

## INTRACRANIAL STENOSIS IN PATIENTS WITH ACUTE CEREBROVASCULAR ACCIDENTS

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### Abstract

**INTRODUCTION:** This study was conducted to investigate pattern and risk factors associated with the location of atherosclerotic occlusive lesions in cerebral vessels. Previous studies of patients with stroke or transient ischemic attack (TIA) suggest that extracranial atherosclerosis is more common in the white race. Noninvasive techniques such as duplex ultrasound, transcranial Doppler (TCD), and magnetic resonance angiography (MRA) allow vascular assessment of a more representative proportion of the patients, compared to conventional angiography alone.

**METHODS:** We evaluated patients with cerebrovascular problems (stroke and/or TIA) during a period of 6 months, using duplex ultrasonography, TCD and MRA to detect significant stenosis according to standard criteria.

**RESULTS:** Stenosis of extracranial and intracranial arteries was detected in 38% and 29% of cases, respectively. MCA was the most frequent involved intracranial artery (11% bilaterally and 5% unilaterally). Intracranial lesions tend to be multiple. There was no significant difference between men and women in terms of frequency and distribution of stenosis. No correlation was found between opium use and stenosis. The women had significantly more poor windows than men ( $P < 0.05$ ). The extracranial stenosis was significantly more frequent than intracranial stenosis ( $P < 0.01$ ).

**CONCLUSION:** The relations between hypertension and extracranial stenosis, and diabetes and MCA stenosis were statistically significant. TCD seemed to be a better technique for evaluating intracranial lesions in men than in women.

**Keywords:** Atherosclerosis, Stenosis, Carotid artery, Doppler Sonography.

**ARYA Atherosclerosis Journal 2008, 3(4): 206-210**

*Date of submission:* 10 Oct 2007, *Date of acceptance:* 21 Feb 2008

### Introduction

Stroke is the third leading cause of human mortality. The condition has a high prevalence and is associated with high economic burden. Stroke has both modifiable and non-modifiable risk factors and interestingly, there is effective preventive measures.<sup>1,2</sup>

Atherosclerosis is a systemic, multifocal disease causing various symptoms and signs. Atherosclerotic lesions occur mainly in large vessels first, and more distal lesions occur with aging.<sup>3</sup> From prognostic and therapeutic aspects, the lesions can be located in the extracranial carotid or intracranial arteries.<sup>4,5</sup> As with

carotid lesions, intracranial atherosclerosis is an important cause of stroke.<sup>1,6</sup> Symptomatic atherosclerotic intracranial stenosis in large arteries accounts for approximately 10% of ischemic strokes.<sup>7</sup> Risk of stroke in patients with MCA stenoses is reported to be around 24% during a 6-year follow-up study.<sup>8</sup> In patients with large artery disease, studying the cerebral hemodynamic state and following its alterations may be a good indicator for long-term outcome.<sup>9</sup> On the other hand, knowledge of intracranial and carotid disease in the symptomatic and especially the

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asymptomatic high-risk patients may be useful for evaluating future treatment modalities.<sup>10</sup> Patients with 50% or higher intracranial arterial stenosis require more rigorous therapies for stroke prevention.<sup>11</sup>

Prevalence of stenosis in extracranial and intracranial arteries is not the same in different regions.<sup>2,12-20</sup> Asians and blacks have more intracranial stenosis than whites.<sup>2</sup> Extracranial atherosclerotic lesions in thrombotic stroke was found to be more frequent than intracranial vessel involvement in some studies in Iran. Nevertheless, intracranial occurrence was more frequent than in western studies.<sup>21</sup>

The apparent differences in risk factors for extracranial and intracranial atherosclerosis are not well defined.<sup>3,4,15,22-25</sup> However, risk of a cerebrovascular accident (CVA) is nearly 3 to 5 times greater in the diabetic population than in non-diabetics.<sup>2,26</sup> The intracranial circulation should be evaluated in these patients in view of the high frequency of intracranial stenoses.<sup>26</sup>

In light of these facts, the importance of accessible, convenient, inexpensive and noninvasive techniques to investigate the intracranial and extracranial arteries can be better understood.

Noninvasive methods such as transcranial Doppler ultrasound (TCD) and magnetic resonance angiography (MRA) to study intracranial atherosclerosis are nowadays in extensive use.<sup>27</sup> They are reported to be able to determine 50-99% of intracranial large vessel stenosis with substantial negative predictive value.<sup>28</sup> In fact, they can reliably exclude the existence of intracranial stenosis.<sup>28</sup> For the non-invasive evaluation of extracranial vessels, MRA is less portable and more expensive than ultrasonography but has higher sensitivity and specificity for carotid stenosis.<sup>29</sup> Carotid duplex imaging is the method of choice for the diagnosis of high-grade stenosis of the carotid artery.<sup>30,31</sup>

There are few studies in our region on the frequency of extracranial and intracranial atherosclerotic lesions. Therefore, we performed a prospective study to determine the frequency of these lesions in patients with cerebrovascular manifestations in an Iranian population.

### Methods

In a cross-sectional study, we examined 223 consecutive acute stroke or TIA sufferers with symptoms of anterior or posterior cerebral artery territories from patients of the Emergency Department (ED) of Shafa Medical Center, Kerman University of Medical Sciences (Iran). Investigations included duplex examination of the cervical vessels and TCD.

Patients with a TCD and/or duplex diagnosis of intra- and/or extracranial stenosis were further evaluated by MRA (or CT angiography) as soon as it could be arranged. Information recorded included demographics, risk factors and tests results.

Hypertension was defined as a history of elevated blood pressure (systolic blood pressure >140 mmHg or diastolic blood pressure >90 mmHg) in two separate recordings or elevated blood pressure before admission that required antihypertensive medications. Diabetes mellitus was defined as a history of elevated glucose in two separate tests (fasting level >125 mg/dl) or diabetes treated with medication before admission. Hyperlipidemia was defined as history of an abnormally high lipid level that required either dietary or pharmacologic intervention. Smoking was documented by quantity-frequency assessment at the time of admission.

TCD studies of intracranial vessels were performed on a DWL Multi Dop T unit with a 2-MHz probe for the examination of intracranial circulation. MCA was stenotic if its peak systolic velocity was greater than 140 cm/s or its mean velocity exceeded 80 cm/s.<sup>2</sup> On the other hand, MCA occlusion was diagnosed if all basal arteries except the symptomatic MCA were detectable or if the asymmetry index of the MCA was less than 21% when compared with the other MCA.<sup>32</sup> Diagnosis of V4 segment and the proximal basilar artery stenosis was made if there were focal increases of the peak systolic and mean velocities to 120 cm/s and 80 cm/s or more, respectively.<sup>2</sup>

Carotid duplex studies were performed using a Hitachi AUB 525 ultrasound unit. The degree of stenosis was estimated with B-mode imaging and Doppler flow studies. Extracranial carotid stenosis was diagnosed according to standard criteria.<sup>33</sup>

We used SPSS to save and analyze the data. Independent t-test and chi square test were used to compare the variables.

### Results

We analyzed the TCD and duplex results of the patients whose mean age was 61 years. 45.7% (102) of our patients were women and 54.3% (121) men. Table 1 represents the summary of findings based on gender. 65% patients (145) suffered from hemispheric strokes, 24% (54) had strokes in the posterior system and 11.2% (25) had TIA. We were not able to insonate the intracranial arteries in 10.8% (24) of our patients due to poor trans-temporal window (3.1% unilaterally and 7.7% bilaterally). The women had significantly more poor windows than men ( $P < 0.05$ ).

The vertebral and basilar arteries were not insonated in 1.4% (3) of cases.

Stenosis was detected in 48% (107) of our patients, extracranial artery stenosis in 38% (85) (15.7% unilaterally and 22.4% bilaterally) and intracranial stenosis in 28.7% (64) (12.1% in one artery and 16.6% in more than one). Extracranial stenosis was significantly more frequent than intracranial stenosis ( $P < 0.01$ ). There was no significant difference between men and women in terms of frequency and distribution of stenosis.

Table 2 shows the pattern of intracranial stenosis. MCA was the most frequently involved intracranial artery. Carotid siphons stenosis was reported in 12.5% (28) of cases.

At the vertebrobasilar system, 10.8% (24) of the patients showed stenosis (7.7% unilaterally and 3.1%

bilaterally). This pattern showed no significant differences between sexes. The Basilar artery (17) had been more commonly involved than the vertebral arteries (9) (7.7% vs. 4%).

The most frequent risk factor for atherosclerosis was hypertension with a frequency of 37.2% (83). Diabetes mellitus, hyperlipidemia and smoking had frequencies of 27.8% (62), 22% (49) and 15.2% (34), respectively. Opium addiction was found in 14% (31). 21.5% (48) of the cases had one risk factor and 35.4% (79) more than one risk factor (17.5% two, 14.3% three, 3.6% four) and 15.2% (34) had no risk factors.

There was a significant relationship between the number of risk factors and frequency of stenosis in ICA and MCA. The relations between hypertension and extracranial stenosis, and diabetes and MCA stenosis were statistically significant.

**TABLE 1.** Summary of findings in men and women.

Findings	Woman	Men
Age (year)	60.7	63
Frequency	45.7% (102)	54.3% (121)
Stenosis		
ECS	40% (41)	36% (44)
ICS	27% (28)	30% (36)
Total	51% (52)	45% (55)
Poor windows	19% (19)	4% (5)

ECS: extracranial stenosis, ICS: intracranial stenosis.

Values in parenthesis show the number of patients.

**TABLE 2.** Frequency of intracranial stenosis found by transcranial Doppler ultrasonography.

Vessel	Unilateral	Bilateral
MCA	11% (25)	5% (11)
ACA	6% (13)	1% (2)
PCA	1% (2)	0.5 (1)
CS	9.4% (21)	3% (7)

MCA: middle cerebral artery, ACA: Anterior cerebral artery, PCA: Posterior cerebral artery, CS: Carotid siphon.

Values in parenthesis show the number of patients.

## Discussion

The findings of this study are in agreement with those of the previous studies, suggesting that atherosclerotic occlusive lesions of the extracranial carotid artery are more common in Iran (as in whites).<sup>2,21</sup> In our experiment, intracranial lesions appeared to be the cause of atherosclerotic occlusive disease in about one-fourth of patients. However, this figure may be an overestimation because we excluded patients with poor temporal windows (mostly elderly women).

About 40% of our patients with neurovascular problems had significant stenosis over carotid arteries. Iranmanesh et al. (2006) reported a somewhat similar pattern in Rafsanjan in central Iran.<sup>21</sup>

Multiple intracranial stenoses were found to be more prevalent than single-artery lesions, a finding that is in agreement with some other studies.<sup>16</sup> Our data showed that MCA was the most frequent stenotic intracranial artery. TCD insonates MCA more than other intracranial arteries<sup>34</sup> and this adds to the value

of TCD as a noninvasive technique. But it should be remembered that apart from atherosclerotic stenosis, increase in flow velocity can also be found in recanalization of an occluded MCA.<sup>35</sup> Therefore, follow-up TCD examination of occluded or stenotic vessels is indispensable in differentiating in situ stenosis from recanalization of the MCA.<sup>35</sup>

Despite some previous suggestions,<sup>18</sup> we found no statistical difference in the frequency of intracranial lesions between men and women. But due to better trans-temporal windows, one may suggest that TCD is a better device for studying intracranial arteries in men.

An interesting finding in our study is that intracranial (MCA) stenosis and extracranial stenosis are more frequently detected in patients with history of diabetes mellitus and hypertension, respectively. This finding is in agreement with some studies<sup>7,15,24,26,36</sup> and in disagreement with some others.<sup>3,23,37</sup> Although we found no association between location of lesion and history of known lipid disorder, blood lipids and lipoprotein concentrations were not systematically measured in our study.

In our study, no correlation could be found between extracranial and intracranial atherosclerosis and opium use, although denial of use may have been an obstacle to drawing an accurate conclusion.

Because we can now detect intracranial occlusive diseases safely and reliably with TCD and MRA, study of the prevalence of intracranial stenosis in asymptomatic patients with multiple risk factors is feasible.<sup>7,8,11,28,29,38,39</sup> Identifying patients with asymptomatic intracranial stenosis may enable us to implement preventive measures early in this high-risk population. This is particularly important because limited success of pharmacological interventions in preventing stroke has now been replaced by technological developments offering improved methods for endovascular therapy of cerebral artery stenosis.

Although TCD and MRA reliably exclude the presence of intracranial stenosis, abnormal findings on TCD or MRA require a confirmatory test such as angiography to definitely identify stenosis.<sup>28</sup> None of our patients performed a conventional angiography.

### Acknowledgement

Authors would like to express their appreciation to Ms. Lida Ketabi and Dr. Reza Zarei (faculty member of Isfahan University of Technology) for their critical reading and constructive comments and guidance all though this manuscript.

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