Transcranial Doppler detection of microembolic signals in clinical practice[1]

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Summary

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The potential value of microembolic signal detection by transcranial Doppler sonography in the clinical evaluation of patients with cerebrovascular disease is investigated and particular attention given to the prevalence of microembolic signals in different clinical groups. The present study was conducted on 158 patients, 100 of whom had 120 stenoses (moderate-grade in 69 arteries, high-grade in 38) or occlusions of the carotid artery (13 cases), and 58 of whom suffered from stroke of other aetiologies in the anterior circulation. Among the 120 stenoses and occlusions, 87 were asymptomatic and 33 were symptomatic. The cerebral vessels of the patients were evaluated by continuous wave Doppler sonography, colour-coded duplex scanning, transcranial Doppler sonography and digital substraction angiography. Cardiac examination included electrocardiography, Holter monitoring and echocardiography.

Microembolic signals were found in patients only when a source of cerebral embolism was detected. Patients with vascular or cardiac embolism were likely to show microembolic signals, the frequency being not significantly different. microembolic signals were found in 33% of patients with carotid artery disease and in 31% of patients with cerebral embolism of cardiac source, 4 of the latter patients having a prosthetic cardiac valve. Microembolic signals were less prevalent in patients with moderate-grade (3/69) ICA stenosis than in patients with high-grade (9/38) stenosis ($p < 0.01$), but more prevalent in patients with symptomatic high-grade (7/15) stenosis than in cases with asymptomatic (2/23) ones ($p < 0.05$). Patients with moderate-grade stenoses and detectable microembolic signals should be further studied, as they might benefit from a more aggressive therapy, such as endarterectomy.

Keywords: microembolic signals; transcranial Doppler sonography; cerebrovascular disease; carotid artery disease; cardiopathy

Introduction

In recent years there has been much interest in the detection of microembolic signals by transcranial Doppler sonography as a new method for evaluating embolic phenomena in cerebral vessels. Most investigators have studied groups of patients comparing cerebral embolism known to be of the same origin, for example, internal carotid artery (ICA) stenoses [1–6] or heart diseases [6–9]. Other investigators [10–13] have monitored patients with ischaemic stroke of various aetiology, particular attention given, for example, to solving particular problems, such as the relation between microembolic signals and brain CT scan imaging, the source of embolism, and the effect of therapy. The main goal has been to evaluate the clinical relevance of the microembolic signals and to determine their predictive value [14].

This study attempts to show the potential role and place of microembolic signal detection in the clinical evaluation of patients with cerebrovascular disease. The goal is to define what relevance this method might have in standard practice to patients including those suffering from stroke of mixed aetiology and carotid artery disease, taking into account that it is a time consuming and laborious technology. To this end, we investigated the prevalence of microembolic signals, detected by TCD

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monitoring of the middle cerebral artery in two groups of patients: (1) those with carotid artery disease – symptomatic as well as asymptomatic, and (2) those with acute stroke of other aetiology.

Patients and methods

Patients

The first group included 100 consecutive patients (76 men, 24 women, mean age 69 years, range 52–92) with moderate-grade (30–69% reduction in diameter) or high-grade (70–99%) ICA stenosis and occlusion. Eighty patients had unilateral and 20 had bilateral ICA lesions, a total of 120 ICA stenoses or occlusions. ICA stenosis was found to be of moderate-grade in 69/120 arteries, of high-grade in 38/120 arteries, and ICA occlusions were present in 13/120. In the group with high-grade ICA stenosis, 23/38 were asymptomatic and 15/38 were symptomatic (with TIA or stroke in the previous 120 days). In the group of moderate-grade ICA stenosis, 56/69 were asymptomatic and 13/69 were symptomatic. Five of the 13 ICA occlusions were symptomatic, the remaining 8 patients with occluded ICA having never had symptoms. All these patients received antiplatelet therapy or, for some of them, anticoagulant at the moment of transcranial Doppler sonography examination.

The second group included 58 consecutive patients with anterior circulation ischaemic stroke or transient ischaemic attack of aetiology other than carotid artery disease (mean age 63 years, range 38–84). Of this group 22.4% (13/58) had cardioembolism. The sources of cardioembolism were classified as follows: prosthetic cardiac valve, atrial fibrillation, recent myocardial infarction (<4 weeks), mitral valve prolapse, patent foramen ovale, and calcific aortic stenosis. None of the prosthetic valve patients (4 patients) had received sufficient anticoagulation therapy (international normalised ratio of 1.5). In addition, one of the prosthetic valve patients had atrial fibrillation, 2 a left atrial thrombus, one a left ventricular thrombus, and one an ejection fraction <35%. Of 58 examined patients 17 (29%) had lacunar infarcts. Of the 58 patients 8 (14%) suffered stroke of other determined aetiology. These were rare and unusual causes of stroke – haematologic disorders or nonatherosclerotic vasculopathies. In 20/58 cases (35%) the cause of the stroke could not be determined with any degree of confidence. Of these patients, only 2 received neither antiplatelet therapy nor anticoagulant.

Methods

All patients underwent a full clinical and diagnostic work-up, including evaluation of cerebrovascular risk factors, laboratory tests, and brain imaging. The cerebral vessels of all patients were examined by continuous wave Doppler sonography (Spectradop 2, DMS Montpellier, France) and colour-Doppler duplex scanning (Acuson 128XP/10). The degree of carotid stenosis was assessed according to established criteria [15]. Digital substraction angiography was performed in 46 patients and degree of carotid stenosis was determined using NASCET criteria [16]. Cardiac disease was diagnosed by clinical examination, electrocardiography, Holter monitoring, and echocardiography (transthoracic or transoesophageal).

Simultaneous transcranial microembolic signals monitoring of the right and left middle cerebral arteries on each patient was done with a computer-controlled Doppler ultrasound device (Multi Dop X4 TCD-8 DWL) with a 2-MHz transducer (14 mm diameter). The recording time was 30 minutes. Each middle cerebral artery was recorded simultaneously at two insonation depths (range 45–55 mm), a 5 mm intergait distance with axial extension of the sample volume 8 mm. Detection of microembolic signals was performed using embolidetection software (TCD-8 for MDX, version 8.00 K). The signal intensity measurement algorithm uses the whole screen as background. A 64-point fast Fourier transform was used, having a FFT length of 2 ms. The FFT time window overlap was set at 60%. The high-pass filter was set at 100 Hz, the scale at 100 cm/s. An on-line investigator (E.V.) was looking for characteristic spectral displays indicative of microembolic signals and for audible Doppler shifts. The recording was analysed off line by two independent observers (H.S., O.P.), both blinded to the clinical data. Microembolic signals were identified in accordance with the criteria established by the Consensus Committee of the Ninth International Cerebral Hemodynamic Symposium [17] (with a higher intensity threshold – 9 dB). This intensity threshold was set after analysing 100 high intensity Doppler speckles of the normal Doppler signal. All high intensity transient signals not showing time lag at the two insonation depths were classified as artifacts.

Student's t-test for independent samples was used to determine whether degree of stenosis was significantly higher in those patients who showed emboli than in those who did not. Chi-square test and Fisher's exact test were used to test whether patients with high-grade ICA stenosis had emboli more frequently than those with moderate-grade

ICA and whether microembolic signals were more prevalent in symptomatic stenosis.

Results

Microembolic signals and carotid artery disease

Microembolic signals were detected in 24% (9/38) of patients with high-grade stenosis, in 4% (3/69) with moderate-grade ICA stenosis, and in 8% (1/13) with carotid occlusion. The mean number of microembolic signals during 30 minutes of recording time, averaged for this group, was 3.8 (range 1–8). Microembolic signals were significantly correlated with the severity of ICA stenosis ($p < 0.01$). The mean degree of ICA stenosis in patients without microembolic signals was 56.3% reduction in diameter (s.d. 15.6), and the mean degree in those with emboli was 72.5% (s.d. 15.7) ($p < 0.001$).

In the group with high-grade symptomatic stenosis, 47% (7/15) showed microembolic signals. Microembolic signals were less prevalent in asymptomatic patients with high-grade stenosis – 9% (2/23) showed microembolic signals ($p < 0.05$). In the moderate-grade group, microembolic signals were detected in 15% (2/13) of symptomatic stenoses and in 2% (1/56) of asymptomatic moderate-grade ICA stenoses. There were differences in the frequency with which microembolic signals were detected in high-grade and moderate-grade symptomatic stenoses. Microembolic signals were more often detected in symptomatic high-grade stenoses, being detected in 46.7% (7/15) as compared to 15.4% (2/13) in symptomatic moderate-grade stenoses, but the difference was not statistically significant.

Microembolic signals seemed to be more prevalent in symptomatic moderate-grade ICA stenosis (15.4% [2/13]) than in asymptomatic high-grade ICA stenosis (8.7% [2/23]), but the difference was not statistically significant ($p > 0.05$).

In the group with ICA occlusion, microembolic signals were detected in one asymptomatic patient.

Microembolic signals in stroke of other aetiologies

Transcranial Doppler sonography monitoring showed indication of microembolic signals in 7% (4/58) of all examined cases with acute stroke of aetiology other than carotid artery disease. The mean number of microembolic signals during 30 minutes recording time was 2.8 (range 1–6). Microembolic signals were found in 31% of patients (4/13) with cerebral embolism of cardiac source. These 4 patients corresponded to those with prosthetic valve and too low anticoagulation; 3 of them had an associated intracardiac thrombus. Two microembolic signals-positive patients with cardioembolism showed microembolic signals in the symptom-related middle cerebral artery. In one patient, microembolic signals were registered only in the contralateral middle cerebral artery (the ipsilateral middle cerebral artery was occluded). Microembolic signals were bilateral in one case. No significant difference was found between the frequency of microembolic signals in patients with cardioembolism and patients with ICA stenosis ($p > 0.05$). No microembolic signals were found in patients with lacunar infarcts. The cases with stroke of other determined aetiology did not show microembolic signals. No microembolic signals were found in patients with stroke of undetermined aetiology.

Discussion

In the groups studied, it was only when the mechanism of cerebral ischaemia was clearly embolism – either artery-to-artery or cardiogenic – that microembolic signals were found. The question whether bilateral transcranial Doppler sonography monitoring helps discriminate between cardiac and vascular embolic sources has been discussed in other studies [18, 19]. Analysis of the present data shows a variety of localisation of microembolic signals in the middle cerebral artery of patients with cardioembolic infarction. Microembolic signals were found in the symptom-related middle cerebral artery, in the contralateral or in both middle cerebral arteries. Cardioembolism does not necessarily produce bilateral microembolic signals. The results in patients with lacunar stroke are consistent with other published results [10–12] and show that transcranial Doppler sonography monitoring for microembolic signals has no diagnostic value in this particular type of cerebral ischaemia. Despite the present study's showing absence of microembolic signals in patients with stroke of undetermined aetiology, microembolic signals detection might yet be helpful in determining the pathogenetic mechanism. Sacco et al. [20], using angiography, found embolism, though of unknown source, associated with stroke of undetermined aetiology. Perhaps we only detected so few microembolic signals because the great majority of our patients were already treated by antiplatelet agents or by anticoagulants when we examined them.

Microembolic signals were found in 10.8% of all patients with carotid artery disease. In accordance with the results of comparable previous studies [5, 21, 22], these results demonstrate that microembolic signals are significantly more prevalent in patients with high-grade than in patients with moderate-grade carotid stenosis. Microembolic signals were significantly more often detected in the group of patients with symptomatic high-grade ICA stenosis than in patients with asymptomatic high-grade stenosis. Similar results have been reported in previous studies, including studies that examined the relationship between microembolic signals and symptomatology in high-grade stenosis [2, 23], as well as those that compared all degrees of stenosis (moderate- and high-grade) [7, 24].

Furthermore, microembolic signals were more likely to be associated with degree of symptomatic ICA stenosis, though the number of patients in this study was insufficient to demonstrate statistical significance. Previous studies which showed the presence of microembolic signals in symptomatic moderate- or high-grade ICA stenosis also failed to find a statistically significant correlation [5, 25].

Detection of microembolic signals in symptomatic high-grade stenosis confirms mechanism of stroke, but it is already well known that carotid endarterectomy is clearly indicated in this group [16, 26]. In patients with asymptomatic high-grade stenosis, also potentially benefiting from endarterectomy [27], discovery of microembolic signals might help decide in favour of carotid endarterectomy when other indicators are less clear.

While patients with moderate stenoses of less than 50% do not benefit from surgery [28, 29], endarterectomy may be the preferred treatment in patients with 50 to 69% stenoses, when there are no other complicating conditions. A recent study described five baseline variables predictive of increased surgical risk: hemispheric versus retinal transient ischaemic attack, left-sided operation, contralateral carotid occlusion, ipsilateral ischaemic lesion on CT scan and ulcerated ipsilateral plaque [30]. In our study the prevalence of microembolic signals in symptomatic moderate-grade ICA stenosis was slightly higher than in asymptomatic high-grade stenosis, a difference not statistically significant. A subgroup of patients, suffering from symptomatic moderate-grade ICA stenosis of 50 to 69% and having detectable microembolic signals, may be at risk of stroke and might benefit from more aggressive therapy, such as endarterectomy or anticoagulation therapy. Therefore, further studies should be done on patients with symptomatic moderate-grade ICA stenosis showing detectable microembolic signals, comparing frequency of microembolic signals with subsequent clinical development and different modalities of therapy.

Conclusion

In a routine laboratory as ours, transcranial Doppler sonography monitoring for microembolic signals seems to have limited practical interest in patients suffering of stroke with undetermined aetiology (no microembolic signals found) and in patients having high-grade ICA stenosis, symptomatic or not, for whom endarterectomy is clearly indicated (cf NASCET and ECST studies). In our opinion, the most interesting group to be studied further is the group of moderate-grade symptomatic ICA stenoses because the detection of microembolic signals could help to decide on endarterectomy in these patients.

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