The Value of Carotid Doppler Ultrasound in Asymptomatic Extracranial Arterial Disease

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ABSTRACT: Carotid Doppler is an accurate, safe and repeatable method of assessing arterial calibre, for distinguishing harmless neck bruits and to identify the stroke prone individual. It is completely non-invasive and can be used serially to monitor progression in carotid stenosis. It is a valuable clinical tool in diagnosis and management in patients at risk of stroke, but has definite limitations, such as in differentiating carotid occlusion from severe stenosis. B-mode imaging, although valuable in identifying arterial anatomy, and detecting plaques, cannot accurately evaluate the degree of stenosis. It is of limited value in identifying plaque hemorrhage and ulceration. Doppler ultrasound technology has advanced rapidly in the last decade, especially in the combination of B-mode imaging and Doppler (Duplex), as well as in evaluating of the intracranial circulation (transcranial Doppler). In the next decade, it may become the new gold standard for evaluating the extracranial and intracranial circulation.

RÉSUMÉ: Valeur de l'ultrasonographie carotidienne par effet Doppler dans la maladie artérielle extracrânienne asymptomatique Le Doppler carotidien est une méthode exacte, sécuritaire et pouvant être répétée à volonté pour évaluer le calibre artériel, pour distinguer les souffles anodins au niveau du cou et pour identifier les individus à risque de présenter un accident cérébro-vasculaire. C'est une technique non-invasive qui peut être utilisée de façon sériée pour surveiller la progression d'une sténose carotidienne. Cet outil clinique précieux dans le diagnostic et le traitement des patients à risque de présenter un accident cérébro-vascuaire a cependant des limites précises, notamment pour différentier une occlusion carotidienne d'une sténose sévère. L'imagerie en mode B, quoique utile pour identifier l'anatomie artérielle et détecter les plaques, ne peut évaluer précisément le degré de sténose. Elle a une valeur limitée pour identifier l'hémorragie et l'ulcération au niveau des plaques. L'ultrasonographie par effet Doppler est une technologie qui a progressé rapidement depuis dix ans, surtout par la combinaison de l'imagerie en mode B et le Doppler (Duplex), ainsi que dans l'évaluation de la circulation intracrânienne (Doppler transcrânien). Au cours de la prochaine décennie, cette technique pourrait devenir le nouvel étalon or pour l'évaluation de la circulation extra et intracrânienne.

Can. J. Neurol. Sci. 1988; 15: 378-383

In the western world, stroke ranks as the third leading cause of death.[1] Cerebral thromboembolism is the commonest type of stroke and 70% of cases are associated with extracranial carotid disease specifically, at the carotid bifurcation.[2] Carotid plaques occur preferentially at the carotid sinus and on the posterior and lateral wall where shear stress is high.[3] Therefore, knowledge of the site and degree of stenosis are critical to clinical decision-making in patients with ischemic cerebral symptoms.

Since its introduction in 1927 by Moniz,[4] cerebral arteriography has been considered the only acceptable method for quantifying *in vivo* the extent and severity of atherosclerotic lesions. However, in addition to the cost, length of the procedure and patient discomfort, a major concern about angiography is its safety since it still carries a morbidity and mortality risk of 0.6-1.0% which precludes its repetitive application.[5,6] Recent advances in non-invasive techniques such as Doppler ultrasound have considerably improved and extended the capacity for assessing progressive changes in the carotid bifurcation. The technique is non-invasive, easily repeatable and without any discomfort or risk for the patient. However, the main challenge

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This paper is based on a special presentation given at the Canadian Congress of Neurological Sciences in London, Ontario in June 1987.

Dr. Bornstein was the 1987 recipient of the Francis McNaughton Award which is presented annually by the Canadian Neurological Society for the best paper submitted by a junior member of the society.

Received April 4, 1988. Accepted July 5, 1988

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and demand for each carotid Doppler laboratory is to evaluate the validity or accuracy and reliability or reproducibility of their test procedure.

Accuracy of Carotid Doppler

The principle of Doppler ultrasonography is that an ultrasound beam emitted by the crystal in the Doppler probe (applied to the skin over an artery) is reflected back by the moving column of blood. The frequency difference between the emitted and received signals is the "shift", measured in kiloHertz. The faster the blood moves, for instance through an area of stenosis, the greater the shift.

The emitted ultrasound signal may be continuous ("continuous wave") or be emitted in short bursts ("pulse wave"). The combination of real-time imaging of the artery (B-mode) and Doppler ultrasound is termed "duplex scanning". B-mode imaging shows a magnified picture of the arterial wall, demonstrating the shape, size and consistency of the plaque. However, it is not an accurate method of assessing stenosis which is still best measured by the Doppler method.

The overall accuracy of the continuous-wave Doppler is 90% for lesions greater than 50% stenosis, with a sensitivity of 87-89% and specificity of 92-99%.[7-10]

For detecting serial changes in the arterial calibre (i.e., progression), a basic requirement is to evaluate the reliability of the diagnostic test. The reliability of a diagnostic test is its ability to reproduce its findings and to provide consistent results on repeated applications to the same unchanged subject. Reliability

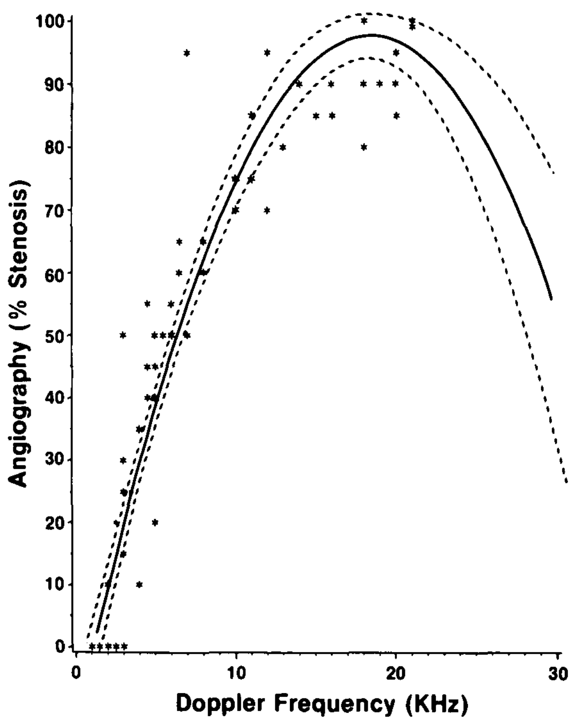

Figure 1 — Correlation between the Doppler shift in kiloHertz and the percent stenosis on angiography using quadratic regression model.

needs:[11] 1) overall agreement with the Gold Standard (angiography — Doppler correlation curve); 2) unbiased interpretation (intra- and inter-observer variation); 3) reproducibility — consistency and precision (intra-observer reliability).

1. Overall agreement with the Gold Standard

In 84 consecutive internal carotid arteries, continuous-wave directional Doppler ultrasound examination was carried out with a 5 mHz probe with a colour coded spectral analyzer (Carolina Medical Electronics model 1050) placing the probe against the neck at a 60 degree angle and recording the maximum peak Doppler shifted frequencies. The Doppler peak frequencies in kiloHertz were compared to the percent stenosis of conventional biplane angiographic investigation. Angiographic and carotid Doppler investigations were interpreted independently. The angiographic films were interpreted by a neuroradiologist, unaware of the carotid Doppler results and were expressed as a percent narrowing of the arterial diameter. A Pearson's correlation coefficient was calculated.

A very good correlation was found between kiloHertz Doppler shift and percent stenosis on angiography ($r = 0.91$). The relationship between the peak frequency in kiloHertz and the percent stenosis on angiogram was plotted using a quadratic regression model ($p < 0.0001$) (Figure 1).

Percent stenosis on angiography =
$-13.70 + (12.1)$ (Doppler frequency) +
(-0.33) (Doppler frequency)^2

2. Unbiased interpretation

In order to eliminate the intra- and inter-observer (interpreter) variation, the internal carotid artery stenosis was reported as percentage reduction in luminal area converted directly from the actual kiloHertz Doppler shift displayed on the screen using the Angiography-Doppler Correlation Curve (Figure 1). The periorbital directional flow was reversed only in high grade stenosis (> 90%).

3. Reproducibility

We tested the intra-observer reliability in 21 patients; the examinations were then repeated by the same technician two days later, without access to any of the previous results. The intra-observer reliability was calculated using the Fleiss method.[11]

Twenty-one patients were tested to determine the intra-observer reliability. We divided the patients into three groups (Table 1). In ten patients there was total agreement, in another seven patients there was only one kiloHertz Doppler shift between the two observations and in only four patients there was a two kiloHertz Doppler shift difference (in one of them there were technical difficulties detecting the internal carotid artery). The intra-rater reliability coefficient was 0.98, with a lower 95% confidence limit of 0.98.

Accuracy of B-Mode Imaging

High-resolution real-time B-mode imaging is a unique non-invasive technique that images the atherosclerotic plaque and its surface much better than is possible by angiography. Although the angiogram has long been considered the gold standard, this is now challenged.[12-14]

Table 1: Intra-observer comparison of peak frequencies (evaluated "blindly" by the same technician on successive days) in 21 patients

Patient	Left ICA 1st Day	Left ICA 2nd Day	Right ICA 1st Day	Right ICA 2nd Day
Total Agreement				
1	4	4	12	12
2	0	0	8	8
3	4	4	3	3
4	2	2	7	7
5	15	15	2	2
6	15	15	0	0
7	3.5	3.5	8	8
8	14	14	10	10
9	10	10	8	8
10	8	7.5	0	0
1 kHz Disparity				
11	8	7	2	2
12	14	14	12	11
13	5	4	20	20
14	0	0	7	8
15	3	4	20	20
16	11	10	2	3.5
17	2	2	8	6.5
2 kHz Disparity				
18	12	12	10	8
19	16	18	0	0
20	2	2	14	16
21	7	7	8	11*

*Technical difficulty.

We prospectively evaluated 56 consecutive carotid plaques removed at carotid endarterectomy. Pre-operatively each patient had B-mode ultrasound imaging of the carotid artery in both sagittal and transverse planes using a 5 mHz probe (CME-1060) and either conventional or intra-arterial digital subtraction, biplane angiography. Angiographic and B-mode imaging investigations were interpreted independently.

Ulcers on B-mode imaging were diagnosed by the following criteria: 1) an isolated crater; 2) proximal and distal lipping, usually with sharp demarcation of the overhanging echogenic border; 3) visualization in at least two views.

Plaque hemorrhage on B-mode imaging was defined as the presence of distinct echolucent areas within the plaque. The presence or absence of ulceration and intraplaque hemorrhage was recorded at endarterectomy. Each specimen was also examined with light microscopy. Intraplaque hemorrhage was observed in 85% (48/55) of the specimens, but only 12 of the 48 were correctly detected by B-mode imaging and all were large plaques. There were 14 small (microscopic) hemorrhages in the remaining 36 (false negative) cases.

These results indicate a sensitivity of 25%, specificity of 86%, positive predictive value of 92% and negative predictive value of 86%. Although we cannot detect small hemorrhages, the positive predictive value for large hemorrhages is high.

Several reports indicate results superior to our data in detecting intraplaque hemorrhages,[14-17] but the definitions of intraplaque hemorrhage in those studies were different. O'Donnell et al defined hemorrhage as gross macroscopic hematoma,[14] and others only distinguished between homogeneous and heterogeneous patterns rather than looking for a distinctive echolucent area.[15-17]

The sensitivity and specificity of B-mode imaging in the detection of ulcers compared to angiography were 67% and 72%, respectively, and when compared to the surgical inspection of the specimen, the sensitivity was 50% and specificity was 90%. When the angiography results were compared to the surgical appearances, the sensitivity was 72% and specificity was 95%. These results are in accordance with other published data,[14,18,19] and indicate that B-mode imaging can provide valuable anatomical information and compares favourably with angiography.

Clinical Applications

1. Screening asymptomatic neck bruits

Discovery of an asymptomatic neck bruit during routine examination poses a dilemma for most physicians. Asymptomatic cervical bruits occur in 4% of persons older than 40 years and are markers of extracranial carotid artery disease as well as risk factors for stroke.[20,21] Clinical examination alone is inadequate to determine location and severity of the underlying arterial stenosis.[22] Carotid Doppler allows identification of underlying arterial disease.

Patients with newly discovered asymptomatic neck bruits should have non-invasive carotid evaluation with Doppler ultrasound to determine the site, extent and severity of the extracranial arterial disease. If the bruit is benign (e.g., subclavian artery stenosis or external carotid artery disease), both patient and physician are reassured and no further investigation is needed.

The presence of detectable stenosis in the internal carotid artery indicates a definite stroke risk. Data from the Toronto asymptomatic cervical bruit study, indicate that the likelihood of ischemic cerebral events (TIA and stroke) in patients with internal carotid stenosis is determined by severity and subsequent progression of carotid stenosis (Figure 2). The overall annual incidence of stroke was 1.7%, but for patients with severe (> 75%) internal carotid artery stenosis, the annual stroke rate in all territories was 6% (Table 2).

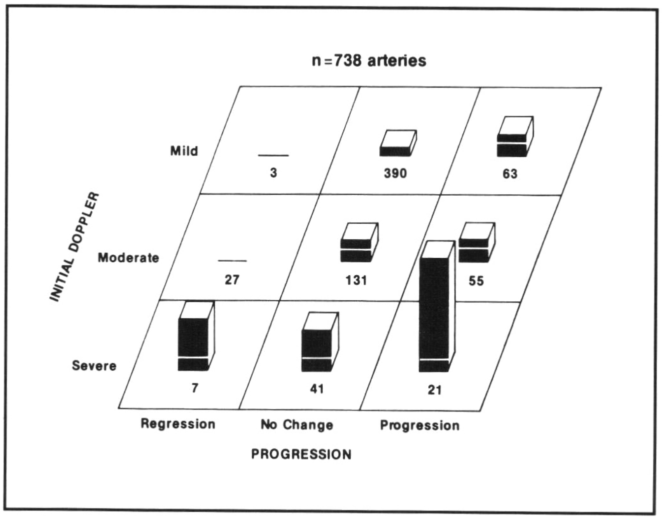

Figure 2 — Relationship between severity of carotid stenosis, progression of the lesion, and the occurrence of ischemic cerebral events.

https://doi.org/10.1017/S0317167100028080 Published online by Cambridge University Press

Table 2: Annual stroke rate (%) in all vascular territories in 498 patients (996 carotid arteries) with asymptomatic cervical bruits (Kaplan-Meier method)

	Patients	Arteries
Carotid Stenosis (Doppler)	% Stroke	% Stroke
< 35%	0.9	0.3
35-50%	0.0	0.0
50-75%	0.9	0.6
>75%	6.0	3.0
Overall	1.7	0.6

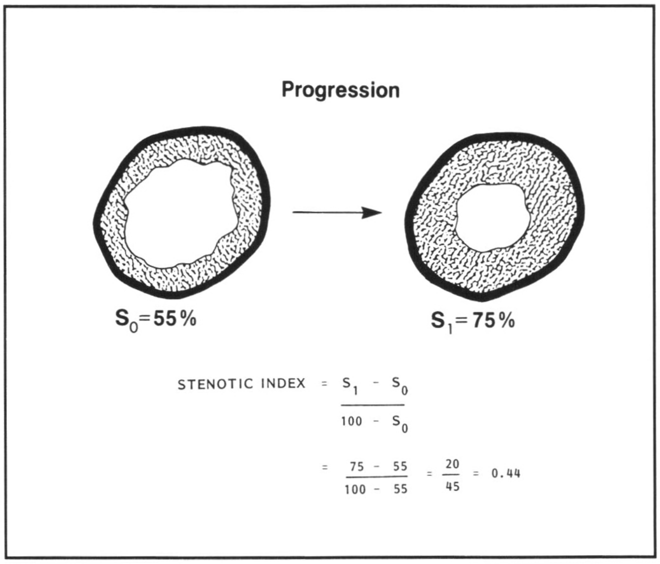

Figure 3 — Stenotic Index equation expressing luminal changes reflecting progression of the stenosis.

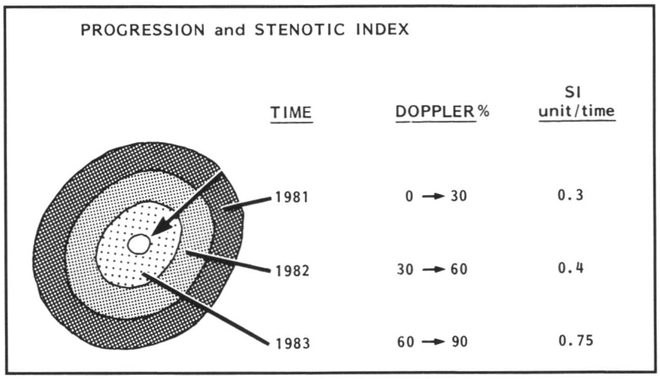

Figure 4 — Example of progressing stenosis over three years and the increased risk of stroke indicated by the higher value of Stenotic Index as the lumen decreases.

When assessing serial changes in arterial calibre, small increments at severe stenosis produce critically severe loss of lumen, while at mild degrees of stenosis, the same amount of disease has little effect. To overcome this, we have developed the "Stenotic Index". This relates the new calibre to the previous lumen in a simplified way (Figure 3). The higher the index value, the greater the threat to the brain (Figure 4).

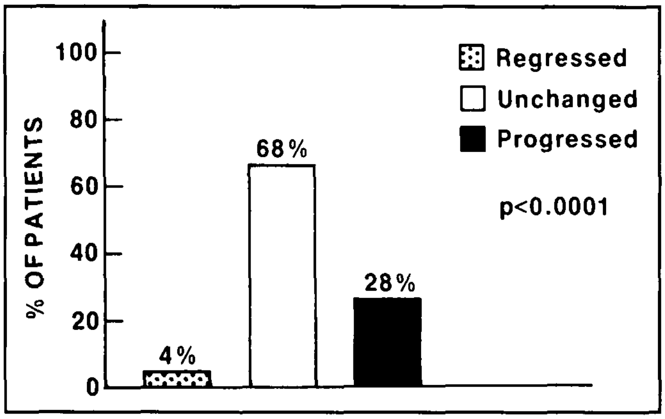

Figure 5 — Percentage of arteries that have progressed (28%), regressed (4%) and remained unchanged (68%) over two years follow-up with continuous-wave Doppler.

Using the Stenotic Index in 496 arteries over a period of 24 months follow-up, we divided the arteries into progressers, regressers and those which remained unchanged. The majority of arteries (68%) were unchanged, 28% progressed and 4% regressed (Figure 5).

Progression of carotid stenosis evaluated with continuous-wave Doppler was a potent factor in the development of symptoms in our study. Progression of stenosis probably reflects "plaque instability".[23] Neurological outcome in asymptomatic carotid stenosis correlates with acute local changes in complex, severely stenosing plaques, such as intra-plaque hemorrhage.[24,25] These local intra-plaque events can be detected with the high resolution duplex systems now available.[14,16] Most (78%) of the ischemic cerebral events were TIAs ipsilateral to the most severely stenosed internal carotid artery (ICA).

The patient with asymptomatic cervical bruit from underlying ICA stenosis should be instructed of warning symptoms and report them immediately to facilitate early carotid angiography in potential surgical candidates.

2. Occlusion of the internal carotid artery

Carotid Doppler evaluation

Distinguishing between occlusion and severe stenosis is critical for patient management since occluded arteries are inoperable. We evaluated the accuracy of carotid Doppler ultrasonography in differentiating severe carotid stenosis from occlusion by comparing the results of angiography to duplex scanning in 124 carotid arteries and to continuous-wave Doppler in 662 carotid arteries.

The ultrasonographic criteria for ICA occlusion were a combination of: 1) failure to detect a flow signal from ICA with continuous-wave Doppler; 2) asonic arterial image on pulse-wave Doppler associated with plaque seen with B-mode imaging and longitudinal pulsation of the artery walls; 3) reversed flow in the ophthalmic, frontal or supraorbital arteries.

The specificity was 95-99%, sensitivity was 86-96% and accuracy was 95-98%. Duplex scanning wrongly identified occlusion in four arteries and failed to detect occlusion in one artery.

For making decisions prior to carotid endarterectomy even such infrequent errors are unacceptable and clearly Doppler diagnosis is inadequate. Therefore, we recommend angiography

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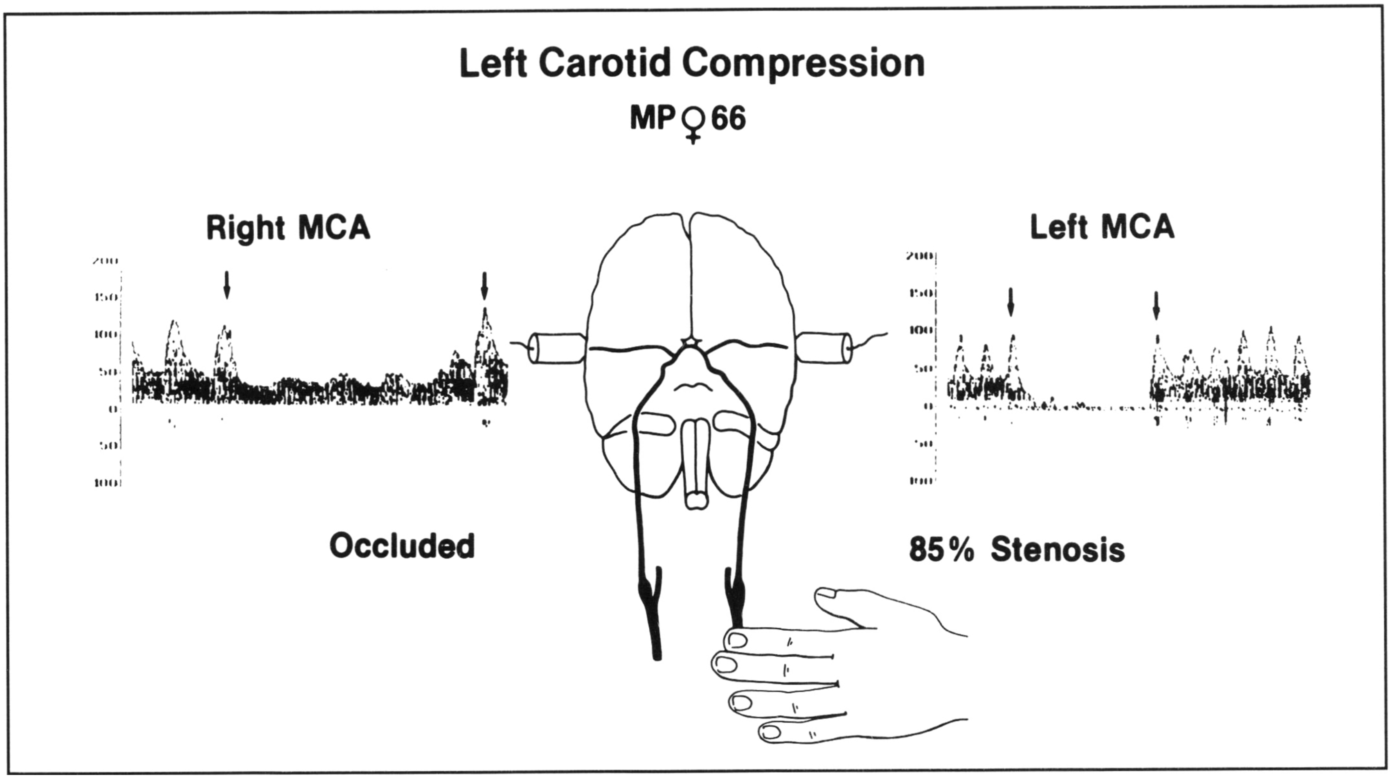

Figure 6 — Left common carotid artery compression of asymptomatic 65 year-old woman. During compression the left middle cerebral artery flow was obliterated, and the right middle cerebral artery flow velocity was reduced from 150 to 48 cm/sec, demonstrating that the patent left internal carotid artery supplies the left middle cerebral and most of the right middle cerebral artery territories.

of all surgical candidates with apparent severe stenosis when the internal carotid artery cannot be clearly identified on duplex, to distinguish apparent occlusion from undetectably low blood flow.

Transcranial Doppler evaluation

We followed 40 patients with unilateral carotid occlusion by serial clinical and Doppler evaluation over six years. In 30 of these, there was angiographic confirmation of the occlusion. The overall annual TIA and stroke rate was 10% with TIAs predominating. The annual stroke rate ipsilateral to the occluded artery was only 1.2% and no stroke occurred after detection of occlusion. However, in some patients occlusion was followed by a devastating stroke, without warning. It is essential to identify this high risk subgroup where prophylactic carotid surgery is justified. Transcranial Doppler (TCD), an accurate diagnostic technique to estimate the adequacy of hemispheric collateral circulation,[26-28] may solve this dilemma. The degree of dependency of each cerebral hemisphere (MCA velocity) on its ipsilateral (occluded) and contralateral (patent) carotid artery can be evaluated using digital compression of each common carotid artery (Figure 6).

In 25 patients with unilateral ICA occlusion, we assessed hemispheric dependency by transcranial Doppler in conjunction with digital compression of the common carotid artery. A 2 mHz pulsed Doppler probe (EME - TC2-64) was placed over each temporal area to continuously monitor the middle cerebral artery (MCA) blood velocities. A 10 mHz continuous-wave Doppler probe over the ipsilateral superficial temporal artery monitored the pulse on a screen to confirm complete cessation of flow in the common carotid artery. Each MCA velocity was evaluated with right and left carotid compression to determine its relative dependency on carotid flow.

Ipsilateral MCA flow was completely dependent upon the patent carotid artery in 50% and partially dependent in 30%. Compression of the common carotid artery on the side of the ICA occlusion had no effect on MCA flow in either hemisphere. Therefore, it may be possible to identify a high-risk subgroup with inadequate collateral circulation by the use of TCD in conjunction with common carotid artery compression and so justify prophylactic carotid endarterectomy in those asymptomatic patients with progressing carotid lesions.

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