High-Risk Plaque for Carotid Artery Stenting Evaluated With 3-Dimensional T1-Weighted Gradient Echo Sequence

Hiroshi Tanemura, MD; Masayuki Maeda, MD, PhD; Naoki Ichikawa, MD; Yoichi Miura, MD; Yasuyuki Umeda, MD, PhD; Seiji Hatazaki, MD, PhD; Naoki Toma, MD, PhD; Fumio Asakura, MD, PhD; Hidenori Suzuki, MD, PhD; Hiroshi Sakaida, MD, PhD; Satoshi Matsushima, MD, PhD; Waro Taki, MD, PhD

Background and Purpose—Preventing cerebral embolisms is a major concern with carotid artery stenting (CAS). This study evaluated 3-dimensional T1-weighted gradient echo (3D T1GRE) sequence to predict cerebral embolism related to CAS.

Methods—We performed quantitative analyses of the characteristics of 47 carotid plaques before CAS by measuring the signal intensity ratio (SIR) and plaque volume using 3D T1GRE images. We used T1-weighted turbo field echo sequence to obtain 3D T1GRE images. We also evaluated diffusion-weighted images (DWI) of the brain before and after CAS to detect ischemic lesions (DWI lesions) from cerebral emboli.

Results—SIR (2.17 [interquartile range 1.50–3.07] versus 1.35 [interquartile range 1.08–1.97]; P=0.010) and plaque volume (456 mm³ [interquartile range 256–696] versus 301 mm³ [interquartile range 126–433]; P=0.008) were significantly higher in the group of patients positive for DWI lesions (P-group: n=26) than DWI lesion-negative patients (N-group: n=21). In multivariate logistic regression analysis, SIR (β=0.007) and plaque volume (P=0.042) were independent predictors of DWI lesions with CAS. Furthermore, SIR (rs=0.42, P=0.005) and plaque volume (rs=0.36, P=0.012) were positively correlated with the number of DWI lesions. From analysis of a receiver-operating characteristic curve, the most reliable cutoff values of SIR and plaque volume to predict DWI lesions related to CAS were 1.80 and 373 mm³, respectively.

Conclusions—Quantitative evaluation of carotid plaques using 3D T1GRE images may be useful in predicting cerebral embolism related to CAS. (Stroke. 2013;44:105-110.)

Key Words: carotid arteries ■ intracranial embolism ■ plaque, atherosclerotic ■ stents

As the practice of carotid artery stenting (CAS) becomes more common, preventing cerebral embolism is a major concern with CAS. The CREST trial (Carotid Revascularization Endarterectomy versus Stenting) showed that there was a higher risk for stroke with CAS than carotid endarterectomy during the periprocedural period.1 In addition, there is an earlier report that asymptomatic ischemic lesions on diffusion-weighted image (DWI) are detected more often in CAS than carotid endarterectomy.2

Recently, vulnerability of carotid plaque has been implicated in evaluating risk for plaque rupture that causes artery-to-artery embolism.3-5 Development of magnetic resonance (MR) imaging with high contrast and resolution enabled noninvasive assessment of carotid plaque vulnerability.3-14,18 High signal intensity plaques on T1-weighted images are considered to correspond to vulnerable plaques that represent a lipid-rich necrotic core or intraplaque hemorrhage (IPH).3,4,6,9-12,14,16,17 Among T1-weighted sequences, 3-dimensional (3D) T1-weighted gradient echo (T1GRE) sequences demonstrated higher diagnostic capability to detect IPH,19 and now evaluating plaque vulnerability using 3D T1GRE images is gaining popularity in clinical settings.3,4,6,9-11,14,16 Evaluating plaque vulnerability also is important in CAS because mechanically ruptured plaques release debris from atherosclerotic plaque. Carotid plaque with T1 high intensity on 2-dimensional (2D) turbo spin echo images are reported to be predictive for cerebral embolism related to CAS,20 whereas the similar usefulness of T1 high intensity on 3D T1GRE images has not been evaluated. In addition, a larger plaque presumably carries a higher risk that more debris will be released during CAS as a result of its large burden. However, the impact of plaque volume on cerebral embolism related to CAS has not been examined. Accurate estimation of such plaque characteristics is important clinically to plan strategies that reduce cerebral embolism related to CAS. In the present study, we retrospectively assessed the usefulness of quantitative plaque characteristics, including signal intensity on T1-weighted images and plaque volume.
evaluated with MR plaque imaging using 3D T1GRE sequence, in predicting cerebral embolism related to CAS.

**Methods**

**Study Population**

Our group performed 48 CAS from January 2008 to December 2009. Patients diagnosed with carotid lesions that were either symptomatic with >50% stenosis or those that were asymptomatic with >80% stenosis, by digital subtraction angiography according to the method used in the North American Symptomatic Carotid Endarterectomy Trial, met our criteria to perform CAS. Carotid artery stenosis was defined as symptomatic if the patient had a history of ipsilateral ischemic events attributed to the affected carotid artery within the previous 120 days before CAS. Outside of this window, carotid artery stenosis was considered asymptomatic. The patient characteristics were collected retrospectively through a review of the medical records. Laboratory parameters were examined within 1 month before CAS.

**Magnetic Resonance Imaging Protocol**

MR examinations, including DWI and 3D T1GRE carotid plaque imaging, were performed after diagnostic angiography on all patients within 3 days before CAS. There were no ischemic events, such as transient ischemic attack or stroke, between preprocedural DWI and CAS. DWI were obtained within 48 hours after CAS. Carotid plaque images and preprocedural DWI were achieved with a 3.0T MR imaging system (Achieva Quasar Dual, Philips Medical Systems, Best, The Netherlands). DWI after CAS was performed with a 1.5T MR imaging system (Intera Achieva Nova, Dual, Philips Medical System, Best, The Netherlands).

We used 3D T1-weighted turbo field echo (T1TFE) sequence to obtain 3D T1GRE images. This imaging was performed in the coronal plane with null blood conditions (effective inversion time 600 msec; TR/TE 5.0/2.3 msec) and the water excitation technique to suppress fat signals. Other scanning parameters were as follows: FOV 260 mm; voxel size = 0.68x0.68x1.00 mm; flip angle = 13°, 56 partitions, covering 70 mm around the carotid bifurcation; and data acquisition time of 4 min 2 sec.

Preprocedural DWI was performed with the following parameters: TR/TE shortest/60; slice thickness = 3 mm; spacing, 0 mm; b value = 1000 sec/mm²; and FOV = 230 mm. Postprocedural DWI was obtained with following parameters: TR/TE shortest/60 msec; slice thickness = 3 mm; spacing, 0 mm; b value = 1000 sec/mm²; and FOV = 230 mm.

**Quantitative Evaluation of Carotid Plaques Using 3D T1TFE Sequence**

All MR images were reviewed by 2 neurointerventionalists blinded to clinical data. Regions of interest were drawn manually on a workstation around the carotid plaque and adjacent sternocleidomastoid muscle with coronal 3D T1GRE images that detected a largest carotid plaque segment. The signal intensity ratio (SIR) was defined as a value of the signal intensity of carotid plaque divided by that of sternocleidomastoid muscle, and was measured in each patient.

Carotid plaques were contoured manually in long-axis reconstruction 3D T1GRE images of the carotid plaque on a workstation, and the area (mm²) of the carotid plaque was calculated automatically. The area measurement was repeated in all images that showed carotid plaques, and plaque volume (mm³) was then calculated as a sum of the areas (mm²) determined in each slice multiplied by the slice thickness (1mm).

**Detection of Cerebral Embolism Using DWI**

Pre- and postprocedural DWI images were compared, and any new ipsilateral hyperintense lesion (DWI lesion) was regarded as an ischemic lesion related to cerebral embolism caused by CAS. The number of new ipsilateral DWI lesions was counted by section-to-section comparison of the pre- and postprocedural DWI.

| Table 1. Patient Characteristics With or Without Ischemic Lesions on Diffusion-Weighted Image |
|----------------------------------------|-----------------------------------|-----------------|-----------------|
|                                        | P-Group  (n=26)                  | N-Group (n=21)  | P Value         |
| Mean age, y                           | 74.0±4.9                        | 72.2±6.5       | 0.276           |
| Degree of stenosis (%)                | 80.3±2.3                        | 81.7±2.6       | 0.687           |
| Men, n (%)                           | 24 (92.3%)                      | 19 (90.5%)     | 1.000           |
| History                               |                                  |                |                 |
| Symptomatic stenosis                  | 13 (50.0%)                      | 10 (47.6%)     | 1.000           |
| Coronary artery disease              | 4 (15.4%)                       | 2 (9.6%)       | 0.687           |
| Hypertension                          | 20 (76.9%)                      | 14 (66.7%)     | 0.521           |
| Diabetes mellitus                     | 11 (42.2%)                      | 4 (19.1%)      | 0.121           |
| Hypercholesterolemia                  | 18 (69.2%)                      | 15 (71.4%)     | 1.000           |
| Smoking                               | 5 (19.2%)                       | 7 (33.3%)      | 0.270           |
| Contralateral ICA occlusion           | 13 (50.0%)                      | 10 (47.6%)     | 1.000           |
| Proximal balloon protection           | 15 (57.7%)                      | 16 (76.2%)     | 0.227           |
| Laboratory parameters                |                                  |                |                 |
| HDL-Cholesterol, mg/dl                | 48.4 [42.3–54.4]                | 44.6 [37.8–58.3]| 0.703           |
| LDL-Cholesterol, mg/dl                | 111.0 [101.0–137.8]             | 98.0 [83.0–117.0]| 0.040           |
| Triglycerides, mg/dl                  | 142.0 [104.0–188.0]             | 127.0 [81.5–182]| 0.451           |
| C-reactive protein, mg/dl             | 0.23 [0.06–0.38]                | 0.15 [0.06–0.229]| 0.870           |
| Carotid plaque characteristics       |                                  |                |                 |
| SIR                                   | 2.17 [1.50–3.07]                | 1.35 [1.08–1.97]| 0.010           |
| Plaque volume (mm³)                   | 477.7 [256.4–696.3]             | 300.7 [125.6–433.0]| 0.008           |

HDL, high-density lipoprotein; ICA indicates internal carotid artery; LDL, low-density lipoprotein; and SIR, signal intensity ratio.
CAS Procedure

All patients received the combination of aspirin (100 mg per day) with clopidogrel (75 mg per day) or cilostazol (200 mg per day) as antiplatelet therapy at least 7 days before CAS. All CAS procedures were performed under local anesthesia via a percutaneous transfemoral route and by an experienced neurointerventional team. A heparin bolus of 100 U/kg was administered intravenously just after the introducer sheath was placed to increase the activated clotting time to a minimum of 300 sec. Two different types of distal embolic protection devices were used: Angioguard XP (Johnson & Johnson, Cordis, Minneapolis, MN; n=46) or Percusurge Guardwire (Medtronic, Santa Rosa, CA; n=2). In the 31 cases protected with Angioguard Xp, proximal balloon protection using Optimo (Tokai Medical Products, Aichi, Japan) was also performed. All of the patients were treated with self-expandable stents: Precise (Johnson & Johnson, Cordis, Minneapolis, MN) after dilation with a balloon catheter. Post dilation was performed as necessary. After completing CAS, heparin was not reversed, leaving its effect to disappear spontaneously.

Neurological examinations were carried out in each patient before CAS, the day after CAS, and 30 days after CAS. Thirty-day morbidity was defined as any new neurological deficit that persisted 30 days after CAS.

Statistical Analysis

Normally-distributed continuous variables were expressed as mean ± standard deviation (SD). Median values and the interquartile range (IQR) were computed for non-normally distributed variables. Because most of the continuous variables were not distributed normally, we made a common logarithmic or square-root transformation of these variables. Baseline characteristics were compared by using Student t test for continuous variables and Fisher exact test for categorical variables. A 2-sided P value of less than 0.05 was considered to indicate a statistically significant difference. Multivariate logistic regression analysis with DWI lesion-positive or -negative as the outcome was then performed using those variables with a P value < 0.25 from the univariate analysis. Factors included were as follows: diabetes mellitus, proximal balloon occlusion, SIR, plaque volume, and low-density lipoprotein cholesterol (LDL-C) were analyzed for the incidence of DWI lesion related to CAS. Then, with the variables in which significance was indicated by the multivariate logistic regression analysis, correlation with the number of DWI lesions were further analyzed by calculating Spearman’s correlation coefficients (rs).

The cutoff values of SIR and plaque volume with the best sensitivity and specificity for evaluating the probability of newly appearing DWI lesions were identified by analyzing the receiver operating characteristic curve. To determine intra- and inter-reader reproducibility, the intraclass correlation coefficient (ICC) with 95% confidence interval (CI) was calculated for the level of agreement. All of the statistical analyses were performed with IBM SPSS Statistics 19 software.

Results

Forty-eight consecutive CAS procedures were completed successfully with satisfactory angiographic results. Thirty-day morbidity and mortality were 2.1% and 0%, respectively. No myocardial infarctions or adverse events related to devices were observed. Characteristics of patients with or without DWI lesions (DWI positive, P-group; or DWI negative, N-group) are shown in Table 1. One patient was excluded from evaluation because the quality of the 3D T1GRE images was inadequate for evaluation. In this case, flow artifact around the carotid plaque obscured the plaque–lumen interface. Thus, 47 carotid plaques were evaluated in this study. Representative 3D T1GRE images and DWI of P-group and N-group are presented in Figures 1 and 2.

New ipsilateral DWI lesions were detected after 26 CAS procedures (55%). The majority of new ipsilateral DWI lesions were asymptomatic; however, 1 patient experienced a minor stroke from a cerebral embolism related to CAS. To clarify the ability of SIR and plaque volume to predict cerebral embolism related to CAS, the relationship between these variables and DWI lesions with CAS were investigated. The results of univariate analysis are summarized in Table 1. Among the
clinical variables, SIR (2.17 [IQR 1.50–3.07] and 1.35 [IQR 1.08–1.97], respectively; P=0.010), plaque volume (456 mm³ [IQR 256–696] and 301 mm³ [IQR 126–433], respectively; P=0.008), and LDL-C (111 mg/dL [IQR 101–138] versus 98 mg/dL [IQR 83–117] respectively; P=0.040) were significantly related to new ipsilateral DWI lesions (Figure 3). The multivariate logistic regression analysis that we subsequently performed, with DWI lesion-positive or –negative as the outcome, indicated SIR (P=0.007), plaque volume (P=0.042), and LDL-C (P=0.021) as independent predictors of new ipsilateral DWI lesions (Table 2).

We then calculated Spearman correlation coefficients between those independent predictors and the numbers of DWI lesions and found significant correlation for SIR (rs=0.42, P=0.005) or plaque volume (rs=0.36, P=0.012), but not for LDL-C (rs=0.23, P=0.110; Figure 4).

Receiver operating characteristic curves indicated that the most reliable cutoff values of SIR and plaque volume to predict new ipsilateral DWI lesions related to CAS were 1.80 and 373 mm³, respectively (areas under the curve were 0.70 and 0.971). Inter-reader reproducibility (ICC, 95% CI) was excellent for the number of DWI lesions (0.996; 0.993 to 0.998), SIR (0.971; 0.948 to 0.984), and plaque volume (0.913; 0.850 to 0.951).

Discussion

The present study demonstrated that MR plaque imaging using the 3D T1GRE images could identify plaques representing high risk for cerebral embolism related to CAS. SIR and plaque volume were significantly higher in the P-group than the N-group. In addition, the numbers of new ipsilateral DWI lesions were correlated positively with SIR and plaque volume. Because the number of new DWI lesions after CAS has been reported to have a clear association with the incidence of minor or major stroke, SIR and plaque volume could be a useful predictors not only for DWI lesions but also for minor or major stroke. To our knowledge, this is the first report that describes the relationship between carotid plaque characteristics evaluated with 3D T1GRE sequence and risk of cerebral embolism related to CAS.

Preventing cerebral embolisms is a major concern with CAS. In contrast to carotid endarterectomy, CAS could mechanically rupture a plaque by applying high-pressure balloons and stents and could release plaque debris and soluble factors into the circulating blood. Therefore, accurate evaluation of carotid plaque characteristics is clinically important to reduce cerebral embolisms related to CAS, especially when the targeted carotid plaque is vulnerable. Vulnerable plaques that contain lipid-rich necrotic core or IPH as determined by ultrasonography or MR imaging are considered to be 1 of the risk factors for ischemic complications after CAS. Recent developments in MR imaging with high-contrast resolution have enabled noninvasive assessment of carotid plaque vulnerability. Yamada et al evaluated the usefulness of T1 high intensity in the 2D T1 turbo spin echo images to predict cerebral embolism related to CAS and concluded that an SIR of 1.25 was the most reliable cutoff value.

Recently, 3D T1GRE sequences have been used in clinical settings and attracted considerable attention for evaluating vulnerability of carotid plaques. Those sequences vary depending on the vendor, including 3D fast spoiled gradient recalled echo, 3D TFE, and magnetization prepared rapid acquisition with gradient echo. 3D

![Figure 3. Scatterplot of Signal intensity ratio (A), plaque volume (B), and LDL-C (C) in the P- and N-groups. These variables were significantly different between the P-group and N-group in univariate analysis. Because SIR, plaque volume, and LDL-C were not distributed normally, we suitably made a common logarithmic or square root transformations of these variables to perform statistical analysis.](http://stroke.ahajournals.org/)

Table 2. Statistical Values From the Results of the Multivariate Logistic Regression Analysis That Show Independent Predictors for a New DWI Lesion Related to CAS

<table>
<thead>
<tr>
<th>Coefficients</th>
<th>Standard Error</th>
<th>P Value</th>
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<tbody>
<tr>
<td>Diabetes mellitus</td>
<td>0.644</td>
<td>0.442</td>
</tr>
<tr>
<td>Proximal balloon protection</td>
<td>0.687</td>
<td>0.456</td>
</tr>
<tr>
<td>LDL-cholesterol (log)</td>
<td>8.300</td>
<td>3.703</td>
</tr>
<tr>
<td>SIR (log)</td>
<td>4.207</td>
<td>1.828</td>
</tr>
<tr>
<td>Plaque volume ((\sqrt{\text{V}}))</td>
<td>0.157</td>
<td>0.056</td>
</tr>
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LDL indicates low-density lipoprotein; SIR, signal intensity ratio.
3D GRE sequences could overcome several limitations of 2D T1 turbo spin echo sequence, including imaging direction restricted to the cross-sectional transaxial plane, lack of contiguous anatomic coverage, quantification errors resulting from partial volume effect, requirement for electrocardiogram or peripheral pulse unit for pulse-synchronized image acquisition to minimize effects of intraluminal flow signals, and inadequate examination time-efficiency. Therefore, 3D T1GRE is more practical in clinical settings. In addition, 3D T1GRE sequences have been reported to demonstrate higher diagnostic capability to detect IPH compared with the 2D fast spin echo or turbo spin echo sequences. Although 3D T1GRE sequences are gaining popularity for evaluation of plaque vulnerability, no studies have been performed to determine the usefulness of those sequences in predicting cerebral embolism related to CAS. Our results demonstrated that 3D T1GRE images are useful in predicting the risk of cerebral embolism related to CAS and the most reliable cutoff value to predict cerebral embolism related to CAS was 1.80. Because the plaque signal on T1-weighted images varies considerably with different magnetic field strength, TR, and sequence, no reported cutoff value, including ours, achieved general validity. However, higher T1 intensity is certainly a risk factor for cerebral embolism related to CAS.

Larger plaques have more atherosclerotic burden and exposed surface, and hence presumably carry a higher risk of releasing more plaque debris during CAS. However, to date, no study has evaluated the association between carotid plaque volume and increased risk for cerebral embolism related to CAS. The severity of carotid stenosis is an important risk factor for stroke and is used to decide which patients could benefit from carotid intervention. Unfortunately, luminal stenosis does not necessarily reflect the amount of atherosclerotic plaque. Degree of stenosis could underestimate the plaque volume, because enlarged arterial lumen resulting from positive remodeling cannot be accounted for with angiography. Long and continuous lesions with mild to moderate stenosis might have more atherosclerotic plaque materials than a severe stenosis that covers only a short segment. Our results clearly show that carotid artery stenosis with higher plaque volume carries more risk for cerebral embolism related to CAS, and that the cutoff value of plaque volume that most reliably predicts cerebral embolism related to CAS was 373 mm$^3$. We propose that plaque volume should also be considered a risk factor of cerebral embolism related to CAS.

Several limitations must be considered for the present study. First, it was performed retrospectively, and the number of patients enrolled was too small to evaluate the association with the incidence of stroke. A prospective study that includes an analysis for incidence of stroke with a larger number of patients would provide more evidence for the association we indicate in the present study. Second, the choice of embolic protection devices and other variables, such as the pressure applied for pre/post dilatation, differed in each case. Third, all the patients were treated with an open-cell–type stent. In a recent study, patients treated with open-cell–type stents had significantly higher stroke and death rates after CAS than those treated with closed-cell–type stents, indicating that the latter type of stent might have an intrinsically greater potential to prevent cerebral embolism of plaque debris. Therefore, we might have experienced more embolism cases with CAS. Use of closed-cell–type stents would further help decreasing incidence of cerebral embolism related to CAS. Finally, assessment of carotid plaque using signal intensity might fail to diagnose vulnerable plaques when they are composed of large lipid-rich necrotic core without IPH, because the regional signal intensity of lipid-rich necrotic core without IPH may not be demonstrated with high intensity signals on T1-weighted images.

Conclusion
The 3D T1GRE sequence was useful to identify vulnerable plaques at high risk for cerebral embolism related to CAS. Higher SIR and plaque volume evaluated with 3D T1GRE images correlated significantly with the appearance of DWI lesions related to CAS. We suggest that higher T1 intensity and larger plaque volume on 3D T1GRE images should be recognized as additional risk factors for cerebral embolism related to CAS.

Acknowledgement
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Disclosures
None.
References


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背景および目的：脳塞栓の予防は、頸動脈ステント留置術（CAS）に伴う大きな課題である。本研究では、CASに関連する脳塞栓の予測に対する3D T1強調グラディエントエコー（3D T1GRE）シーケンスを評価した。

方法：CAS実施前に、3D T1GRE画像を用いて信号強度比（SIR）およびプラーク容積を測定し、頸動脈プラーク47病変の特徴を定量解析した。3D T1GRE画像は、T1強調ターボフィールドエコー（TFE）シーケンスを使用して取得した。また、CASの前後に脳の拡散強調画像（DWI）を評価し、脳塞栓による虚血性病変（以下「DWI病変」とする）を特定した。

結果：SIR [2.17（四分位範囲：1.50～3.07）、p = 0.010]およびプラーク容積 [456 mm³（四分位範囲：256～696）、p = 0.008]は、DWI病変陽性患者群（P群：n = 26）においてDWI病変陰性患者群（N群：n = 21）よりも有意に高かった。多変量ロジスティック回帰分析では、SIR（p = 0.007）およびプラーク容積（p = 0.042）が、CASに伴うDWI病変の独立予測因子であった。さらに、SIR（rs = 0.42、p = 0.005）およびプラーク容積（rs = 0.36、p = 0.012）は、DWI病変の数と正の相関を示した。ROC曲線の解析から、CASに関連するDWI病変の予測において最も信頼できるカットオフ値は、SIRが1.80、プラーク容積が373 mm³であった。

結論：3D T1GRE画像を使用した頸動脈プラークの定量的評価は、CASに関連する脳塞栓を予測するうえにおいて有用である。
本研究では、CAS関連の脳塞栓予測におけるプラックの量的特徴の有用性を後向きに評価した。プラックの量的特徴として、T1強調画像のシグナル強度、3D T1GREシーケンスを用いたMRプラック画像で評価したプラック容積を用いた。

研究対象集団
2008年1月から2009年12月までにCASを実施した48例を研究対象とした。

North American Symptomatic Carotid Endarterectomy Trialで使用された方法に従って、デジタルサブトラクション血管造影により、狭窄が50%以上の症候性頸動脈病変または狭窄が80%以上の無症候性頸動脈病変と診断された患者がCAS実施の適格例であった。頸動脈狭隘症において、CAS実施前の120日以内に、頸動脈病変に原因する同側虚血性イベントを発症している場合は症候性と定義した。これ以外は、無症候性頸動脈病変とみなした。患者特性は診療記録のレビューを通じて後向きに収集した。CAS実施前1カ月以内に臨床検査パラメータを評価した。

磁気共鳴画像法のプロトコル
CAS実施前3日以内に全患者に対し、診断的血管造影を実施した後に、CAS実施前のDWIおよび3D TIGREによる頸動脈プラックイメージングを含む、MR検査を実施した。CAS実施後のDWIからCAS実施までの間、一過性脳虚血発作または脳卒中の虚血性イベントはみられなかった。CAS実施後48時間以内に、頸動脈プラック画像およびCAS実施前のDWIは、3.0T MRイメージングシステム(Achieva Quasar Dual, Philips Medical Systems社,Best,オランダ)により得た。CAS実施後のDWIは、1.5T MRイメージングシステム(Intera Achieva Nova、Dual, Philips Medical System社,Best,オランダ)を使用した。

3D T1ターボフィールドエコー(T1TFE)シーケンスを用いて3D TIGRE画像を取得した。3D TIGREは、血液をnullポインタに設定して、冠状面において実施し(実効反転時間600msec、TR/TE 5.0/2.3msec)、水励起法により脂肪信号を抑制した。その他のスキャンニングパラメータ:FOV 260mm、ボクセルサイズ=0.68 × 0.68 × 1.00mm、フリップ角＝13°、パーセッション56、頸動脈分岐部の間隔70mmをカバー、データ取り込み時間4分2秒。CAS実施前のDWIは以下のパラメータで実施した：TR/TE最短/60msec、スライス厚＝3mm、スペーシング、

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<th>表1拡散強調画像における虚血性病変を有するまたは有さない患者の特性</th>
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<td><strong>P群(n=26)</strong></td>
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<td>年齢平均値、歳</td>
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<td>狭窄率（%）</td>
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<td>近位バリュープロテクション</td>
</tr>
<tr>
<td>臨床検査値</td>
</tr>
<tr>
<td>HDLコレステロール、mg/dl</td>
</tr>
<tr>
<td>LDLコレステロール、mg/dl</td>
</tr>
<tr>
<td>トリグリセリド、mg/dl</td>
</tr>
<tr>
<td>C反応性タンパク質、mg/dl</td>
</tr>
<tr>
<td>頸動脈プラックの特徴</td>
</tr>
<tr>
<td>SIR</td>
</tr>
<tr>
<td>プラック容積（mm³）</td>
</tr>
</tbody>
</table>

HDL:高比重リポタンパク、ICA:内頸動脈、LDL:低比重リポタンパク、SIR:信号強度比。
抗血小板療法として全患者にアスピリン（100 mg/日）とクロピドグレル（75 mg/日）の併用、またはアスピリン（100 mg/日）とシロスタゾール（200 mg/日）の併用でCAS実施前に7日間以上投与した。CASはすべて、局所麻酔下で経験豊かな脳神経系血管内治療チームにより経皮的大腿動脈経由で実施された。イントレポーターのシースを留置した直後にヘパリン100 U/kgを静脈内にボラス投与して、活性化凝固時間（ACT）を300秒以上に延長した。2種類の遠位塞栓予防デバイス【Angioguard XP（Johnson & Johnson, Cordis社,ミネアポリス,ミネソタ州, n = 46）, または Percusurge Guardwire (Medtronic AVE 社, サンタローザ, カリフォルニア州, n = 2)】を使用した。患者31例は、Angioguard XPにより遠位塞栓を予防し、近位塞栓予防にはバルーンカテーテル、Optimo（東海メディカルプロダクツ社, 愛知,日本）を使用した。全患者に対し、バルーンカテーテルで応張後の自己応張型ステント【Precise (Johnson & Johnson,Cordis社,ミネアポリス,ミネソタ州)】による治療を実施した。ポスト応張は必要に応じて実施した。CAS終了後、ヘパリンのリバースは実施せず、作用を自然に消失させた。

図1 P群患者の頸動脈ブラークの典型的な画像。（A）：3D T1GRE画像。（B）：拡散強調画像。画像は重度の無症候性頸動脈狭帯を有する70歳男性から取得した。高信号の頸動脈ブラークが長軸再構成3D T1GRE画像において明確に描出されている。頸動脈ブラークの信号強度は3.07, およびブラーク容積は1,133 mm³であった。頸動脈ステント留置術後の拡散強調画像において、多発性・無症候性脳塞栓が判明した。

図2 N群患者の頸動脈ブラークの典型的な3D T1GRE画像。画像は、重度の症候性頸動脈狭帯を有する65歳男性から取得した。等強度の頸動脈ブラークが長軸再構成3D T1GRE画像において描出されている（白矢印）。頸動脈ブラークの信号強度は1.04, およびブラーク容積は100 mm³であった。頸動脈ステント留置後の拡散強調画像において、脳塞栓は認められなかった。
CAS実施前、実施の翌日および30日後に各患者に対して神経学的検査を実施した。30日有病率は、CAS実施後30日時点で残存する何らかの新規神経学的徵候と定義した。

統計解析
正規分布する連続変数は、平均値±標準偏差 (SD)で示した。非正規分布する変数に関しては、中央値および四分位範囲 (IQR) を算出した。連続変数の大部分は、正規分布を示さなかったため、これらの変数を対数変換または平方根変換した。ベースライン特性は、連続変数に関してStudent t検定を用いて比較し、分類変数に関してはFisherの正確確率検定を用いて比較した。両側のp値が0.05未満の場合に、統計的有意差を示すとみなした。各変数の単変量解析にあって、P群とN群の間には有意差を認めた。SIR、プラック容積、LDL-Cは、正規分布を示さなかったので、これらの変数に対して一般的な対数変換および平方根変換を適切に行い、統計解析を実施した。

結果

統計解析

cas実施前、実施の翌日および30日後に各患者に対して神経学的検査を実施した。30日有病率は、cas実施後30日時点で残存する何らかの新規神経学的徵候と定義した。

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表2 多変量ロジスティック回帰分析の結果による統計値。CASに関連する新規のDWI病変に対する独立予測因子を示す。

<table>
<thead>
<tr>
<th>因子</th>
<th>係数</th>
<th>標準誤差</th>
<th>p 値</th>
</tr>
</thead>
<tbody>
<tr>
<td>糖尿病</td>
<td>0.644</td>
<td>0.442</td>
<td>0.145</td>
</tr>
<tr>
<td>近位バルーンプロテクション</td>
<td>0.687</td>
<td>0.456</td>
<td>0.132</td>
</tr>
<tr>
<td>LDLコレステロール (log)</td>
<td>8.300</td>
<td>3.703</td>
<td>0.021</td>
</tr>
<tr>
<td>SIR (log)</td>
<td>4.207</td>
<td>1.828</td>
<td>0.007</td>
</tr>
<tr>
<td>プラーク容積 (√)</td>
<td>0.157</td>
<td>0.056</td>
<td>0.042</td>
</tr>
</tbody>
</table>

LDL:低比重リポタンパク。SIR:信号強度比。
うプラークを特定し得ることを示した。SIR およびプラーク容積は, N 群よりも P 群において有意に高値であった。さらに, 新規の同側性 DWI 病変の数は, SIR およびプラーク容積と正の相関を示していた。CAS 実施後の新規の DWI 病変の数に関しては, 軽度または重度の脳卒中発症との明確な関連性が報告されていることから 22, SIR およびプラーク容積は DWI 病変の有用な予測因子であることが示された (表 2)。

さらに, これらの独立予測因子と DWI 病変の数との間の Spearman 相関係数を算出したところ, SIR (rs = 0.42, p = 0.005) またはプラーク容積 (rs = 0.36, p = 0.012) との間に有意な相関がみられたが, LDL-C (rs = 0.23, p = 0.110) との間にはみられなかった (図 4)。

ROC 曲線により示された CAS に関連する新規の同側性 DWI 病変を予測する上で最も信頼できるカットオフ値は, SIR が 1.80, プラーク容積が 373 mm³であった (曲 線下表面積は, SIR が 0.70, プラーク容積が 0.73)。SIR のカットオフ値が 1.80 の場合, 感度 73%, 特異度 72%, 陽性適中率 71%, 陰性適中率 75%であった。プラーク容積のカットオフ値が 373 mm³の場合, 感度 69%, 特異度 71%, 陽性適中率 75%, 陰性適中率 65%であった。

検者内の再現性は, DWI 病変の数 (ICC = 0.996, 95% CI: 0.993 ～ 0.999), SIR (ICC = 0.985, 95% CI: 0.973 ～ 0.991) およびプラーク容積 (ICC = 0.949, 95% CI: 0.911 ～ 0.971)において優れていた。検者間の再現性は, DWI 病変の数 (ICC = 0.996, 95% CI: 0.993 ～ 0.998), SIR (ICC = 0.971, 95% CI: 0.948 ～ 0.984) およびプラーク容積 (ICC = 0.913, 95% CI: 0.850 ～ 0.951)において優れていた。

考察

本研究では, 3D TIGRE 画像を使用した MR プラークイメージングにより, CAS 関連の脳塞栓の高リスクを伴うプラックを特定し得ることを示した。SIR およびブラーク容積は, N 群よりも P 群において有意に高値であった。さらに, 新規の同側性 DWI 病変の数は, SIR およびブラ ク容積と正の相関を示していた。CAS 実施後の新規の DWI 病変の数に関しては, 軽度または重度の脳卒中発症との明確な関連性が報告されていることから 22, SIR およびブラ ク容積は DWI 病変の有用な予測因子であることが示された (表 2)。

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3D T1 強調グラディエントエコーチェンジスには、2D T1 ターボスピンエコーチェンジスと比べ、顕著な樹状断面に限定された画像の方向、近接部位の解剖学的カバー度の欠如、部分体積効果に起因する定量化誤差、血管壁内の血流による信号を最小化するため、バーラス同期化画像の獲得のための心電図または末梢脈拍ユニットの必要性、不適切な検査時間効率など克服し得る。したがって、臨床現場においては 3D T1GRE の方が実用的である。さらに、3D T1GRE シーケンスは、IPH の特徴において、2D ファーストスピンエコーまたはターボスピンエコーチェンジスよりも高い診断能力を示すといわれている4,19。3D T1GRE シーケンスが、プラククの不安定性評価において好評を博しているにもかかわらず、CAS に伴う脳塞栓予防に関する 3D T1GRE シーケンスの有用性を判定することは、実施されていなかった。本研究の結果では、3D T1GRE 画像が CAS に伴う脳塞栓のリスク評価において有用であること、さらに、CAS に伴う脳塞栓を予測する、最も信頼性あるカットオフ値が 1.80 を示した。T1 強調画像におけるプラクク信号はかなり多様であり、磁場強度 24, TR25, シーケンス 26 により異なるため、我々も含めて、一般的妥当性のあるカットオフ値を示すことができなかった。しかし、T1 信号強度が上昇するほど、CAS 関連の脳塞栓のリスク因子として確実になる。

プラククが大きくなるほど、アテローム性動脈硬化の負荷および露出面は大きくなり、これにより、CAS 実施中により多くのプラクク片を放出するリスクが高くなると推定される。しかし、現在までに、頸動脈プラクク容積と CAS に伴う脳塞栓のリスク上昇との関係性を評価した研究はなかった。頸動脈狭窄の重症度は、脳卒中の危険因子として重要であり、頸動脈介入が患者に有益であるか否かの判断に使用される。残念ながら、血管の狭窄は、アテローム性プラククの量を必ずしも反映するわけではない。狭窄率からプラクク容積を評価する時に過小評価する懸念があるのは、再構築により拡大した動脈内径を血管造影的に評価する困難がある。しかし、プラクク容積の増加は、頸動脈狭窄の重症度を反映していると考えられる。

結論

3D T1GRE シーケンスは、CAS に伴う脳塞栓の危険が高い不安定プラククの特定に有用である。3D T1GRE 画像の評価では、SIR およびプラクク容積の増加が CAS に関連の DWI 病変の発現に有効であることが示唆された。プラクク容積の増加は、CAS 関連の脳塞栓の危険因子が増加したと認識されるようであることが示唆された。

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