Correlation of Hemodynamically Significant Internal Carotid Stenosis with Pulsed Doppler Frequency Analysis

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Systolic and mean pressure gradients across internal carotid stenoses were measured at the time of carotid endarterectomy in the arteries of 90 patients, all of whom underwent angiography. Eighty-two of these patients also had pulsed Doppler ultrasonic arteriography with real-time spectrum analysis. There were 71 (79%) high grade stenoses of greater than 50% diameter reduction by angiography. Significant systolic pressure gradients (≥10 mmHg) were identified in 41 patients (46%), 38 (46%) of whom underwent ultrasonic evaluation. A pulsed Doppler frequency measured within the stenosis equal to or greater than 6.5 kiloHertz had a sensitivity of 94.7% (36/38) in identifying pressure reducing lesions with a specificity of 47.7% (21/44). Positive predictive value was 61% (36/59). Angiographic criteria (50% diameter reduction) exhibited a sensitivity of 97.6% (40/41), a specificity of 36.7% (18/49) and a positive predictive value of 56.3% (40/71). Negative predictive value was 94.7% for angiography and 91.3% for ultrasonic arteriography. A pulsed Doppler frequency equal to or greater than 6.5 kiloHertz appears to accurately identify lesions that are at risk to reduce distal internal carotid pressure under operative conditions with a sensitivity similar to angiography. This criterion has a positive predictive value and specificity that is slightly superior to angiography and a high negative predictive value. Pulsed Doppler spectrum analysis provides physiologic information relative to blood flow velocity that is complimentary to the anatomic data provided by angiography for assessing the potential for hemodynamic significance of internal carotid stenoses.

EVALUATION AND OPERATIVE MANAGEMENT of asymptomatic carotid stenoses is based primarily on the assumption that a high grade stenosis that produces a drop in distal internal carotid pressure may increase the risk of stroke, especially in patients undergoing general anesthesia for a major operation.[1,2] Busuttil et al.[3] have demonstrated that patients with hemodynamically significant carotid lesions as measured by noninvasive testing are at increased risk for stroke. Although data to support the practice of prophylactic carotid endarterectomy for the asymptomatic high grade stenosis are conflicting, many surgeons continue to recommend endarterectomy for these lesions.[4-6]

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Preoperative identification of stenoses that reduce internal carotid pressure rely primarily on indirect noninvasive techniques that measure parameters related to ocular blood pressure and flow.[7,8] These physiologic methods are accurate when positive, however, they can identify only those lesions that are hemodynamically significant under laboratory conditions in the awake patient and are further limited by their inability to differentiate between high grade stenosis and occlusion.[9] Marginally compensated stenoses that may become significant when systemic hemodynamics are altered under anesthesia or by intraoperative blood loss may thus go undetected. Alternatively, estimation of percentage angiographic diameter reduction may serve to identify potentially hemodynamically significant lesions.[10,11] However, since carotid plaques are often asymmetric, the degree of stenosis determined angiographically is at best only an estimate.

Ultrasonic arteriography and pulsed Doppler spectrum analysis have been demonstrated to be highly accurate in the identification and quantification of internal carotid stenosis and in differentiating high grade lesions from internal carotid occlusions.[12-14] High grade stenoses characteristically produce a marked increase in Doppler frequency within the area of narrowing due to an increase in flow velocity at this location. Although Doppler frequency elevation is clearly related to the degree of luminal area reduction,[12,14] a precise relationship between hemodynamically significant carotid stenosis and Doppler frequency has not been determined.

The present study was performed in an attempt to correlate the results of pulsed Doppler frequency analysis with hemodynamically significant carotid stenoses and to compare these results with standard angiographic criteria for identifying pressure reducing lesions by measuring

mean and systolic pressure gradients across carotid lesions at the time of endarterectomy.

Materials and Methods

Ninety patients with varying degrees of internal carotid stenosis who underwent carotid endarterectomy form the basis for this study. Twenty (22%) were asymptomatic and operation was performed prophylactically prior to anticipated subsequent major operative procedure. The remainder were symptomatic with transient ischemic attacks (TIAs), prior stroke, or symptoms of generalized cerebral ischemia. Informed consent was obtained from all subjects.

All patients underwent preoperative arteriography. In most cases, selective multiview carotid arteriograms were obtained; however, in some patients technical problems precluded selective studies and aortic arch injections were utilized. All arteriograms were interpreted independently by one of three radiologists who was unaware of the results of noninvasive testing. Each arteriogram was graded by percentage diameter reduction from the projected normal diameter of the internal carotid artery at the point of maximum stenosis. A 50% diameter reduction was recorded as a potentially pressure-reducing stenosis. Stenoses greater than 75% diameter reduction were also analysed separately to evaluate the sensitivity and specificity of this angiographic criterion.

Eighty-two of these patients also had ultrasonic arteriography (P-1 Ultrasonic Arteriograph, D. E. Hokanson, Inc., Issaquah, WA) with pulsed Doppler spectrum analysis (Angioscan I Spectrum Analyzer, Unigon Industries, Mt. Vernon, NY). All examinations were performed and interpreted by nurse technologists. Ultrasonic arteriography utilized a 6-gated pulsed Doppler to generate a flow map of the carotid bifurcation, specifically identifying the internal carotid artery.[10,12] After identification of the internal carotid, a single pulsed Doppler sample volume was passed through the vessel while the real-time spectrum was recorded. Changes associated with carotid stenosis, including systolic frequency elevation and spectral broadening, were noted. The point of maximum stenosis was identified by the examiner and the highest peak systolic frequency recorded from within this region was measured from the real-time Doppler spectrum. Examples of Doppler spectra recorded from within carotid stenoses of varying degree are shown in Figure 1.

At the time of subsequent carotid endarterectomy, the bifurcation was exposed and the point of maximum stenosis identified with a sterile continuous wave Doppler by audible evaluation of the Doppler signal. After systemic heparinization, a needle connected to a pressure transducer was inserted into the carotid bulb proximal to the point of maximum stenosis. Mean and systolic pressure was measured from the digital readout of the transducer. Immediately thereafter, similar pressure determinations were made from the internal carotid artery distal to the point of stenosis. The external carotid remained open during all measurements. Systemic blood pressure was monitored with an intra-arterial catheter in the radial artery during the pressure measurements and all patients were normotensive and normocarbic.

In order to compensate for small variations in systolic and mean pressure from beat to beat since internal and common carotid measurements were not simultaneous, a gradient of 10 mmHg was arbitrarily selected as significant. Both systolic and mean pressure gradients were correlated with peak internal carotid frequency and with angiography. Sensitivity, specificity, and positive and negative predictive value for angiography and Doppler frequency analysis in identifying pressure reducing lesions were also calculated.

Results

There were 19 vessels (21%) with a stenosis of less than 50% diameter reduction. A stenosis of 50% to 74% diameter reduction was present in 34 vessels (38%) and a stenosis greater than or equal to 75% was present in 37 vessels (41%). Thus, there were 71 lesions (79%) that had the potential to reduce distal internal carotid pressure based on angiographic criteria. A significant systolic pressure gradient equal to or greater than 10 mmHg was identified in 41 vessels (46%), 38 (46%) of which had frequency analysis.

Systolic pressure gradients measured at operation are compared with angiographic percentage diameter reduction in Figure 2. These data are illustrated in tabular form in Table 1. Only one vessel with a significant systolic pressure gradient had a stenosis of less than 50% and this vessel was only minimally below the critical value. Thus, the sensitivity of angiographic criteria (50% diameter reduction) in identifying pressure reducing lesions was 97.6% (40/41). Thirty-one high grade stenoses, however, did not produce a distal pressure reduction so the specificity of this angiographic criterion was only 36.7% (18/49). The positive predictive value of a 50% stenosis in identifying a pressure reducing lesion was 56.3% (40/71) and the negative predictive value was 94.7% (18/19).

Table 1 also illustrates the results of pressure gradient determination compared to angiographic criteria using 75% diameter reduction (90% area reduction) as a significant stenosis. Clearly, this criterion is inadequate since 15 of the lesions that reduced distal internal carotid pressure were missed. Sensitivity was only 63.4% (26/41) and the positive predictive value was 70.3% (26/37). Specificity was increased, however, by using this criterion to 77.6% (38/49). Negative predictive value was 71.7% (38/53).

Mean pressure gradients compared with angiography (50% diameter reduction) are illustrated diagramatically

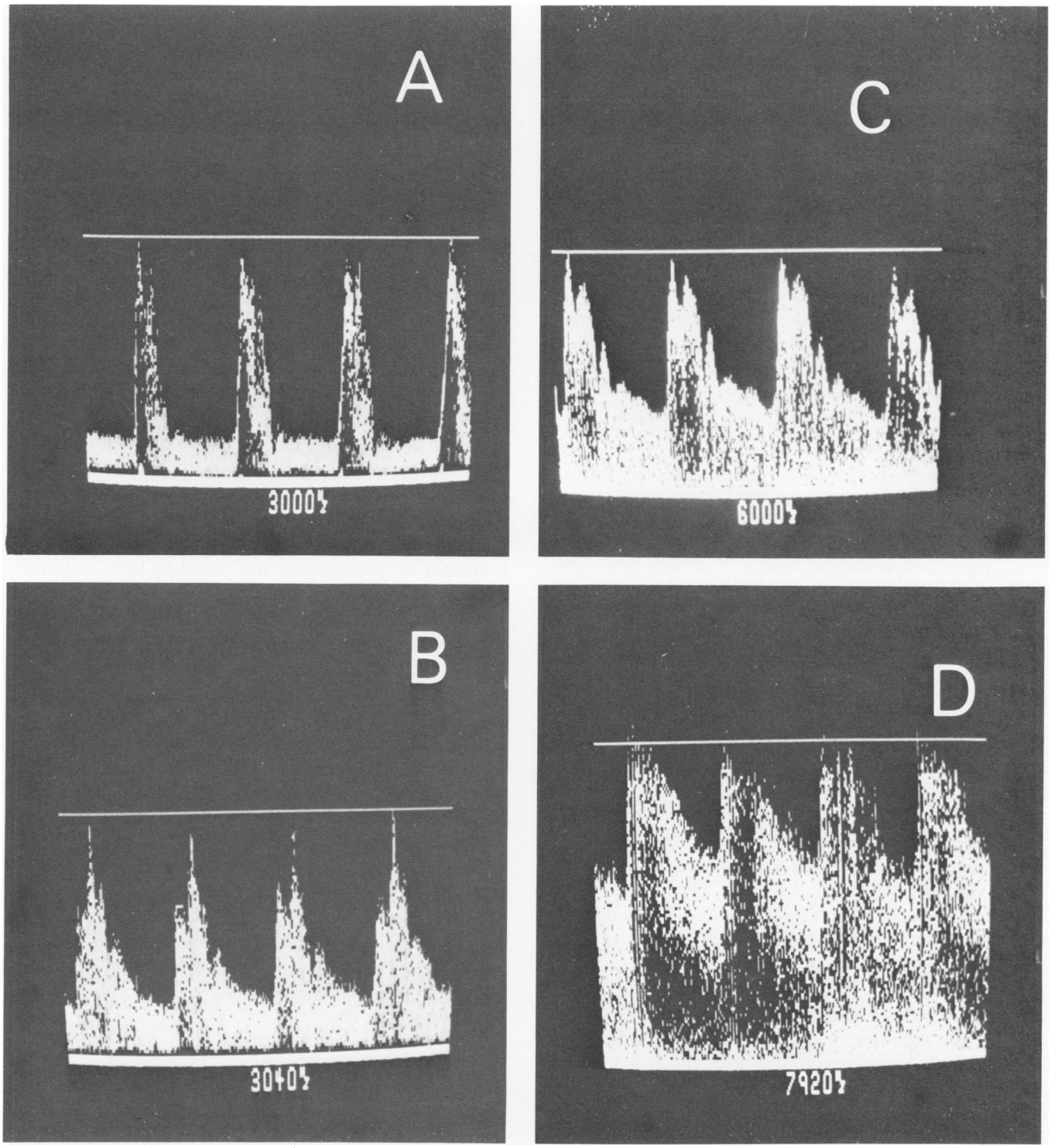

FIG. 1. Pulsed Doppler spectra recorded from internal carotid arteries with varying degrees of disease determined by angiography. Spectrum A from a normal vessel exhibits a low peak frequency with no spectral broadening in systole. Spectrum B recorded from a mild 25% stenosis also has a low peak frequency with spectral broadening due to flow disturbance produced by the plaque. Spectrum C recorded from a moderate 50% stenosis shows disturbed flow associated with a moderate elevation of peak systolic frequency (6.0 kiloHertz), while spectrum D from a high grade 80% stenosis has a marked systolic frequency elevation (7.9 kiloHertz). (Scale on A and B 0-5 kiloHertz; scale for C and D 0-10 kiloHertz).

in Table 2. Again, only one vessel exhibited a significant reduction in internal carotid pressure with a stenosis of <50% diameter reduction. Thus, the sensitivity of angiography for identifying a significant mean pressure gradient was 96.9% (31/32). Specificity was 31% (18/58) and positive predictive value was 43.7% (31/40). The negative

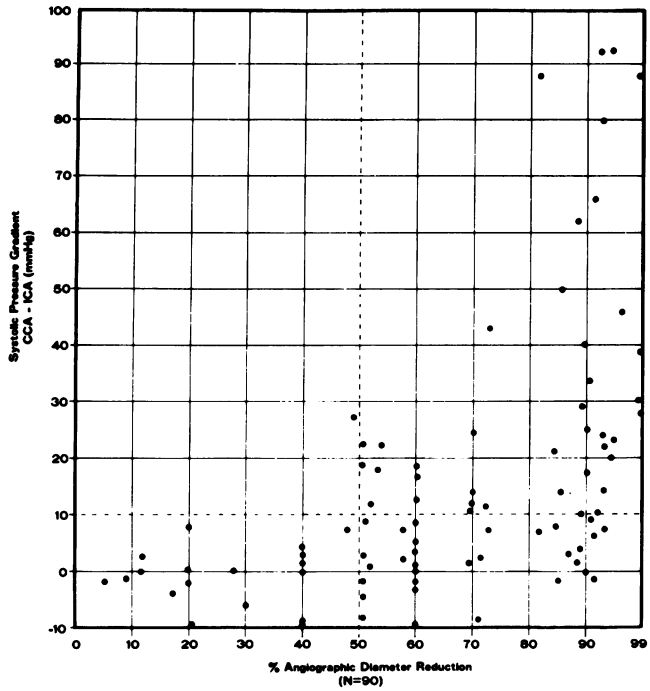

FIG. 2. Systolic pressure gradients measured at operation *versus* angiographic diameter reduction. The horizontal dotted line divides these vessels with significant gradients (≥10 mmHg) from those with gradients of lesser degrees. The vertical dotted line marks a 50% diameter reduction.

predictive value for a significant mean pressure gradient was 94.7% (18/19).

Pressure gradients compared to systolic peak frequency are illustrated in Figure 3. Using 6.5 kiloHertz (kHz) as the criterion for distinguishing between pressure reducing and nonpressure reducing lesions, only two vessels were identified with significant systolic pressure gradients and a peak frequency below this level. These data are illustrated diagramatically in Table 3. The sensitivity of Doppler frequency analysis was 94.7% (36/38) and the specificity was 47.7% (21/44). Positive predictive value of a frequency of 6.5 kHz in identifying a systolic pressure reduction was 61% (36/59), whereas the negative predictive value of a peak frequency below 6.5 kHz in identifying a lesion that did not reduce internal carotid pressure was 91.3% (21/23). Mean pressure gradients compared to peak systolic frequency using 6.5 kHz as a criterion are illustrated in Table 4. Sensitivity is 90% (27/30) and specificity is 38.5% (20/52). Positive predictive value is 45.8% (27/59) while negative predictive value is 87% (20/23).

TABLE 1. *Systolic Pressure Gradient Correlated with Angiography (n = 90)*

Gradient (mm Hg)	Angiographic Diameter Reduction (%)			
	<50	≥50	<75	≥75
≥10	1	40	15	26
<10	18	31	38	11

A review of the operative and noninvasive findings in the two cases with a significant systolic pressure gradient in which a peak frequency less than 6.5 kHz was detected with the Doppler suggests that examiner errors may have affected the results in both of these cases. In the first instance a patient with an internal carotid stenosis of moderate degree had a peak frequency of 5.4 kHz identified within the stenosis. This patient was the first in our series. At operation some technical difficulties were encountered with the transducer and a systolic pressure gradient of 28 mmHg was identified but no mean gradient could be detected. It was the impression of the surgeon that a technical error was involved in the common carotid systolic measurement since the lesion did not appear to be extraordinarily tight on angiography, but it was felt unwise to perform repeated carotid punctures to verify this impression.

In the second case a patient with a stenosis of 85% as measured by angiography was noted to have a systolic pressure gradient of 50 mmHg. Peak systolic frequency recorded from this internal carotid artery measured only 4.7 kHz; however, it was the impression of the examiner that a much higher frequency signal was present from this vessel. Technical difficulties arose during the ultrasonic study due to dense calcification within the internal carotid artery. In addition, the patient was unable to maintain a steady position for the examination for any length of time. A high frequency signal was detected very transiently but the peak frequency could not be recorded.

If it is true that technical errors with the pressure measurements in the first case and ultrasonic arteriography in the second case provided erroneous data, the sensitivity of a peak frequency of 6.5 kHz in identifying pressure reducing lesions would rise to 100%, as would negative predictive value. Positive predictive value and specificity would not change significantly.

Discussion

Carotid endarterectomy is well established therapy for symptomatic carotid stenosis of any degree.[15] Controversy still exists, however, regarding the wisdom of surgical intervention for asymptomatic carotid lesions. Moore et al.[16] have demonstrated an increased risk of stroke and TIA in patients with asymptomatic severe ulcerations and Thompson and associates[4,5] report a significant late spontaneous stroke rate in asymptomatic patients with cervical bruits. Humphries et al.,[6] however, have presented

data to suggest that even high grade asymptomatic lesions will produce symptoms of transient cerebral ischemia prior to stroke in most cases. Although a number of studies have failed to demonstrate an increased risk of stroke during major operation in patients with asymptomatic cervical bruit,[17-22] it is still common practice to perform prophylactic endarterectomy for high grade lesions of potential hemodynamic significance because of the possibility of stroke in the perioperative period.[1,5]

It seems clear that patients with high grade carotid stenosis are particularly prone to develop symptoms.[23,24] Busuttil et al.[3] have reported that asymptomatic patients with positive oculopneumoplethysmography are more likely to develop TIA and stroke. Similarly, Kartchner and McRae[8] have noted a significant late stroke rate in patients with ocular pulse wave delay as measured by oculoplethysmography. These indirect studies, which measure parameters related to ophthalmic artery pressure and flow, are useful for identifying hemodynamically significant internal carotid lesions; however, they cannot distinguish between high grade stenosis and occlusion when used alone. Furthermore, a well compensated stenosis with intracranial collateral flow from other sources may go undetected, although it is presumably still at risk to produce embolization.

Reliance on these studies has been criticized because they are performed in the awake patient under laboratory conditions.[9] When systemic hemodynamics are altered by operation, blood loss, or drug therapy, the pressure significance of a stenotic carotid lesion may change. In addition, it appears that indirect carotid studies are most likely to be positive when the degree of distal pressure reduction is severe, thus a number of pressure significant lesions may be missed.[14,23]

Standard angiographic criteria for assessing the potential of a carotid stenosis to produce a decrease in distal pressure and flow are well defined.[10,11] A 50% reduction in luminal diameter, which corresponds to a 75% reduction in area, is the point at which distal internal carotid pressure may decrease. In practice, however, it is often difficult to assess the precise area of an asymmetric carotid plaque. The morphology of the lesion with reference to ulceration and length are of particular importance in determining the hemodynamic effects and criteria for the evaluation of a specific lesion remain subjective.

Direct imaging noninvasive studies such as ultrasonic arteriography are particularly useful as a screening procedure for carotid occlusive disease. Not only can they differentiate between high grade carotid stenosis and occlusion but, when combined with pulsed Doppler spectrum analysis, they can detect many low grade stenoses and identify vessels that are essentially normal. As the arterial lumen is progressively narrowed by an atherosclerotic plaque, a corresponding increase in flow velocity and thus Doppler frequency within the stenosis occurs.[12,14]

TABLE 2. *Mean Pressure Gradient Correlated with Angiography (n = 90)*

Gradient (mm Hg)	Angiographic Diameter Reduction (%)			
	<50	≥50	<75	≥75
≥10	1	31	11	23
<10	18	40	42	14

The results of this study confirm the utility of angiographic criteria (50% diameter reduction) in identifying pressure significant stenoses. This criterion has a relatively low specificity and positive predictive value, however, so if angiography is used alone to select asymptomatic patients for operation a greater number of well compensated lesions will undergo endarterectomy.

Our results further suggest that physiologic frequency information from preoperative pulsed Doppler spectrum analysis can also be used to assess the potential of an internal carotid stenosis to reduce distal pressure under

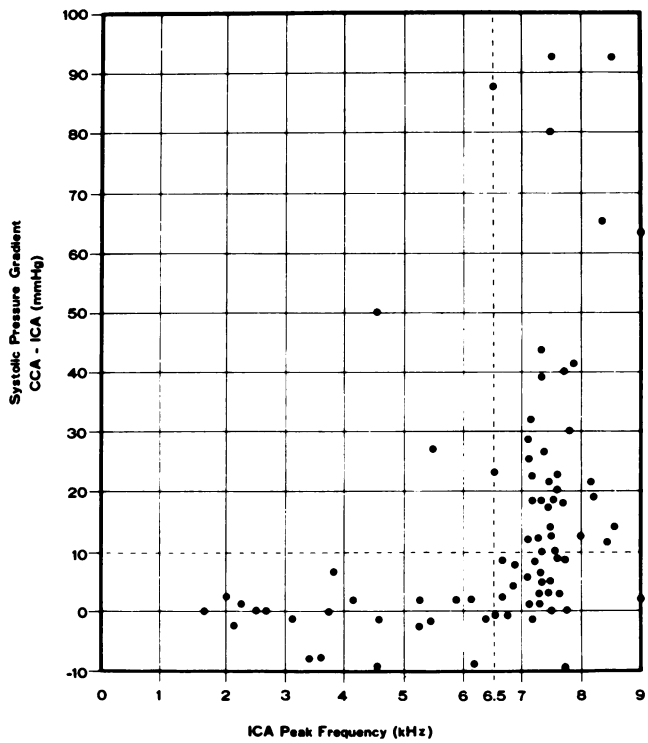

FIG. 3. Systolic pressure gradients measured at operation *versus* peak systolic frequency. The horizontal dotted line divides those vessels with significant gradients (≥10 mmHg) from those with gradients of lesser degrees. The vertical dotted line marks a frequency of 6.5 kiloHertz (kHz).

TABLE 3. *Systolic Pressure Gradient Correlated with Peak Doppler Frequency (n = 82)*

Gradient (mmHg)	Peak Systolic Frequency (kHz)	
	<6.5	≤6.5
≥10	2	36
<10	21	23

operative conditions. A frequency of 6.5 kHz appears to accurately identify lesions that are at risk to significantly reduce distal internal carotid systolic and mean pressure during operation. The sensitivity of this criterion compares favorably with standard angiographic criteria. The positive predictive value and specificity were slightly superior to angiography. Thus, more precise selection of lesions at risk to produce pressure drops is possible than with angiography alone. Importantly, a Doppler frequency below 6.5 kHz appears to have a high negative predictive value in excluding a pressure reducing lesion.

Tight internal carotid stenosis of greater than 80% diameter reduction invariably yields pulsed Doppler frequencies above 6.5 kHz with the ultrasonic arteriograph. This criterion should be of particular use in evaluating the intermediate carotid stenosis with irregular morphology with regard to its potential for intraoperative hemodynamic significance. Thus, this direct noninvasive study can provide complimentary information to the anatomic data provided by angiography, which permits a more thorough assessment of the hemodynamic potential of a carotid lesion.

Finally, it should be noted that these results only apply to a 5 megaHertz pulsed Doppler. A Doppler with a different base frequency would produce a different Doppler shifted frequency although the shifted frequency corresponding to 6.5 kHz should be calculable from the Doppler equation. The Nyquist limit of the ultrasonic arteriograph is approximately 8.0 kHz. It is clear from inspection of the spectra in our studies that many of the high grade lesions exhibited aliasing. This did not occur at the level of 6.5 kiloHertz, however, so aliasing does not appear to be a factor in the two false-negative examinations. Although we have no experience with continuous wave Doppler imaging and spectrum analysis, peak frequency information should be similar to the pulsed Doppler within the range below 7.5 kHz, so similar results might be expected with the 5 megaHertz continuous wave Doppler.

TABLE 4. *Mean Pressure Gradient Correlated with Peak Doppler Frequency (n = 82)*

Gradient (mm Hg)	Peak Systolic Frequency (kHz)	
	<6.5	≥6.5
≥10	3	27
<10	20	32

Doppler frequency depends both on flow velocity at the point of measurement and the angle of the incident Doppler beam. Although some variation in Doppler angle clearly is present between patients with ultrasonic arteriography, it appears that variation in angle with lesions of this degree is not sufficient to markedly influence the results. However, flow velocity calculation considering Doppler angle might be expected to yield even more precise criteria for evaluating carotid lesions.

From this study it is evident that the physiologic data provided by pulsed Doppler spectrum analysis can provide an important complimentary parameter to be used in conjunction with the anatomic appearance of a lesion demonstrated by angiography. Frequency criteria will permit a more accurate assessment of the potential of an asymptomatic carotid stenosis to cause subsequent cerebral ischemia, increasing the utility of direct carotid imaging and flow velocity analysis in patient evaluation.

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References

1. Moore WS, Boren C, Malone JM, Goldstone J. Asymptomatic carotid stenosis. Immediate and long-term results after prophylactic endarterectomy. Am J Surg 1979; 138:228–233.
2. Yatsu FM, Hart RG. Asymptomatic carotid bruit and stenosis: a reappraisal. Stroke 1982; 17:21–25.
3. Busuttil RW, Baker JD, Davidson RK, Machleder HI. Carotid artery stenosis—Hemodynamic significance and clinical course. JAMA 1981; 245:1438–1441.
4. Thompson JE, Kartchner MM, Austin DJ, et al. Carotid endarterectomy for cerebrovascular insufficiency (stroke): follow-up of 359 cases. Ann Surg 1966; 163:751–763.
5. Thompson JE, Patman RD, Talkington CM. Asymptomatic carotid bruit: long-term outcome of patients having endarterectomy compared with unoperated controls. Ann Surg 1978; 188:308–316.
6. Humphries AW, Young JR, Santilli PH, et al. Unoperated asymptomatic carotid artery stenosis: a review of 182 instances. Surgery 1976; 80:695–698.
7. Gee W, Mehigan JT, Wylie EJ. Measurement of collateral cerebral hemispheric blood pressure by ocular pneumoplethysmography. Am J Surg 1975; 130:121–127.
8. Kartchner MM, McRae LP. Noninvasive evaluation and management of the "asymptomatic" carotid bruit. Surgery 1977; 82:840–847.

9. O'Hara PJ, Brewster DC, Darling RD, Hallett JW Jr. Oculopneumoplethysmography. Relationship to intraoperative cerebrovascular hemodynamics. Arch Surg 1980; 115:1156–1158.
10. May AG, DeWeese JA, Rob CG. Haemodynamic effects of arterial stenosis. Surgery 1963; 53:513–524.
11. Berguer R, Hwang NHC. Critical arterial stenosis: a theoretical and experimental solution. Ann Surg 1974; 180:39–50.
12. Blackshear WM Jr, Phillips DS, Thiele BL, et al. Detection of carotid occlusive disease by ultrasonic imaging and pulsed Doppler spectrum analysis. Surgery 1979; 86:698–706.
13. Sumner DS, Russell JB, Ramsey DE, et al. Noninvasive diagnosis of extracranial arterial disease. A prospective evaluation of pulsed Doppler imaging and oculoplethysmography. Arch Surg 1979; 114:1222–1229.
14. Blackshear WM Jr, Strandness DE Jr. Angiographic imaging by ultrasound compared with indirect methods. *In* Nicolaides AN, Yao JST, eds. Investigation of Vascular Disorders. New York: Churchill Livingstone, 1981; 165–200.
15. Moore WS, Hall AD. Importance of emboli from carotid bifurcation in pathogenesis of cerebral ischemic attacks. Arch Surg 1970; 101:708–716.
16. Moore WS, Boren C, Malone JM, et al. Natural history of nonstenotic asymptomatic ulcerative lesions of the carotid artery. Arch Surg 1978; 113:1352–1359.
17. Barnes RW, Liebman PR, Marszalek PB, et al. Natural history of symptomatic carotid disease in patients undergoing cardiovascular surgery. Surgery 1981; 90:1075–1081.
18. Ropper AH, Wechsler LR, Wilson LS. Carotid bruit and the risk of stroke in elective surgery. N Engl J Med 1982; 307:1388–1390.
19. Evans WE, Cooperman M. The significance of asymptomatic unilateral carotid bruits in preoperative patients. Surgery 1978; 83:521–522.
20. Treiman RL, Foran RF, Cohen L, et al. Carotid bruit. A follow-up report on its significance in patients undergoing an abdominal aortic operation. Arch Surg 1979; 114:1138–1140.
21. Turnipseed WD, Berkoff HA, Belzer FO. Postoperative stroke in cardiac and peripheral vascular disease. Ann Surg 1980; 192:365–368.
22. Carney WI, Stewart WB, DePinto J, et al. Carotid bruit as a risk factor in aortoiliac reconstruction. Surgery 1977; 81:567–570.
23. Riles TS, Lieberman A, Kapelman I, Imparato A. Symptoms, stenosis, and bruit: interrelationships in carotid artery disease. Arch Surg 1981; 116:218–220.
24. Imparato AM, Riles TS, Mintzer R, Baumann FG. The importance of hemorrhage in the relationship between gross morphologic characteristics and cerebral symptoms in 376 carotid artery plaques. Ann Surg 1983; 197:195–203.