Asymptomatic Carotid Lesions and Silent Cerebral Infarction

Hidetaka Hougaku, MD; Masayasu Matsumoto, PhD; Nobuo Handa, PhD; Hiroaki Maeda, MD; Taiji Itoh, MD; Yoshitane Tsukamoto, MD; Takenobu Kamada, PhD

Background and Purpose  Few studies have investigated the relationships between asymptomatic carotid lesions and silent infarcts confirmed on magnetic resonance imaging.

Methods A consecutive series of 117 subjects (average age, 62±9.4 years) who were free from neurological deficit but had at least one established risk factor for stroke were investigated by B-mode carotid ultrasonography and magnetic resonance imaging of the brain. Carotid lesions were evaluated by plaque score, maximum percent stenosis, and the existence of ulcerated lesions. The relations between the carotid lesions and the incidence, size, or localization of the brain lesions were investigated.

Results The incidence of silent infarcts was 42% in all subjects and significantly increased with advancing age (P<.05). Most lesions were smaller than 1 cm in diameter and were usually localized in the subcortical white matter or the basal ganglia. The percentage of subjects with infarcts increased significantly as the plaque score increased (P<.05) or when subjects had high-grade stenosis (P<.05) or ulcerated lesions (P<.01). These relationships were also noted in each decade of age. A higher incidence of larger lesions (>1 cm) was found in the brain hemisphere ipsilateral to the carotid lesion, particularly in subjects with high-grade stenosis or ulcerated lesions (P<.01). Multivariate analysis indicated significant correlations with silent infarcts for age, hypertension, and plaque score.

Conclusions Both the severity and characteristics of asymptomatic carotid lesions estimated by B-mode ultrasonography were closely related to the appearance of silent infarcts. These results demonstrate that noninvasive assessment of carotid lesions can be useful in predicting the existence of silent cerebral infarction even in patients free from neurological deficits. (Stroke. 1994;25:566-570.)

Key Words  • carotid arteries • cerebral infarction • magnetic resonance imaging • ultrasomics

Silent cerebral infarction (SCI) is considered the preliminary stage of accidental stroke, and investigating its clinicopathology may elucidate the underlying mechanism of stroke onset and help to prevent this disabling disease. Several studies have examined the incidence of SCI and its relation to stroke risk factors. However, few reports have detailed the relationship between each risk factor for stroke and SCI detected by magnetic resonance imaging (MRI).2,7 The most sensitive method for evaluating organic changes in the brain.

Considerable controversy exists regarding the management of asymptomatic carotid lesions (ACL). Although there is no doubt that the existence of carotid lesions is one of the major risk factors for systemic atherosclerotic disease (such as ischemic heart disease and cerebrovascular accident10-12), the efficacy of surgical treatment for ACL has not been established.13,14 In 1992 Norris and Zhu15 investigated the relationship between carotid stenosis and silent stroke detected by x-ray computed tomography (CT) to determine the danger of progression from ACL to stroke.15 They demonstrated that asymptomatic carotid stenosis was associated with infarcts ipsilateral to the stenosis at a higher rate as stenosis increased, and they suggested that SCI was an indication for carotid endarterectomy (CEA) even in asymptomatic patients. Although their research was valuable, they did not have asymptomatic subjects without carotid stenosis as controls to determine the effect of carotid stenosis alone. They also did not have sufficient data on risk factors, particularly hypertension, to comment on SCI localizations.

In this study, to clarify the role of ACL in the appearance of SCI, we attempted to evaluate the effects of carotid lesions on brain vessels, including (1) direct effects from carotid stenosis and ulcerated carotid lesions and (2) the possible relationships between small cerebral penetrator arteriosclerosis and carotid atherosclerosis. By using B-mode ultrasonography, we evaluated ACL by three indexes (plaque score to indicate the severity of systemic atherosclerosis, maximum percent stenosis, and existence of ulcerated lesions) and compared these with the rate of occurrence, size, and localization of SCI confirmed on MRI. Risk factors for stroke were also investigated.

Subjects and Methods

Between May 1989 and March 1991, 117 consecutive patients (mean±SD age, 62.0±9.4 years) who had at least one stroke risk factor but did not have a history of stroke were randomly chosen to be evaluated by B-mode carotid ultrasonography and brain MRI. These patients were outpatients of the First Department of Medicine (including diabetology, cardiology, hypertension, and stroke sections) and were investigated for their atherosclerotic or arteriosclerotic involvement with these examinations. Those who had cardiogenic risk factors such as atrial fibrillation, valvular heart disease, and myocardial infarction were excluded. Careful history taking...
Plaque score = subject+(contralateral plaques)

![Diagram of carotid bifurcation and measurements obtained from B-mode ultrasonography. Plaque score was computed by summing maximum thickness in millimeters of plaques in each segment of both sides (a+b+c+contralateral plaques). S1 indicates region of internal carotid artery (ICA) <15 mm distal to its bifurcation from the common carotid artery (CCA); S2, region of ICA and CCA <15 mm proximal to bifurcation; S3, region of CCA >15 mm and <30 mm proximal to bifurcation; and S4, region of CCA >30 mm proximal to bifurcation below flow divider. Length of individual plaques was not considered in determining plaque score. From HANDA et al.]

Carotid Lesions and Silent Infarction

Hougaku et al.

Results

The incidence of stroke risk factors in all subjects (n=117) was as follows: hypertension, 65%; diabetes mellitus, 31%; hypercholesterolemia, 58%; and ischemic heart disease, 12%. Ischemic heart disease was the only risk factor that increased with advancing age (P<.05).

The incidence of SCI was 42% in all 117 subjects. It increased significantly with advancing age from 18% in those aged 40 to 49 years to 29% in those aged 50 to 59 years, 46% in those aged 60 to 69 years, and 63% in those aged 70 to 79 years (P<.05). A total of 256 SCI lesions were detected, and most were localized in the subcortical white matter or the basal ganglia. Only one subject had two transcortical infarctions in the bilateral parietal regions. Three lesions were located in the infratentorial area. Among the 253 supratentorial lesions, there were more lesions in the right hemisphere than the left (134 versus 119). The average number of lesions in all subjects was 2.2±3.8 (5.2±4.3 in the subjects with SCI). Ninety-two percent of all lesions were less than 1 cm in diameter.

Seventy-five of 117 subjects (64%) had plaques on at least one side of the carotid arteries (47% on the right carotid and 49% on the left). The proportions of the four groups divided by plaque score were as follows: none, 36%; mild, 38%; moderate, 15%; and severe, 11%. Fig 2 shows the relationship between age and severity of the plaque score. The percentage of subjects with moderate to severe plaque scores significantly increased with advancing age (P<.05), while there was no significant increase in the percentage of subjects with mild to severe plaque score because the incidence was relatively high even in those aged 40 to 49 years or 50 to 59 years. However, the incidence of risk factors in the group with moderate to severe plaque scores was as follows: hypertension, 77%; diabetes mellitus, 37%; hypercholesterolemia, 60%; and ischemic heart disease, 30% (61%, 29%, 58%, and 6%, respectively, in the
Fig 2. Bar graph shows relationships between age and severity of carotid atherosclerosis (plaque score). Open bars indicate the percentage of the group with plaque score of none; hatched bars, those that scored mild; and closed bars, those that scored moderate to severe.

group that scored none to mild), and only ischemic heart disease significantly correlated with the appearance of the moderate to severe plaque score \( (P<.01) \). As the number of risk factors increased, the severity of the plaque score increased, although without statistical significance. For those with one risk factor \((n=51)\), 19% had a moderate to severe plaque score; for those with two risk factors \((n=46)\), 27% had similar plaque scores, as did 41% of the 22 patients with three or four risk factors. The average ages of these three groups were 62.0±9.9, 62.5±9.2, and 61.7±9.2 years, respectively.

The rate of high-grade stenosis was 6% in the right 117 vessels and 5% in the left 117 vessels. The percentage of ulcerated lesions was 7% in the right vessels and 6% in the left vessels. Almost all subjects who had high-grade stenosis and/or ulcerated lesions had severe plaque, except two in the moderate plaque score group (one with a high-grade stenosis and another with an ulcerated lesion).

Fig 3 shows that the higher the plaque score, the higher was the incidence of SCI; the difference was statistically significant \( (P<.05) \). In particular, subjects with moderate to severe plaque scores had a markedly higher incidence of SCI than those with plaque scores of none to mild \( (P<.01) \). In subjects without hypertension \((n=40)\), the incidence of SCI in those with moderate to severe plaque scores was 43% \((3/7)\), double that of those with plaque scores of none to mild \((21%, 7/33)\). The SCI rate increased significantly when subjects had high-grade stenosis \((P<.05)\) or ulcerated lesions \((P<.01)\). In subjects with SCI, all those with high-grade stenosis \((n=7)\) had subcortical border-zone infarcts; 74% of subjects without high-grade stenosis \((n=42)\) had border-zone infarcts, and the remaining 26% \((n=11)\) had infarcts only in the basal ganglia.

In regard to the number of SCI lesions in each subject, the number of SCI lesions was significantly correlated with the plaque score \( (r=.22, P<.05) \). Furthermore, the average number of lesions in the subjects with high-grade stenosis or ulcerated lesions \((n=12)\) was 4.3±4.2, significantly higher than that in those without such severe lesions \((1.9±3.7; n=105, P<.05)\).

The SCI rate ipsilateral to each vessel in subjects with no \((n=121)\), low-grade \((n=100)\), or high-grade \((n=13)\) stenosis was 31%, 33%, or 77%, respectively. This difference was significant \( (P<.01) \). Moreover, the incidence of SCI ipsilateral to each vessel in subjects with an ulcerated lesion \((n=15)\) was 80%, significantly higher than that in those without an ulcerated lesion \((32%; n=219, P<.01)\). These results are also shown in Fig 3.

The Table shows the relationships between the severity of carotid atherosclerosis and the rate of SCI in each decade of age \((50 to 59 years, 60 to 69 years, and 70 to 79 years)\). The SCI rate in patients with moderate to severe plaque scores was rather high at more than 50% in those aged 50 to 59 years and significantly increased with advancing age \( (P<.05) \), while that of subjects without carotid lesions was 17% in those aged 50 to 59 years and 50% in those aged 70 to 79 years. Furthermore, subjects with high-grade stenosis or ulcerated lesions had a surprisingly high SCI rate \( (75%); n=37, P<.01)\). Particularly in those aged 50 to 59 years, the SCI rate in those with high-grade stenosis or ulcerated lesions was significantly higher than in those without plaques \( (P<.05)\).

In regard to the relationship between the severity of carotid lesions and the size of SCI lesions, the occurrence of larger lesions \( (>1 cm)\) was significantly more frequent in subjects with high-grade stenosis \((22\%)\).
we evaluate ACL from two different perspectives: the gate how ACL was related to SCI and showed the direct effect from stenosis or ulcerated lesions and the lar accident. In this study we attempted to investi-
sclerotic disease (ischemic heart disease, cerebrovascu-
of carotid atherosclerosis can be a predictor of athero-
progression of arteriosclerotic change in the brain was
was 80% versus 54% for hypertension, 51% versus 38%
indirect effect of the severity of carotid atherosclerosis
assessment of systemic atherosclerosis could pre-
that of carotid atherosclerosis, independently of the
the direct close relationships between carotid athero-
sclerosis and SCI. Since this tendency could be observed
even in the subjects without hypertension, the progres-
seemed to make the SCI rate and the average number of
lesions higher and frequently was associated with mul-
tle small infarcts in the area supplied by perforating
arteries.1
The appearance of SCI was closely associated with
the severity of the plaque score (Fig 3). This tendency
was also observed in the evaluation of each decade of
age (Table), suggesting that the close association did
depend mainly on the increase of both incidence of
carotid lesion and SCI with advancing age but reflected
the direct close relationships between carotid athero-
sclerosis and SCI. Since this tendency could be observed
even in the subjects without hypertension, the progress-
cerebral arteriosclerosis might be paralleled by that
of carotid atherosclerosis, independently of the
effect of hypertension.
We found a strong correlation between the maximum
percent stenosis and appearance of SCI. Furthermore,
the results of the high rate of larger SCI lesions ipsilat-
eral to the high-grade stenosis and the higher rate of
border-zone infarcts in these subjects suggested that
high-grade stenotic lesions had direct hemodynamic
influence on the ipsilateral brain tissues, although the
possibility of embolic events from these lesions could
not be wholly excluded because vessels with high-grade
stenosis often showed combined ulcerated lesions
(85%) [11/13]).
In the evaluation of ulcerated lesions, similar results
were demonstrated that suggested the mechanism of
to-artery embolism. However, we could not de-
t large transcortical infarcts that are sometimes
found in embolism. There are two possible explanations for this. First, the emboli shed from carotid lesions were too small to obstruct the major arteries and produced small infarcts in the peripheral asymptomatic area (subcortical or border zone). The second possibility is that subjects who had large cortical infarcts did not participate in this study because such infarcts frequently produce neurological deficits and signs. Either way, these explanations should be verified by a long-term follow-up study of subjects with ulcerated carotid lesions.

In the relationship between appearance of SCI and various risk factors, the percentage of subjects with SCI increased as the number of risk factors in each patient increased. In particular, age and hypertension strongly and independently correlated with the occurrence of SCI. This is compatible with the results of other studies. 

Our results clearly demonstrate that the severity of carotid atherosclerosis closely correlates with the appearance of SCI. In addition to this correlation, high-grade stenosis or ulcerated lesions had more direct influence on the appearance of SCI. Conversely, these results suggest that the evaluation of ACL by noninvasive B-mode ultrasonography may be useful in predicting the appearance of latent cerebrovascular disease in the form of SCI.

Acknowledgments
This study was supported in part by the Smoking Research Foundation. We acknowledge K. Moriguchi and M. Okumura for their invaluable secretarial assistance.

References
Asymptomatic carotid lesions and silent cerebral infarction.
H Hougaku, M Matsumoto, N Handa, H Maeda, T Itoh, Y Tsukamoto and T Kamada

Stroke. 1994;25:566-570
doi: 10.1161/01.STR.25.3.566

Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1994 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/25/3/566

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/