Incidence of Asymptomatic Extracranial Arterial Disease

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SUMMARY Investigations of the incidence and the extent of the asymptomatic early stages of extracranial arterial disease (EAD) have been restricted for methodical reasons. Direct Continuous Wave-Doppler examination has given highly accurate results in the location and correct estimation of the degree of EAD both for the carotid (97%) and the vertebral arteries (90%), as shown from a detailed comparison with carotid (n = 604) and vertebral (n = 426) angiograms. Compared with this degree of reliability, the validity of normal auscultation for the diagnosis of EAD is shown to be poor: if bruits are taken as the only signs of associated EAD in patients with systemic atherosclerosis, only 27.6% in a group of 123 patients would have been correctly diagnosed. This parallels the number of false-positives (22.6%) in patients with normal results. The frequency and degree of EAD was studied by the use of direct Doppler examination in 2009 neurologically asymptomatic patients admitted either with severe vascular (n = 375) or coronary atherosclerosis (n = 264) or with high-risk factors (n = 1370). The frequency was significantly higher (32.8%) in patients with peripheral vascular disease than in those with coronary artery disease (6.8%) and in risk-factor patients (5.9%). The combination and degree of vessel involvement are presented in detail and their possible prognostic significance discussed.

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A VARIETY of non-invasive techniques have been developed for the detection of extracranial arterial disease (EAD): Some of these methods, such as the supraorbital Doppler,1, 2 ophthalmodynamometry3 and ocular pneumoplethysmography4 are inexpensive and easily performed. Their validity is, however, limited to the detection of high-grade stenosis or occlusion of the carotid arteries.5, 6 An accurate differentiation between stenosis and occlusion of the carotid arteries is impossible and the exact site of obstruction cannot be localized.

The more sophisticated application of the Continuous Wave (CW)-Doppler technique for direct insonation of the carotid arteries in the neck has considerably improved the value and reliability of the non-invasive examination, particularly for the carotid artery system.7-12 By continuous scanning of the course of the extra-cranial arteries from the supraventricular to the submandibular region it is possible to detect with accuracy the size, extent and location of lesions producing an obstruction of the lumen of about 50% or more. The method can be further refined by spectrum analysis of the Doppler signals13 allowing the additional detection of lesions producing obstructions of even less than 50% due to atherosclerotic changes in the normal laminar flow within the vessels.14 With the new combination of real-time B-scan imaging and Doppler systems15-17 it may become possible to achieve a degree of resolution sufficient for the detection of even small ulcerated lesions of the arterial wall.

It has been reported that use of the Doppler technique to detect flow abnormalities in the vertebral arteries (flow reduction or steal phenomena) provides information on the adequacy of the posterior brain circulation.18 Although CW-Doppler does not as yet yield quantitative information about cerebral perfusion, the evidence it provides of significant variations in blood flow velocity between the carotid and vertebral artery systems — as well as knowledge of the collaterals — may be of substantial help in making an

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Since angiographic examination is usually confined to selected patients, knowledge of the incidence of EAD based on this test has so far been limited. On the basis of the advances in non-invasive diagnostic methodology it is now possible to study the incidence and extent of EAD in considerably more detail than was previously possible using more fallible indicators such as a bruit heard over the neck.

The data presented emphasize the reliability and accuracy of both carotid and vertebral direct Doppler examination based on an extensive comparison with angiograms of 1030 patients. It also provides evidence of the incidence and extent of EAD as derived from Doppler investigations obtained from 2009 patients admitted either with severe atherosclerosis of large peripheral arteries, the aorta or the coronaries, or with high-risk factors for atherosclerosis. None of these patients had signs or symptoms of focal cerebrovascular insufficiency. (Among those patients with peripheral vascular disease (n = 375) the frequency rate of detection of EAD by conventional bruit auscultation was compared with that of CW-Doppler examination.)

I. Correlation of Direct CW-Doppler Examination and Angiogram

Methods

A directional CW-Doppler device (Débimètre ultrasonique directionnel Delalande) developed by Pourcelot was used for all recordings with a non-focussed beam at a frequency of 4 MHz. The flow profiles of the supratrochlear arteries, the vertebral arteries (both at the level of the atlas slope and its proximal origin within the supraclavicular fossa) and the subclavian arteries were recorded as well as those of the carotid arteries throughout their course in the neck accessible to direct insonation, i.e., from supraclavicular to submandibular regions (common carotid, internal and external carotid arteries including the bifurcation).

Details of the physical, anatomical, physiological and pathophysiological basis of the Doppler investigation, the examination technique and the interpretation of the velocity curves are described elsewhere. Abnormalities of Doppler flow distribution were correlated with angiography in 604 patients (carotid artery system) and 426 patients (vertebral artery system) according to the criteria reported earlier.

Results

For the carotid artery system, the data presented in table 1 show the very high reliability of the direct Doppler examination (97%) for the detection as well as for the location of stenotic lesions causing more than 50% narrowing of the lumen.

The middle-grade and hemodynamically relevant (> 80%) high-grade stenoses can be reliably graded and differentiated from total occlusion as shown in figure 1.

For the vertebral system, the method is sensitive enough (90%) for the estimation of the cerebral blood flow via these vessels, but not for the differentiation of the underlying vascular disease (table 2).

Irregularities of the arterial wall have not yet been taken into account in these comparisons, since they could not generally be recorded without the addi-

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### Table 1: Correlation Between CW-Doppler and Angiographic Findings in 604 Patients with Different Location and Degree of EAD Within the Carotid Artery System (30 Patients with Severe Intra-Cranial Carotid Lesions as Revealed by CW-Doppler Examination are Included). Lesions with Less than 50% Surface Area Reduction are Disregarded.

<table>
<thead>
<tr>
<th>Doppler</th>
<th>Total (n)</th>
<th>Angiogram in agreement (n)</th>
<th>different (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Internal carotid artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occlusion at the bifurcation</td>
<td>85</td>
<td>79</td>
<td>3</td>
</tr>
<tr>
<td>Stenosis (neck)</td>
<td>140</td>
<td>137</td>
<td>1</td>
</tr>
<tr>
<td>Stenosis (siphon before ophthalmic artery branching)</td>
<td>15</td>
<td>15</td>
<td>-</td>
</tr>
<tr>
<td>Stenosis (siphon after ophthalmic artery branching)</td>
<td>15</td>
<td>14</td>
<td>1</td>
</tr>
<tr>
<td>External carotid artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenosis/occlusion</td>
<td>35</td>
<td>35</td>
<td>-</td>
</tr>
<tr>
<td>Common carotid artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Occlusion</td>
<td>10</td>
<td>10</td>
<td>-</td>
</tr>
<tr>
<td>Stenosis</td>
<td>20</td>
<td>19</td>
<td>1</td>
</tr>
<tr>
<td>Innominate artery</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stenosis/occlusion</td>
<td>21</td>
<td>21</td>
<td>-</td>
</tr>
<tr>
<td>Controls</td>
<td>263</td>
<td>258</td>
<td>2</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>3</td>
</tr>
<tr>
<td>Total</td>
<td>604</td>
<td>588 (97.3%)</td>
<td>16 (2.7%)</td>
</tr>
</tbody>
</table>

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*Note: ABN: Abnormality, TIF: Tubular Stenosis*
tion of measurement of turbulence by pulsed Doppler methods or by spectral analysis of the CW-Doppler signals.15, 21

II. Asymptomatic EAD in Patients with Different Types of Atherosclerosis

Patients

Doppler velocity profiles of the extracranial arteries were studied in 3 groups totalling 2009 patients, all without signs or symptoms of focal cerebrovascular insufficiency. The first group (A) consisted of 375 patients (297 males: mean = 61.5 ± 9.9 years of age and 78 females: mean = 58.4 ± 11.8 years of age) examined before major vascular surgery on the aorta or iliac arteries for aneurysm of the aorta or severe atherosclerotic lesions. The second group (B) comprised 264 patients (227 males: mean = 53.7 ± 6.4 years of age and 37 females: mean = 58.0 ± 5.4 years of age) suffering from severe coronary artery disease with multiple stenotic lesions as revealed by coronary angiography. For both groups the prevalence of additional atherosclerotic processes, i.e., in group A severe coronary artery disease and in group B severe peripheral vascular disease, was identical at 17%. A third group (C) consisted of 1370 patients (1123 males: mean = 58.1 ± 7.1 years of age and 247 females: mean = 56.2 ± 6.8 years of age) otherwise in good health apart from non-specific complaints possibly due to diffuse cerebrovascular insufficiency (poor memory, syncope, vertigo or non-focal visual disturbances not typical of transient cerebral

<table>
<thead>
<tr>
<th>Doppler</th>
<th>Total (n)</th>
<th>Angiogram in agreement (n)</th>
<th>different (n)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Vertebral reverse flow (permanent SSP)</td>
<td>66</td>
<td>66</td>
<td></td>
</tr>
<tr>
<td>Vertebral alternating flow (partial SSP)</td>
<td>17</td>
<td>17</td>
<td></td>
</tr>
<tr>
<td>Vertebral alternating flow (without SSP)</td>
<td>8</td>
<td>5 hypoplasia</td>
<td>3 prox. vert. stenosis</td>
</tr>
<tr>
<td>Vertebral stenosis (atlas slope)</td>
<td>6</td>
<td>5 occlusion/aplasia</td>
<td>1 no stenosis</td>
</tr>
<tr>
<td>No vertebral flow</td>
<td>58</td>
<td>27 occlusion/aplasia</td>
<td>21 hypoplasia</td>
</tr>
<tr>
<td>Orthograde vertebral flow (&gt;75% asymmetry)</td>
<td>28</td>
<td>3 occlusion/aplasia</td>
<td>14 hypoplasia</td>
</tr>
<tr>
<td>Controls</td>
<td>243</td>
<td>216 (90.1%)</td>
<td>27 hypoplasia/prox. stenosis</td>
</tr>
<tr>
<td>Total</td>
<td>426</td>
<td>384 (90.1%)</td>
<td>42 (9.9%)</td>
</tr>
</tbody>
</table>
ischemia) or high-risk factors for atherosclerosis such as hypertension, diabetes, hyperlipidemia, smoking etc. Hypertension — probably the most important risk factor for cerebral ischemia — was present in 40% of the patients with peripheral vascular disease (A), in 35% of those with coronary artery disease (B) and in 38% of the group C patients.

Results

Correlation Between Findings on Auscultation and Extracranial Arterial Disease (EAD)

The reliability of normal auscultation for the diagnosis of extracranial arterial stenotic lesions was studied in 375 patients (group A). Attention was paid to uniformity of procedure in order to exclude all murmurs transmitted from the heart, venous hums and other non-arterial cervical sounds. Arterial bruits were graded only as absent or present, and no attempt was made to describe the intensity of the bruit. The presence of bruits heard at the anterior borders of the sternomastoid muscles was correlated with the Doppler results from the carotid artery system, and those heard in the supraclavicular areas were compared with the Doppler findings in the innominate-subclavian-vertebral artery system.

Figure 2 summarizes the results of this investigation. The results of auscultation correlated positively with the Doppler examination in only 61.2% (9.1% patients with abnormal and 52.1% with normal Doppler results). False positive results from auscultation (i.e., a bruit was heard but the Doppler examination was normal) were found in 22.9%. It is believed that most of these false positives probably resulted from hypertension, thyroid artery flow abnormalities or asymmetric transmission of cardiac murmurs in patients without stenotic lesions of the extracranial arteries (15.2%) and from bruits detected contralaterally to the side of the Doppler abnormality (7.7%). This may be caused by alterations due to an increased collateral flow.

False negative results were found in 15.9% (i.e., no bruit and an abnormal Doppler study). Based on the various degrees of obstruction from vascular lesions, 6.6% might have been missed due to either severe or mild stenotic lesions (> 90% and < 60% surface area reductions of the lumen). If a bruit is used as the only sign of associated EAD, only 27.6% (n = 34) of the 123 patients with asymptomatic extracranial disease would have been correctly diagnosed.

Stenotic lesions of the external carotid arteries were observed in 6 patients, all in combination with an internal carotid artery stenotic lesion. A bruit heard in the neck correlated with these severe arterial processes at the carotid bifurcation in four patients and auscultation was twice falsely negative.

Incidence and Degree of Asymptomatic EAD

Figure 3 shows the prevalence of hemodynamically relevant obstructions of the extracranial cerebral arteries within the 3 groups of patients described. Asymmetries of the vertebral arteries are not considered to be abnormal in instances of orthograde perfusion apart from patients with additional carotid disease, as there is a high percentage of vertebral hypoplasia and aplasia in controls.

A high prevalence of 32.8% (n = 123) of extracranial stenotic lesions was found in patients originally admitted for surgery for severe peripheral vascular disease (A). In contrast, the frequency of asymptomatic EAD was considerably lower in patients with severe coronary artery disease (6.8%, n
FIGURE 3. Incidence of asymptomatic extracranial arterial disease revealed by CW-Doppler examinations in patients originally admitted for surgery of severe vascular disease — 32.8% — (A), in patients with severe coronary artery disease — 6.8% — (B), and in patients with high-risk factors for atherosclerosis or only uncharacteristic complaints possibly due to diffuse cerebrovascular insufficiency — 5.9% — (C). Within these groups the number of vessels involved varies as indicated by the symbols explained on the right.

= 18) (B), and lowest in patients otherwise in good health apart from non-specific complaints possibly due to diffuse cerebrovascular insufficiency or high-risk factors for atherosclerosis (5.9%, n = 81) (C). This correlation of asymptomatic EAD in association with peripheral vascular disease is statistically highly significant (p < 0.001 x²-test). The remarkable difference between groups A and B/C is further emphasized by the varying number of extracranial vessels involved as shown in table 3.

About one-half (48.8%) of the patients with peripheral vascular disease and EAD had abnormalities in 2 or more cerebral arteries on Doppler examination. One-third of the patients with coronary artery disease and EAD (33.4%) and risk-factor patients with EAD (34.6%) had similar findings on Doppler examination.

Figures 4 and 5 further illustrate the degree of extracranial arterial obstruction as revealed by Doppler examination in the group most severely affected with peripheral vascular disease (A). Sixty-three patients showed stenosis or occlusion of only one cerebral artery. In 60 patients more than one vessel was affected. Among the patients with one vessel involved, 29 had mild or moderate stenosis of the carotids near the bifurcation and 10 had severe stenosis or occlusion (fig. 4). Since direct examination of flow velocity is restricted to the extracranial section of the carotid arteries, only a few severe intracranial lumen obstructions have been detected by a marked reduction of the diastolic blood flow velocity in the extracranial common and internal carotid arteries proximal to that lesion (4 patients). In contrast, a subclavian-steal phenomenon is often a result of either severe stenosis (n = 3) or occlusion of the subclavian artery (n = 17), and can be reliably diagnosed by non-invasive methods. Isolated lesions of the external carotid arteries have been observed in 10 patients.

<table>
<thead>
<tr>
<th>TABLE 3 The Incidence of One- and Multi-neck Artery Disease in Different Groups of Arteriosclerotic Patients (A / B / C)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients examined</td>
</tr>
<tr>
<td>--------------------------</td>
</tr>
<tr>
<td>375 A Peripheral vascular disease</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>264 B Coronary artery disease</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>1370 C Risk factor patients</td>
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<td></td>
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</table>
FIGURE 4. The incidence, degree (mild, moderate or severe stenosis and occlusion) and location of one-vessel asymptomatic extracranial arterial disease (total n = 63) in 375 patients with peripheral atherosclerotic disease submitted to CW-Doppler examination. Four cases of severe intracranial obstruction (subtotal or total) of the internal carotid artery as revealed by CW-Doppler examinations are included. Isolated obstructions of the vertebral and external carotid arteries (total n = 30) are indicated on the right side.

FIGURE 5. The incidence, number, degree (stenosis versus occlusion) and location of multi-vessel asymptomatic extracranial arterial disease (total n = 60) in 375 patients with peripheral atherosclerotic disease submitted to CW-Doppler examination. With respect to a poorer prognosis carotid-vertebral lesions versus bilateral carotid lesions in two-vessel disease, and carotid-vertebral-vertebral lesions (CVV) versus carotid-carotid-vertebral lesions (CCV), are separately handled. 4 indicates a retrograde perfusion of the arteries involved. In view of the poorer resolution of CW-Doppler examination within the vertebral system no differentiation between hypo- and aplasia versus stenosis and occlusion of these arteries could be obtained.
Multiple-vessel disease shows considerably more variations in both the number of vessels involved and the degree of the individual obstructions. In 47 (78%) of the 60 patients 2 cerebral arteries were involved, in 12 (20%) 3, and in one both carotid and vertebral arteries were affected by the atherosclerotic process.

As shown in figure 5, combined lesions including one or even both vertebral arteries occur considerably less frequently than bilateral carotid lesions in asymptomatic patients with EAD.

Lesions of both carotid arteries are the most common (n = 32); of 17 patients with bilateral stenosis, 3 had bilaterally mild, 9 mild to moderate or severe, and 5 bilaterally moderate to severe stenosis. In 11 patients a combination of unilateral occlusion of the internal or common carotid artery with stenosis of the contralateral side was observed. Three were mild, one moderate and 7 severe. In 4 patients both carotids were occluded indicating the possible extent of asymptomatic lesions. Carotid lesions of the same extent can be found in 3-vessel disease involving both carotids and one vertebral system (of 4 patients with bilateral stenosis and 7 with occlusion and contralateral stenosis, all but 2 were moderate to severe in degree). As in 2-vessel disease, combinations of carotid-carotid and single vertebral obstructions (n = 11) are more common than vertebral-vertebral and single carotid lesions (n = 1) in asymptomatic patients with 3-vessel disease. Additionally, the incidence of external carotid stenotic lesions was low in patients with multi-vessel disease (n = 8) as well as in those with stenosis or occlusion of only one cerebral artery.

Discussion

TIAs are very often harbingers of stroke. TIA and stroke have been shown to be caused by hemodynamically significant changes in cerebral perfusion by or by thrombo-embolic mechanisms, both commonly arising from extracranial arterial stenotic lesions. There is still controversy about the appropriate therapy, particularly in asymptomatic patients with EAD. One major reason for this is a general lack of data on the incidence and the spontaneous course of extracranial occlusive diseases and individual variability in these patients either to suffer from subsequent stroke or to remain without symptoms of ischemic brain disease, even though the atherosclerotic process proceeds. Most of what is known is from empirical experience based only on individual observations. Apart from limited angiographic studies none of the presently available data dealing with this subject is sufficient to solve this problem. Studies have often been based on inadequate indicators of EAD such as carotid bruits or have disregarded the vertebrabasilar system. When a carotid stenotic lesion is found contralateral to the cerebral hemisphere of a previous stroke, the patient is often somewhat arbitrarily classified as being asymptomatic. Therefore, only a non-invasive method allowing reliable detection of the individual vascular lesion will enable estimation of the prevalence of obstructive therapy, particularly in asymptomatic patients with EAD.

Although cervical bruits or murmurs sometimes indicate an underlying carotid arteriosclerotic lesion, they are often either falsely negative (27.6%), particularly for high and mild grade stenosis, or falsely positive (22.6%), for instance, as a result of misinterpretation of increased collateral flow contralateral to the side of an occluded carotid artery. Our results on the reliability of bruits are in good agreement with those of Gilroy and Meyer, — both 43% — and Ziegler et al., who found an even greater number of false negative results (73%) possibly because of the exclusion of minimal bruits and the inclusion of minor atherosclerotic lesions producing little change in the flow. From bruits no reliable information can be obtained about the degree of the carotid stenotic lesion, its progress during long-term follow up, or about the status of the vertebro-basilar system, whose involvement seems to be important in increasing the stroke risk.

Among the variety of methods which have been developed for the non-invasive evaluation of EAD, the direct Doppler technique has proved to give highly reliable results, as may be seen from the data in table 1. Its validity is crucially dependent on the skill of the examiner — with this proviso, it can be a useful clinical tool comparable to angiography for the detection of hemodynamically relevant carotid stenotic lesions within the extracranial course of these vessels. Although a reliable differentiation between subtotal and total occlusion of the internal carotid artery is not always possible with the Doppler examination (cf. fig. 1), it may also not be possible with arteriography. For additional highly sophisticated angiographic techniques, which usually are not performed, are disregarded. On the other hand, an occlusion can be simulated by spasm during invasive neuroradiologic procedures (cf. table 1) so that even these techniques may fail. The same is true for the detection of such low-grade stenotic lesions as minor irregularities of the arterial wall which may either be detected or undetected by both angiographic and Doppler techniques. The application of refined non-invasive techniques such as spectral analysis, pulsed Doppler and B-scan methods to the study of low grade and nonstenotic ulcerative lesions will probably improve the detection rate for these high and low grade stenoses. The CW-Doppler examination seems to be sensitive and specific enough, as compared with angiography of the cerebral arteries, for a study of the prevalence, extent and natural history of asymptomatic EAD. Since epidemiological studies have shown that about 30% of the patients with TIA and brain infarction have coexisting coronary and peripheral vascular occlusive disease, and/or a variety of risk factors for atherosclerosis, we expected to find a comparable percentage of asymptomatic patients with EAD within these groups.

Our data from 2009 patients, however, reveal a striking, statistically significant (p < 0.001) preference for asymptomatic EAD in association with peripheral vascular disease (32.8%) in contrast to a considerably lower frequency of EAD in patients with coronary
percentage of patients with combined peripheral and coronary occlusive diseases was equal, this difference cannot be explained on the basis of a more or less severe general atherosclerotic process. Neither the age and sex distribution nor the risk-factor profile — particularly with respect to hypertension — seems to be sufficient to account for this striking difference.

The prevalence of EAD in patients with coronary artery disease approximately equals that of EAD in patients with high-risk factors for atherosclerosis (5.9%), but this difference is not statistically significant (table 3). Although the relationship of these distinct occurrences of EAD with different forms of atherosclerosis remains a subject of speculation, the results presented allow some conclusions to be drawn on the management of these patients. Since every third patient (32.8%) undergoing vascular surgery, and 6.8% of those requiring aorto-coronary bypass surgery, are found to suffer from additional asymptomatic EAD, every patient who is a possible candidate for major vessel or bypass surgery should undergo a Doppler examination. The important question of how to use this additional information in the management of patients with asymptomatic EAD remains the subject of further investigation. It is therefore necessary and now possible to study the natural history of EAD in sufficiently large populations of asymptomatic patients and then to compare the course of asymptomatic EAD with that in patients with TIA and stroke.

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