI of BB-MRI, whereas lipid-rich necrotic cores were identified as areas of variable signal intensity in T2WI of BB-MRI [3]. In time of flight (TOF) images, lipid-rich necrotic cores were identified as areas of moderate intensity, but fibrous tissue was identified as moderate-to-low as well. T1WI of BB-MRI can show the borders of intimal plaques more clearly than TOF (3). Therefore, we employed the signal intensity ratio (SIR) (intensity of plaques/intensity of SCM) as a marker to discriminate tissue components of carotid plaques rather than using other MRI settings [10].

The signal intensity of carotid plaque was classified as "high" when the SIR was ≥1.25 using T1WI of BB-MRI according to the criteria that we and other investigators previously reported [10,11].

2.3. Carotid artery stenting procedure

Acetyl salicylic acid (100 mg) and clopidogrel (75 mg) or ticlopidine (100 mg) or cilostazol (200 mg) were given for a minimum of 7 days prior to the procedure. All CAS procedures were done under local anesthesia via the percutaneous transfemoral route. The procedures were carried out by an experienced neurointerventional team. A heparin bolus of 100 U/kg was given immediately before the interventional part of the procedure to increase the activated clotting time (ACT) to a minimum of 300 s. A 6 F, 90-cm-long sheath catheter was guided up into the ipsilateral common carotid artery proximal to the carotid stenosis. Two different types of embolic protection devices were used: Percusurge Guardwire (Medtronic AVE, Santa Rosa, CA) (n = 49) or Angioguard (Johnson & Johnson, Cordis, Minneapolis, MN) (n = 7). In all patients, predilation of the internal carotid lesion was done with a 3.5–4.0-mm balloon catheter. Two types of stents were placed in the stenotic lesion: Precise (Johnson & Johnson, Cordis, Minneapolis, MN) (n = 46) or Wallstent (Boston Scientific, Natick, MA) (n = 10). Postdilation was performed with a 4.5–5.5-mm balloon catheter.

2.4. Carotid endarterectomy procedure

All patients received general anesthesia. An intraluminal shunt was used in all of patients. Shunt insertion was performed immediately after arterectomy before removing the atherosclerotic plaques to provide immediate cerebral protection. Primary closure without patching was performed. After closure, all patients had angiography to confirm the patency of the carotid arteries in the operating room. All patients were transferred to the intensive care unit for 24–48 h.

2.5. Detection of NISIL by DWI-MRI

The MRI instrument used in this study was 1.5-T system (Intera Achieva Nova Dual, Philips Medical Systems, Best, The Netherlands). The MRI studies consisted of DWI with the echo-planar method under the following conditions: TR/TE 2060/67.0, slice thickness 5 mm, spacing 1.5 mm, b value 1000 s/mm^2 and FOV 24 cm.

The baseline DWI-MRI was obtained after diagnostic angiography and prior to CAS or CEA in all patients. The period between the baseline DWI-MRI and CAS or CEA was 11 ± 9 days. There were no new ischemic events such as transient ischemic attack or stroke between the baseline DWI-MRI and CAS or CEA. The second DWI-MRI was performed within 72 h after CAS or CEA.

We determined the interobserver reproducibility of DWI-MRI-positive in 50 randomly selected images that were measured by two observers in a blinded fashion. Likewise, we determined the intraobserver reproducibility of DWI-MRI-positive in 50 randomly selected images that were measured twice by one observer with a 30-day interval between the two measurements. The interobserver and intra-observer reproducibility of DWI-MRI-positive was excellent (Cohen's κ = 0.97 and 1.00, respectively).

2.6. Statistical analysis

Continuous values were expressed as the mean ± SD. Categorical data were summarized as percentages and compared using a Fisher's exact test. Comparisons of continuous variables between the cohorts were performed with an unpaired Student's t test. A value of p < 0.05 was considered to indicate a statistically significant difference. All variables with a p value <0.05 comparing NISIL-positive with NISIL-negative were included in multivariate logistic regression analysis Table 2. However, prescription of "ticlopidine or clopidogrel" was excluded as a confounding factor because we prescribed ticlopidine or clopidogrel to all patients who were scheduled for CAS. All of the statistical analyses were performed with StatView 5.0 (SAS Institute, Cary, NC).

3. Results

3.1. Patient characteristics

The patient characteristics are showed in Table 1). All procedures were completed successfully in all patients. There were two