

Symptomatic low-grade carotid stenosis with intraplaque hemorrhage and expansive arterial remodeling is associated with a high relapse rate refractory to medical treatment

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1 **Abstract**

2 **Background:** Carotid plaque characteristics considerably influence future risk of stroke.  
3 However, the severity of stenosis does not accurately reflect plaque burden in patients  
4 with expansive arterial remodeling.

5 **Objective:** The present study aimed to determine the therapeutic outcome of  
6 symptomatic carotid low-grade stenosis with vulnerable plaque based on MRI  
7 characterization.

8 **Methods:** We studied 25 (male, n = 23; age, 74.2 ± 5.6 years) of 29 consecutive patients  
9 with symptomatic carotid low-grade stenosis (< 50%) and both high-signal plaque and  
10 expansive remodeling on T1-weighted MR images. The remaining four were excluded  
11 due to impending stroke. A single antithrombotic and statin were administered and  
12 recurrent ischemic stroke was treated with dual antithrombotics. We considered carotid  
13 endarterectomy (CEA) when recurrence was refractory to aggressive medical treatment.

14 **Results:** During a 31.3 ± 16.4 month follow-up, 11 of the 25 patients developed a total  
15 of 30 recurrent ischemic events (46.0% per patient-year). The patients' characteristics  
16 did not significantly differ between the groups with and without recurrence (n = 11 and  
17 n = 14, respectively). Seven of 11 patients in the recurrence group who were treated  
18 with CEA remained free of ischemic events during a postoperative follow-up of 19.1 ±  
19 14.6 months.

20 **Conclusion:** Symptomatic low-grade carotid stenosis with vulnerable plaque confirmed  
21 by MRI was associated with a high rate of stroke recurrence that was refractory to  
22 aggressive medical treatment. However, CEA was safe and effective for such patients.  
23 Plaque characterization by MRI has potential for more accurate stroke risk stratification  
24 in the management of carotid low-grade stenosis.

1 Key words: atherosclerosis, carotid artery disease, carotid endarterectomy, magnetic

2 resonance imaging, vulnerable plaque

3

4 Short Title: Carotid stenosis with vulnerable plaque

5

## 1 **Introduction**

2 Several large multicenter trials have established that carotid endarterectomy (CEA)  
3 significantly reduces stroke risk compared with medical treatment in patients with  
4 moderate to high-grade stenosis, but has no apparent benefit for those with low-grade  
5 stenosis.<sup>1-4</sup> The assessment of stroke risk from carotid atherosclerosis and determination  
6 of the need for surgical intervention in these randomized trials have been based on  
7 angiographic or ultrasonographic evaluations of stenosis rates.<sup>5</sup>

8 Accumulating evidence from recent vascular biology studies indicates that plaque  
9 stability depending on several factors such as plaque components, volume and  
10 morphological characteristics has a large impact on the risk of ischemic events from  
11 atherosclerotic disease.<sup>6-9</sup> Therefore, the importance of evaluating not only the severity  
12 of stenosis but also the vessel wall itself has been widely recognized for the  
13 management of carotid stenosis. While carotid plaque is generally assessed by  
14 ultrasonography, MRI has been gaining importance in the evaluation of carotid  
15 atherosclerosis with recent technological developments in MRI equipment and imaging  
16 sequencing. Many investigations have demonstrated that carotid MRI can accurately,  
17 non-invasively and objectively provide a considerable amount of information about  
18 carotid atherosclerosis.<sup>10-13</sup> Moreover, several reports have revealed an important  
19 characteristic of plaque associated with a high risk of stroke on MR images.<sup>14-17</sup>

20 Luminography does not necessarily reflect a significant burden of atherosclerotic  
21 plaque due to expansive arterial remodeling in some patients with carotid stenosis.<sup>18,19</sup>  
22 Some might be at high risk for stroke even if angiography reveals only mild stenosis.  
23 Therefore, meticulous risk assessment for ischemic events based on plaque evaluation  
24 in addition to stenosis rates is significant, particularly for patients with low-grade

1 stenosis. However, few reports have assessed risk for mild stenosis based on plaque  
2 characterization.<sup>20</sup>

3 The present study retrospectively assesses the therapeutic outcomes of symptomatic  
4 carotid low-grade stenosis using MRI plaque evaluation at a single center.

5

## 6 **Methods**

### 7 **Patients**

8 We initially identified 29 consecutive patients with symptomatic carotid low-grade  
9 stenosis (< 50%) accompanied by both high-signal plaque and expansive remodeling on  
10 T1-weighted MR images and a history of presenting at our institution between January  
11 2004 and May 2009. We excluded four with impending stroke and finally studied data  
12 from 25 patients (male, n = 23; age, 74.2 ± 5.6 years).

13 Expansive remodeling was diagnosed using carotid MRI and the criteria of Hardie et  
14 al.<sup>21</sup>

15 Symptomatic patients were defined as those who presented with transient ischemic  
16 attack (TIA), ischemic stroke, or amaurosis fugax in the territory of the ipsilateral  
17 carotid artery at the time of admission. If necessary, patients underwent Holter  
18 monitoring, transesophageal echocardiography or aortic MRI and were checked by  
19 cardiologists. We excluded patients when cardiogenic or aortogenic embolism remained  
20 as the possible etiology.

21 Our institutional Ethics Committee approved the study, and all patients provided  
22 written informed consent to analyze their records and publish the findings.

### 23 **Imaging**

24 The severity of carotid artery stenosis was evaluated by digital subtraction

1 angiography (DSA), computed tomography angiography (CTA), or magnetic resonance  
2 angiography (MRA) using the North American Symptomatic Carotid Endarterectomy  
3 Trial (NASCET) criteria.<sup>3</sup> All patients who were scheduled for CEA were also examined  
4 by DSA.

5 Atherosclerotic plaque associated with intraplaque hemorrhage (IPH) was diagnosed  
6 when axial T1-weighted 3D gradient-echo black blood (BB)-MRI images revealed high  
7 signals relative to the sternocleidomastoid muscle.<sup>22</sup> Using axial MR images of areas  
8 with the highest rate of stenosis, relative overall plaque MR signal intensity (roSI) was  
9 measured and compared with plaque MRI signals as described.<sup>23</sup>

10 Plaque in the patients who underwent CEA was characterized in more detail by  
11 obtaining several additional MR images as follows. Plaque components were precisely  
12 evaluated using 2D spin-echo BB-MRI,<sup>23</sup> plaque distribution was evaluated using  
13 long-axis 3D inversion-recovery turbo field echo BB-MRI,<sup>24</sup> and fibrous cap rupture or  
14 erosion was detected using 3D time of flight (TOF) MRI.<sup>25</sup>

15 The parameters of each MR imaging sequences were as follows.

16 Axial black-blood T1-weighted images (3D gradient-echo): field of view, 220 mm;  
17 matrix size, 179 × 256; TR/TE, 30/5.8 msec; flip angle, 20°.

18 Axial black-blood T1-weighted images (2D double IR-TSE): field of view, 150 mm;  
19 matrix size, 256 × 256; TR/TE, 700-1000 (1 cardiac cycle)/12 msec; flip angle, 110°;  
20 slice thickness, 3.0 mm.

21 Long-axis T1-weighted images (3D IR turbo field echo): field of view, 150 mm; matrix  
22 size, 320 × 512; TR/TE/TI, 10/2.7/500 msec; flip angle, 35°; slice thickness, 1.6 mm.

23

24 Treatment

1 Medical treatment was started essentially with a single antithrombotic drug selected  
2 from among aspirin, ticlopidine, clopidogrel and cilostazol. Concomitant hypertension,  
3 hyperlipidemia or diabetes was also treated if necessary. Angiotensin II receptor  
4 blockers and statins were preferentially administered to control hypertension and  
5 hyperlipidemia, respectively. Dual antithrombotic therapy was administered if patients  
6 developed recurrent ischemic stroke or had other ischemic vascular diseases. Ischemic  
7 symptom recurrence was defined as TIA, MRI-confirmed infarct or amaurosis fugax in  
8 the territory of the ipsilateral carotid artery.

9 We examined the implementation of CEA when patients presented with more than  
10 two recurrences despite maximal medical therapy, had no other general problems and  
11 consented to surgical intervention. Carotid endarterectomy proceeded under general  
12 anesthesia and with intra-operative monitoring of somatosensory evoked potentials  
13 (SEP) and near-infrared spectroscopy (NIRS). An internal shunt was selectively applied  
14 when the SEP amplitude fell by > 50% or the value of NIRS dropped by > 20%.  
15 Patients continued medical treatment with a single antithrombotic after undergoing  
16 CEA.

#### 17 Statistical analysis

18 We investigated the number of recurrences during follow-up under medical treatment  
19 (period between starting medical treatment and surgical intervention for patients who  
20 underwent CEA). Differences in risk factors, medical regimen, roSI on BB-MRI, and  
21 duration of follow-up were analyzed between groups with and without recurrence. We  
22 also analyzed excised specimens, perioperative complications and postoperative  
23 recurrence after CEA.

24 Numerical data are expressed as means  $\pm$  standard deviation. Statistical significance

1 was calculated using Student's *t* test or Fisher's exact test and probability values of <  
2 0.05 were considered significant. All data were statistically analyzed using SPSS 12.0  
3 for Windows.

4

## 5 **Results**

6 During a follow-up period of  $31.3 \pm 16.4$  months while under medical management,  
7 11 (44%) of 25 patients developed a total of 30 ischemic recurrences (mean,  $2.73 \pm 1.85$   
8 each). The annual recurrence rate under medical management was thus 46.0% per  
9 patient-year. None of age, gender, hypertension, hyperlipidemia, diabetes, ischemic  
10 heart disease, atrial fibrillation, medical regimen, roSI and duration of follow-up  
11 significantly differed between the groups with ( $n = 11$ ) and without ( $n = 14$ ) recurrence  
12 (Table 1).

13 Seven of 11 patients with recurrence underwent CEA  $12.1 \pm 10.4$  days after the last  
14 ischemic attack. The duration between the initial event and CEA was  $35.4 \pm 16.9$   
15 months and the number of recurrences before CEA was  $3.29 \pm 2.06$ . The findings of  
16 DSA revealed a stenosis rate of  $27.1 \pm 9.9\%$  and obvious ulceration in two patients.  
17 Distinctly high signals of plaque were found on BB-MRI of all patients and the roSI  
18 was  $1.84 \pm 0.21$ . Preoperative TOF-MRI assessment of fibrous cap predicted ruptured or  
19 thin fibrous cap in four patients and the quality of MR images from one patient was too  
20 low to evaluate. Internal shunts were used in two of the CEA procedures. Histological  
21 assessment of excised plaques confirmed massive and fresh IPH in all specimens. Five  
22 and two plaques had ruptured and eroded fibrous caps, respectively. Postoperative  
23 diffusion weighted images confirmed the absence of perioperative complications such  
24 as new infarcts in all patients, whereas a neck hematoma and transient hoarseness



1 occurred in one patient each.

2 No ischemic events, including those in the contralateral hemisphere, were confirmed  
3 during the postoperative follow-up period of  $19.1 \pm 14.6$  months (Table 2).

4

#### 5 **Illustrative case (Patient No. 5)**

6 This 73-year-old man with a history of minor stroke presented with right arm  
7 weakness at another hospital during July 2006. He remained under treatment with an  
8 antithrombotic until October 2007 when he was admitted to our hospital with TIA  
9 manifesting as right arm weakness and sensory disturbance. While left carotid  
10 angiography revealed only 26% stenosis with slight luminal irregularity (Fig. 1A), axial  
11 and long-axis BB-MRI clearly showed appreciable high-signal plaque in the form of  
12 expansive remodeling at the carotid bifurcation indicating fresh IPH (Fig. 1B and C).  
13 Neither atherosclerotic plaque along the ascending aorta on aortic MRI nor intracardiac  
14 thrombus on transesophageal echocardiography was detected. Hyperlipidemia was  
15 confirmed by laboratory data upon admission.

16 These findings indicated a diagnosis of recurrent ischemic events due to  
17 artery-to-artery embolism originating from the carotid low-grade stenosis with unstable  
18 plaque. The patient was administered with dual antithrombotics and statin. He was  
19 readmitted to our hospital during July 2008 with right arm and leg weakness. Diffusion  
20 weighted images demonstrated fresh multiple minor infarcts in the left hemisphere,  
21 whereas left carotid angiography identified no appreciable elevation in the rate of  
22 stenosis.

23 Because not even maximal medical therapy could prevent recurrent ischemic events,  
24 the patient provided written informed consent to undergo CEA on the seventh day from

1 the last event. The postoperative course was uneventful and no new infarct was  
2 demonstrated on diffusion weighted images obtained two days postoperatively.  
3 Macroscopic observation of an excised specimen identified a disrupted fibrous cap (Fig.  
4 1D) and histological assessment also revealed a ruptured fibrous cap and massive IPH.  
5 The patient was treated only with aspirin after CEA and he has remained stroke-free at  
6 14 months of follow-up.

7

## 8 **Discussion**

9 Carotid atherosclerosis has been widely evaluated by ultrasonography, as it is  
10 noninvasive and can provide information about luminal stenosis and, to some extent,  
11 plaque characteristics.<sup>26, 27</sup> However, limitations are associated with assessing the  
12 carotid artery using this modality since discriminating IPH from a lipid core in  
13 atherosclerotic plaque is less robust. Furthermore, plaque with dense calcification,  
14 stenosis at higher locations and patients with a short neck cannot be fully imaged using  
15 US and interpretation of the results is extremely operator-dependent.<sup>28-30</sup>

16 Since the quality of MR equipment has progressed and technical improvements have  
17 been made in MR sequences, many studies have recently demonstrated the value of  
18 high-resolution MRI for assessment of carotid plaque components, volume and  
19 morphology.<sup>10-13, 23, 31, 32</sup> That IPH, which plays a potent role in plaque vulnerability, can  
20 be visualized as intense signals on T1-weighted MR images is generally accepted and  
21 intense signals are generated more frequently by symptomatic, than asymptomatic  
22 carotid plaque.<sup>10, 15, 33</sup> The MR signal of IPH is obviously high during the acute phase  
23 and declines over time.<sup>34</sup> Prospective studies of carotid atherosclerosis have revealed  
24 that stenosis with IPH detected by MRI confers higher risk for ischemic events than that

1 without IPH in either symptomatic<sup>35</sup> or asymptomatic patients.<sup>17</sup> Considering the many  
2 reports describing MRI plaque evaluation of patients with carotid stenosis, regarding  
3 plaques with high-signal on T1-weighted MR images as being unstable and at high risk  
4 for ischemic stroke seems appropriate.

5 Few studies have examined the outcomes of medical treatment for symptomatic  
6 low-grade carotid stenosis. The European Surgery Carotid Trial (ECST) reported only a  
7 1.3% rate of ipsilateral ischemic strokes lasting beyond seven days in patients with  
8 symptomatic mild (0-29%) carotid stenosis during three years of follow-up (0.43% per  
9 year) when stroke recurrence assessment was based on merely stenosis rate evaluation.<sup>36</sup>  
10 Among patients with < 50% stenosis in the NASCET study, the 5-year rate of any  
11 ipsilateral stroke was 18.7% in the medically treated group (3.74% per year).<sup>3</sup> Fritz et al.  
12 reported an 8.6% rate of ischemic events including TIA and stroke during two years of  
13 follow-up (4.3% per year) in 35 medically treated symptomatic patients with low grade  
14 stenosis (< 50%) or ulcerated plaques.<sup>37</sup> Although the rate of recurrent ischemic events  
15 has some variation among these studies, probably because of differences in the  
16 definition of ischemic events or rate of stenosis, they nevertheless concluded that  
17 patients with symptomatic low-grade stenosis did not benefit from CEA because the  
18 outcome of medical treatment was favorable.

19 To the best of our knowledge, only Altaf et al.<sup>20</sup> prospectively analyzed recurrence  
20 risk based on MRI plaque evaluation in addition to rates of stenosis among patients with  
21 symptomatic carotid low-grade stenosis. They showed that the rates of recurrent  
22 ischemic events in patients with symptomatic mild stenosis (30-49%) treated medically  
23 during a median follow-up period of 28 months were 25% and 10% in plaques with IPH  
24 detected or not by MRI, respectively. They concluded that carotid plaques with intense

1 signals on T1-weighted MR images are at higher risk for ischemic recurrence even  
2 when the rate of stenosis is not significant.

3 The present retrospective analysis found ischemic recurrence in 44% of medically  
4 treated patients who had high-signal plaque and expansive remodeling on T1-weighted  
5 carotid MR images, and an annual recurrence rate reached 46.0% per patient-year. A  
6 detailed comparative discussion is limited because reports on outcomes of medical  
7 treatment for symptomatic mild stenosis based on MRI plaque evaluation are scarce.  
8 Nonetheless, we can offer some explanations for the remarkably high rate of ischemic  
9 recurrence in this study. Recurrence in our report included both stroke and TIA. The  
10 recurrence rate excluding TIA in this study was still high at 36.8% per patient-year.  
11 Stroke was diagnosed based on diffusion-weighted images regardless of the severity of  
12 ischemic symptoms. The chances of an oversight in ischemic events seemed low  
13 because patients were regularly followed up at a single institution. More importantly,  
14 the fact that our study patients had not only carotid plaque with IPH detected by MRI  
15 but also expansive remodeling might explain why our patients were at higher risk for  
16 ischemic events than those described by Altaf et al. Expansive plaque remodeling in  
17 patients with coronary artery atherosclerosis has been considered a major factor in  
18 vulnerable plaque.<sup>18, 19</sup> A study using a murine model of carotid artery lesions found that  
19 the macrophages characteristic of vulnerable plaques assist in expansive remodeling by  
20 promoting matrix degeneration through matrix metalloproteinase secretion.<sup>38</sup> A recent  
21 study of human carotid atherosclerosis using multidetector CT angiography also found  
22 that the incidence of expansive remodeling is much higher among symptomatic, than  
23 asymptomatic carotid plaques and that the extent of expansive remodeling correlated  
24 with atherosclerotic plaque vulnerability.<sup>21</sup>

1 With respect to the safety of CEA for treating symptomatic carotid stenosis, large  
2 clinical trials have shown that the perioperative complication rate does not depend on  
3 the rate of carotid stenosis. Rates of death, disabling stroke, or any other stroke  
4 producing symptoms for more than seven days in the ECST report were 3.7% (70-99%)  
5 and 2.3% (0-29%) for severe and mild stenosis, respectively, with no statistically  
6 significant difference.<sup>36</sup> In addition, NASCET did not find a significant difference in the  
7 rate of disabling stroke at 30 days between groups with moderate (2.8%) and severe  
8 (3.0%) stenosis.<sup>39</sup> The fact that diffusion-weighted MR imaging in the present study  
9 confirmed the absence of perioperative ischemic events demonstrated the safety of CEA  
10 for patients with symptomatic low-grade stenosis. None of the patients described herein  
11 has presented with TIA or any stroke, even though they were treated with only single  
12 antiplatelet drugs after CEA for a median postoperative follow-up of 19 months.  
13 Therefore, our results might also indicate the relevance of CEA for patients with  
14 symptomatic low-grade stenosis accompanied by vulnerable plaque confirmed by MRI,  
15 although this assertion is limited by the number of patients studied and the short period  
16 of postoperative follow-up.

17 Carotid endarterectomy was adopted as a therapeutic option for patients who were  
18 refractory to multidisciplinary medical treatment in this study. However, we could not  
19 find distinctive differences in the patients' characteristics and MRI findings between the  
20 recurrence and non-recurrence groups, which remains an issue. To discriminate patients  
21 with low-grade carotid stenosis refractory to medical treatment before recurrences or  
22 screen extremely vulnerable plaques with diagnostic imaging remains challenging. In  
23 addition to IPH and expansive arterial remodeling, fibrous cap rupture is also an  
24 important feature of vulnerable plaques. In fact, a prospective study of asymptomatic

1 carotid stenosis with MRI plaque evaluation has demonstrated that ruptured fibrous caps  
2 more significantly influence ischemic events than IPH.<sup>17</sup> Precise assessment of fibrous  
3 cap status would thus seem key to discriminating extremely vulnerable plaques. Several  
4 studies of MRI plaque characterization have shown that ruptured or thin fibrous caps  
5 can be detected as “dark bands” on TOF images<sup>25, 32, 40</sup> and have demonstrated a  
6 moderate to good correlation between MRI findings and CEA specimens for diagnosing  
7 ruptured caps. However, these reports also pointed out the limitation of fibrous cap  
8 estimation by MRI due to poor image quality when the internal carotid artery is  
9 obviously angulated or tortuous or when plaques are densely calcified. In fact, 18-34%  
10 of the patients who underwent carotid MRI were excluded from analysis of the fibrous  
11 cap in these studies. The present study found that the preoperative estimation of fibrous  
12 cap from TOF MR images agreed with histological findings of excised plaques in only 4  
13 of 7 patients. Thus, MRI is not yet satisfactory for fibrous cap assessment in the clinical  
14 setting. Improved spatial- and contrast-to-noise ratios, better spatial resolution using a  
15 higher magnetic field and faster imaging procedures will allow the identification of finer  
16 structures within atherosclerotic arterial walls<sup>41</sup> and enable more precise diagnosis of  
17 high-risk plaques for recurrent ischemic events.

18 The preventive effect against ischemic stroke for low-grade vulnerable stenosis  
19 between CEA and medical treatment should be compared. While anti-thrombotic drugs  
20 have been widely used to prevent strokes,<sup>42</sup> more aggressive medical treatment with  
21 dual anti-platelet medication with aspirin and clopidogrel is apparently more effective  
22 than aspirin alone.<sup>43</sup> In addition, statins seem to be appreciably effective against many  
23 disorders caused by systemic atherosclerosis. The ability of aggressive lipid-lowering  
24 therapy with statins to reduce the incidence of ischemic stroke has been verified by

1 several large randomized studies.<sup>44, 45</sup> In addition, high-resolution MRI studies have  
2 demonstrated that statins suppress, stabilize and reduce carotid atherosclerotic  
3 plaque.<sup>46-48</sup> Thus, the outcome of medical treatment for carotid stenosis should be  
4 significantly improved by early multifaceted medical intervention for patients with  
5 high-risk atherosclerotic disease. Comparing the long-term results between CEA and  
6 aggressive medical treatment is mandatory to validate the use of CEA for low-grade  
7 high-risk stenosis.

8 One limitation of the present study is that it was a retrospective analysis of a small  
9 patient cohort over a relatively short follow-up period. Importantly, our patients did not  
10 have symptomatic low-grade carotid stenosis but had plaque with positive remodeling  
11 that was evident on high-signal on T1-weighted images. Therefore, the present findings  
12 are not applicable to symptomatic low-grade stenosis in general. Nevertheless, our  
13 findings promote awareness of the limitations of future stroke risk assessment based  
14 solely on the severity of carotid stenosis.

## 15 **Conclusion**

16 Among patients with symptomatic low-grade carotid stenosis, those with plaque  
17 containing IPH demonstrated by MRI undergoing outward remodeling were associated  
18 with a high rate of stroke recurrence regardless of medical treatment. Carotid  
19 endarterectomy prevented further stroke in patients who were refractory to aggressive  
20 medical therapy and was validated for treating a subset of patients with low-grade, but  
21 high-risk carotid stenosis determined by plaque evaluation.

22

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- 11

1 **Figure legends**

2

3 Figure 1. Angiographic and MR images of left carotid artery obtained from Patient 5.

4

5 A. Preoperative digital subtraction angiography (DSA) image acquired after two strokes  
6 that were refractory to medical treatment. Bulb shows slight luminal irregularity but  
7 only 26% stenosis based on North American Symptomatic Carotid Endarterectomy  
8 Trial (NASCET) criteria.

9 B. Long-axis T1-weighted black-blood MR image of carotid bifurcation shows large  
10 amount of plaque without significant narrowing of internal carotid artery (ICA lumen;  
11 expansive arterial remodeling).

12 C. T1-weighted black-blood MR image perpendicular to long axis of ICA at bifurcation  
13 also indicates expansive remodeling. \*ICA lumen. SCM, sternocleidomastoid muscle.

14 D. Excised carotid plaque has yellowish luminal surface at carotid bifurcation and  
15 extensively thinned and partially disrupted fibrous cap on luminal surface of the ICA.  
16 CCA, common carotid artery.



Figure 1-A



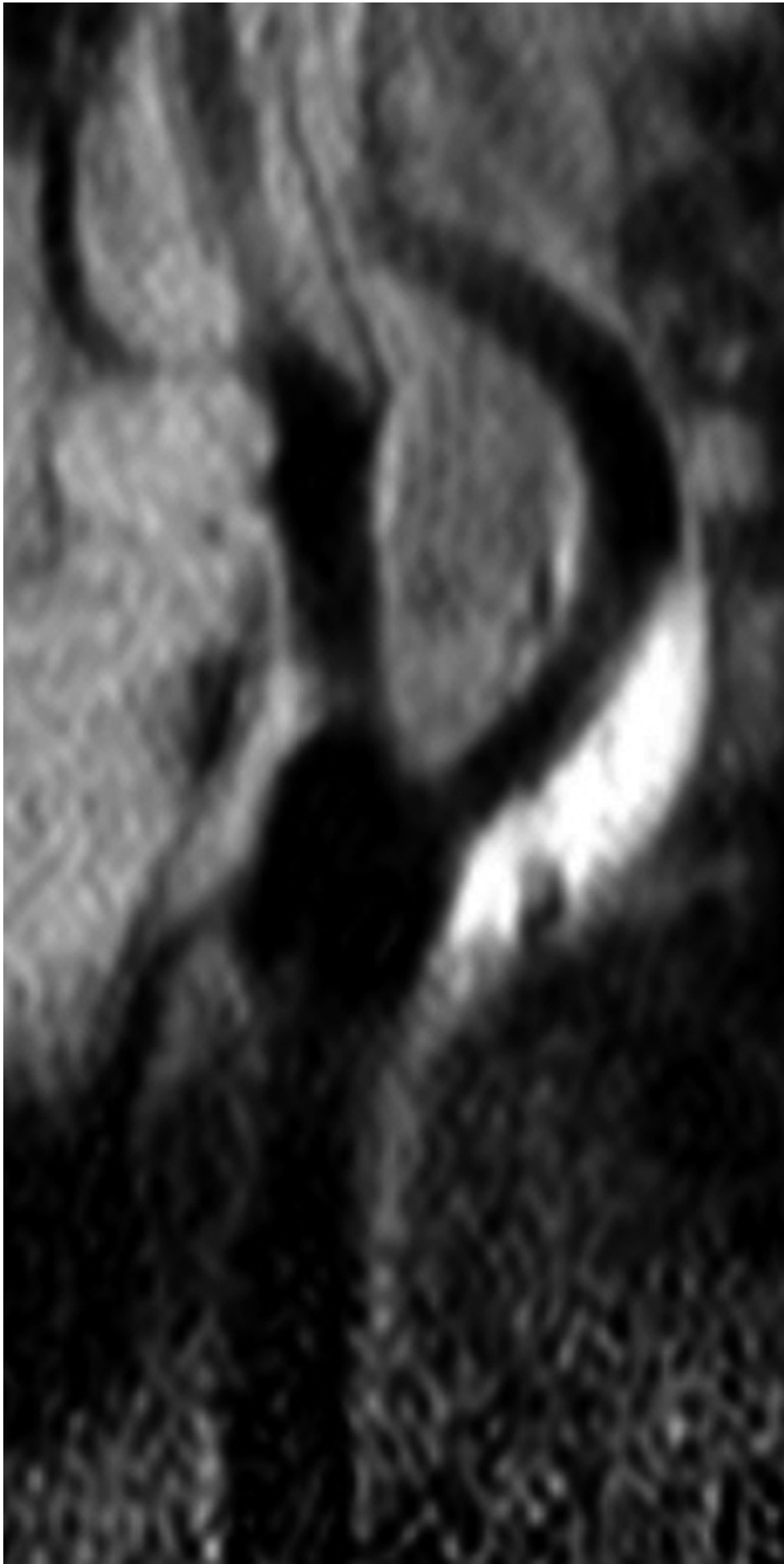


Figure 1-B

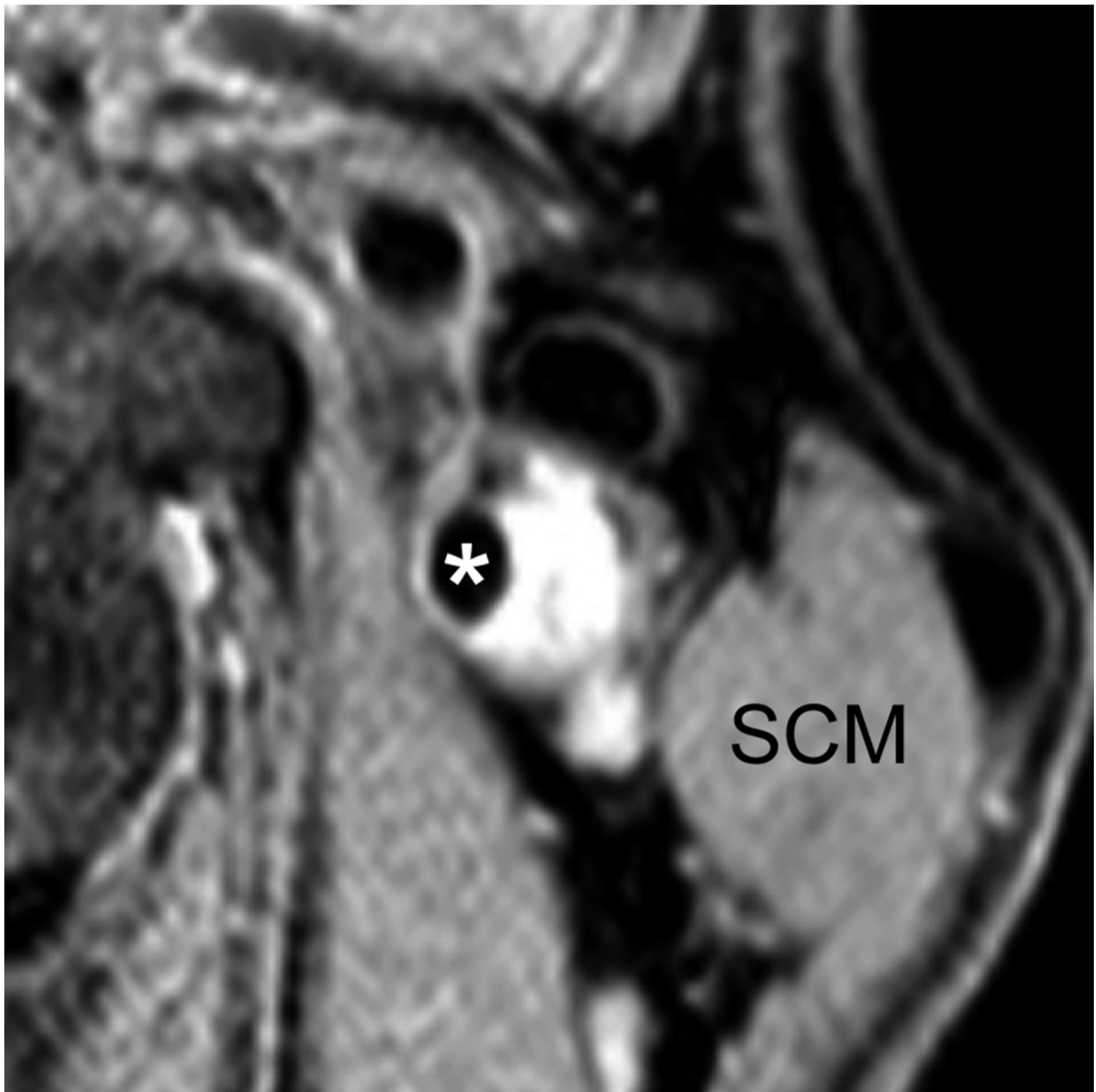
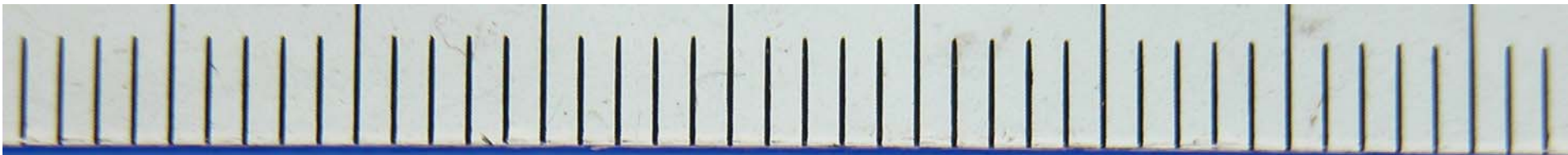


Figure 1-C



ICA



CCA



Figure 1-D

**Table 1. Characteristics of the patients with symptomatic low-grade carotid stenosis.**

	Total (n=25)	Recurrence (n=11)	No recurrence (n=14)	P value
Age (years)	74.2 ± 5.6	73.7 ± 7.2	74.6 ± 4.2	0.716
Gender (male)	23 (92.0%)	10 (90.9%)	13 (92.9%)	0.697
Hypertension	21 (84.0%)	10 (90.9%)	11 (78.6%)	0.396
Hyperlipidemia	18 (72.0%)	9 (81.8%)	9 (64.3%)	0.305
Diabetes	8 (32.0%)	4 (36.4%)	4 (28.6%)	0.504
Ischemic heart disease	10 (40.0%)	4 (36.4%)	6 (42.9%)	0.534
Atrial fibrillation	3 (12.0%)	2 (18.2%)	1 (7.1%)	0.407
<b>Medical treatment</b>				
Statins	17 (68%)	9 (81.8%)	8 (57.1%)	0.19
Dual antiplatelet drugs	15 (60%)	9 (81.8%)	6 (42.9%)	0.058
Warfarin	2 (8%)	2 (18.2%)	0	0.183
roSI of carotid MRI	1.65 ± 0.30	1.70 ± 0.27	1.61 ± 0.32	0.459
Number of recurrences		2.7 (1-6)	0	
f/u period (months)	31.3 ± 16.4	34.3 ± 16.6	29.0 ± 16.4	

roSI, relative overall signal intensity on axial T1-weighted images of whole carotid plaque except for lumen at maximal stenosis relative to adjacent sternocleidomastoid muscle;<sup>23</sup> f/u, follow-up.

Table 2. Carotid endarterectomy for symptomatic low-grade carotid stenosis refractory to aggressive medical treatment.

No. of patients	1	2	3	4	5	6	7	Average	SD
Age (years) /gender (M/F)	80/M	68/M	72/M	74/M	73/M	77/M	73/F	73.9	3.8
Duration from initial stroke to CEA (months)	60	18	46	16	24	49	35	35.4	16.9
No. of recurrences	6	6	2	1	2	2	4	3.3	2.1
Rate of stenosis	25	25	47	13.6	26.3	27.8	25.3	27.1	9.9
Ulceration on DSA	+	-	+	-	-	-	-		
roSI on carotid MRI	2.12	1.58	2.08	1.77	1.87	1.88	1.61	1.84	0.21
<b>Histological findings</b>									
Intraplaque hemorrhage	+	+	+	+	+	+	+		
Status of fibrous cap	Ruptured	Eroded	Ruptured	Eroded	Ruptured	Ruptured	Ruptured		
New DWI lesion after CEA	-	-	-	-	-	-	-		
Other complications	Neck swelling	-	Transient hoarseness	-	-	-	-		
mRS on discharge	1	0	1	1	1	1	1		
Ischemic events after CEA	-	-	-	-	-	-	-		
f/u period (months)	47	24	23	17	14	5	4	19.1	14.6

No, number; SD, standard deviation; DSA, digital subtraction angiography; roSI, relative overall signal intensity; MRI, magnetic resonance imaging; DWI, diffusion weighted image; mRS, modified Rankin scale; f/u, follow-up.