ORIGINAL ARTICLE

# The importance of Doppler studies in asymptomatic intracranial and extracranial arterial disease

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(Received for publication on March 25, 2002)

**Abstract. Knowledge of intracranial and carotid disease in the symptomatic and especially the asymptomatic high risk population may be useful for evaluating future treatment modalities. A group of 204 symptomatic patients and 105 asymptomatic elderly patients at high risk for stroke were tested by carotid duplex ultrasound and transcranial doppler for the presence of carotid and intracranial stenosis. Quantitative measurements of the stenosis were made directly from the hard copy of the carotid duplex and the transcranial doppler. Of the 204 symptomatic patients 168 (83%) had some degree of stenosis: 84 of the 204 (41%) in the intracranial circulation only, 59 (29%) in the internal carotid only, and 26 (13%) in both sets of vessels. Of the asymptomatic patients 85 (81%) had some degree of stenosis; 31 of 105 (30%) in the intracranial circulation only, 35 (33%) in the internal carotid only, and 19 (18%) in both sets of vessels. Statistical analysis did not reveal significant differences between the two groups. The large percentage of intracranial disease in the symptomatic as well as the asymptomatic population at high risk for stroke require further confirmation by good duplex studies of the intracranial circulation. This is important in order to create coherent treatment protocols.** (Keio J Med 51 (4): 189–192, December 2002)

**Key words: transient ischemic attack, transcranial Doppler**

## Introduction

Stroke prevention is of paramount importance.[1] The North American Symptomatic Carotid Artery Endarterectomy Trial (NASCET) study[2] and the Asymptomatic Carotid Artery Stenosis (ACAS) study[3] among others have addressed the issues of identying patients with carotid stenosis most at risk for stroke and in need of intervention. Both studies examined the effects of pharmacologic and surgical therapy of the extracranial carotid system on the mortality and morbidity resulting from ischemia. A few studies of intracranial circulation in symptomatic patients are on record,[4,5] and studies on abnormalities of intracranial circulation in high risk asymptomatic patients have been recently reported.[6]

The question asked in this study concerned is the incidence of intracranial vessel abnormalities in a symptomatic group of patients as definied below versus an asymptomatic group.

We compared the intracranial and extracranial Doppler findings in an elderly group of asymptomatic high-risk and symptomatic patients. We then compared the prognostic implication of these sonographic findings with the prognostic implications of the modified Framingham questionnaire[7,8] (a one page document modified by Wolf and this author which interrogates the various risk factors of a potential candidate study. See Appendix A) and the history of stroke-TIA and/or carotid bruits. The Framingham questionnaire was modified for this study by the addition of four additional risk factors: alcohol consumption, family history of stroke, elevated cholesterol >200 and overweight. Each added factor was assigned a maximum weight of 2 points equivalent to the weight points of other risk factor. The cut-off scores as described in the Framingham questionnaire were adjusted upward by ≈25% to reflect the increase in total possible score adding these new 4 factors.

Although the study population does not reflect the epidemiologic incidence of stroke risk and symptomatology in the general population, the conclusions of this study regarding the utility of Doppler sonography in the

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better identification of elderly patients at risk for stroke remain valid.

## Material and Methods

Patients were culled from a population of seniors who were living in retirement centers in New York state and were attending stroke prevention programs presented as part of a health care symposia between 1993 and 1996. Attendees filled out a risk assessment questionnaire, which was subsequently reviewed with a physician.

High risk but asymptomatic patients were definied in accordance with the modified Framingham clinical assessment criteria[8] as discussed above. Risk factors included hypertension (BP > 140/90); cardiovascular disease including a history of MI, angina, atrial fibrillation; peripheral vascular disease; excessive alcohol[9] (>2 glasses per day); history of smoking (>40 packs/year); diabetes mellitus; cholesterol >200 mg/dl; and excess weight.[10] Patients were considered to have a 50% or greater chance of incurring a stroke if the accumulated score exceeded 23 for males and 22 for females on the modified Framingham scale (similar to the Framingham Score). Symptomatic patients were definied for this study as those with a history of transient ischemic attack, stroke, or carotid bruits. Patients who met these criteria were invited to join the study.

Of the 309 patient studied, 204 (66%) were symptomatic, and 105 (34%) were asymptomatic high-risk. Carotid duplex (Biosound) and transcranial Doppler (Medasonic) sonography were performed by vascular technicians on these 309 patients and the results of the two groups were compared. Results were evaluated by the author (PH), a clinician with 12 years experience in duplex interpretation.

The abnormalities of the carotid arteries were definied by the degree of stenosis at the site of maximum plaque dimension and compared to the arterial diameter before the stenosis as suggested by Taylor and Strandness.[11] Patients were categorized into one of three groups based on the degree of stenosis: less than 50% reduction in diameter, 50–70% reduction, and more than 70% reduction.

Intervals were based on the indications for medical therapy (>50% stenosis) and surgery (>70% stenosis). Plaque size was measured with a caliper calibrated in millimeters directly from the hard copy generated by the duplex. Although Doppler flow velocities were obtained in each case we chose to measure arterial caliber diameter just as performed in the ACAS[3] study.

Abnormal intracranial circulation was defined as a 50% or more change (decrease or increase) in the flow velocity (in cm/sec) in the middle cerebral artery compared to the normal fellow artery,[12] or total absence of the arterial signal on one side. Normal values were obtained from the study of Hansen *et al.*[13] Statistical analysis was performed using the Wilcoxon-Mann-Whitney test (StatXact 3 for Windows, Cytel Software Corporation, Cambridge, Mass.).

## Results

Of the 204 symptomatic patients, 169 (83%) had some degree of stenosis: 84 of 204 (41%) in the intracranial circulation only, 59 (29%) in the internal carotid only, and 26 (13%) in both sets of vessels (Fig. 1), intracranial circulation abnormalities were therefore more common than extracranial circulation disease in this group.

Of the 105 asymptomatic patients, 85 (81%) had some degree of stenosis: 31 of 105 (30%) in the intracranial circulation only, 35 (33%) in both sets of carotid only, and 19 (18%) in both sets of vessels (Fig. 2).

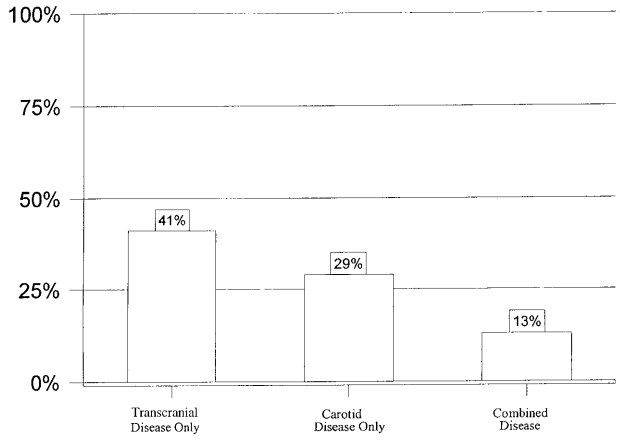


**Fig. 1** Results of Doppler studies in 204 symptomatic patients.

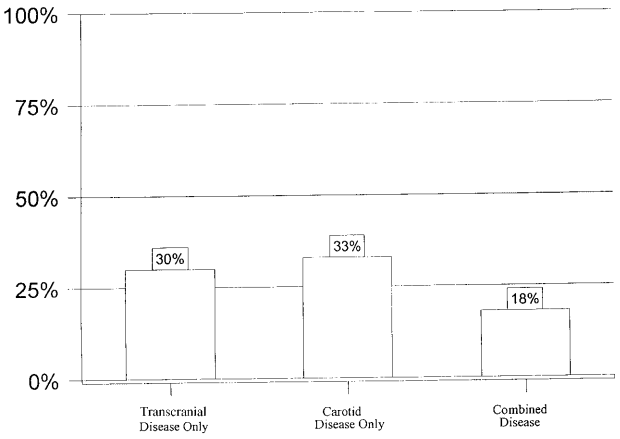


**Fig. 2** Results of Doppler studies in 104 asymptomatic patients.

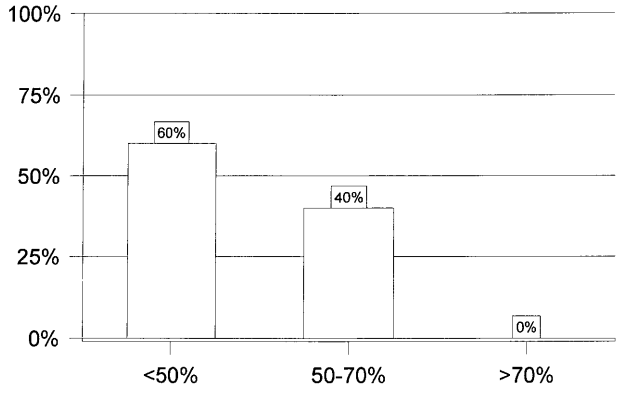


**Fig. 3** Severity of carotid stenosis in 59 symptomatic paitents.

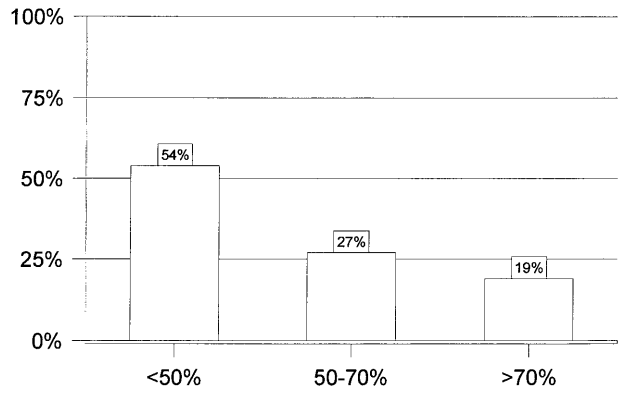


**Fig. 4** Severity of carotid stenosis in 35 asympotomatic patients.

The Wilcoxon-Mann-Whitney test was used to compare the frequency of stenosis in symptomatic versus high-risk asymptomatic patients. The test revealed no significant difference between the two groups (Mann-Whitney statistic $= 2.767 \times 104$, $p = 0.4648$). These data indicate that the lack of symptoms does not indicate an absence of arterial disease. Furthermore, the likelihood of finding stenosis in a high-risk asymptomatic patient is significant.

We then compared the degree of stenosis in the 59 symptomatic and 35 asymptomatic patients with only carotid stenosis. We found less than 50% stenosis in more than half the cases in both symptomatic and asymptomatic groups. Stenosis of 50–70% was found in 27% of symptomatic patients, and 40% of asymptomatic patients. Nineteen percent of symptomatic patients, but no asymptomatic patients, had stenosis more than 70% (Figs. 3, 4).

## Discussion

The findings of this study corroborate the findings of the ACAS study[3] regarding the presence of carotid disease in asymptomatic patients with risk factors, in particular that asymptomatic patients with multiple risk factors may have as much or more carotid stenosis as symptomatic patients. Importantly, this study extends this concept to the intracranial circulation, showing the presence of intracranial abnormalities in asymptomatic high-risk patients. Furthermore, these data help to further establish the usefulness of the modified Framingham questionnaire for identifying this high risk ''asymptomatic population''.

Of the symptomatic patients within this study, 41% had intracranial disease vs. 29% with carotid disease (see Fig. 1 $p > 0{,}05$). The fact that patients with symptomatic carotid disease have 30% more intracranial stenosis is surprising. This may be partially accounted for by the extracranial artery disease stenosis which may cause increased intracranial flow.[14] It is also important to note that the NASCET subset analysis has found intracranial artery stenosis an independent risk factor for stroke in patients with carotid stenosis.[15]

If the above findings are corroborated in large studies it may become critical to use antiplatelet therapy in intracranial stenosis grater than 50% even if the extracranial circulation is normal.

Furthermore our findings demonstrated the presence of intracranial abnormalities in asymptomatic patients even without carotid abnormalities. The large percentage of abnormal intracranial or extracranial arteries in the asymptomatic population was surprising. In this group the combined rate of abnormalities was 81% with equal distribution between the intracranial and carotid circulation. This is much higher than reported previously.[16,17] Nevertheless intracranial artery stenosis is a dynamic lesion which can both progress and regress.[18]

A number of studies have described various therapeutic modalities in intracranial symptomatic stenosis.[19–21] A small number of patients were mainly treated with anticoagulation. These are uncontrolled studies and although widely used in the medical and neurological practice lack supporting hard data.

In our study only the velocity shift of the middle cerebral artery was analysed. A number of medical conditions can cause marked changes in the velocity shift such as anemia, increased viscosity, or congestive heart failure. Usually, these conditions cause bilateral changes. Furthermore, tandem stenosis and concomitant extracranial stenosis may alter TCD results.[22] Until the B-mode results of intracranial circulation become more sophisticated, a clear-cut reading of the arterial wall abnormalities is difficult.[23] Intra-arterial ultrasound has become available[24] for the carotid artery but its use in the intracranial vessels has not yet been published. Although a very good correlation and up to 90% sensitivity and specificity are reported between angiography and carotid Duplex,[22] such a correlation has not

been shown between angiography and transcranial Doppler. With the advent of good B-mode studies of intracranial circulation,[23] validation studies should be forthcoming.

The large percentage of intracranial disease in the symptomatic population as well as the asymptomatic population at high risk, surprisingly high in our study, requires further confirmation by good Duplex studies of the intracranial circulation, confirmed by angiography.[14,24] Randomized treatment studies for intracranial circulation stenosis may follow. This is important since there is no recognized therapeutic protocol for intracranial vascular disease with solid supporting data and since a large segment of the at-risk population may benefit from available medical or surgical therapeutics.[25–27]

Although ultimate clinical outcomes over an extended period of time are not known for this patient group at this time, the findings reported are significant in and of themselves, as they suggest that these diagnostic tests are useful and may increase the clinician's ability to identify patients in whom intervention might be warranted.

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