Prospective Comparison of a Cohort With Asymptomatic Carotid Bruit and a Population-Based Cohort Without Carotid Bruit

David O. Wiebers, MD, Jack P. Whisnant, MD, Burton A. Sandok, MD, and W. Michael O'Fallon, PhD

This study is a prospective analysis of the predictive value of diffuse and localized carotid bruit. Patients with asymptomatic carotid bruits are compared with a population-based age- and sex-matched control group known not to have carotid bruit, in regard to subsequent transient ischemic attack, stroke, and death. Each person was followed until death or for 5 years. Among the 566 patients with asymptomatic carotid bruit, the annual stroke rate given survival was 1.5%/yr or 7.5% at 5 years by actuarial analysis. The annual stroke rate given survival for the 428 patients in the population-based cohort was 0.5%/yr or 2.4% at 5 years. Patients with localized carotid bruit were not significantly different from those with diffuse carotid bruits in regard to subsequent cerebral ischemic events ($p=0.11$). These data indicate that patients with asymptomatic diffuse or localized carotid bruit are approximately three times more likely to have ischemic stroke than an age- and sex-matched population sample known not to have carotid bruit. (Stroke 1990;21:984–988)

The proper management of patients with asymptomatic carotid bruits remains controversial. The number of patients with this disorder is large; approximately 12.6% of the population aged >45 years have been noted to have some type of cervical murmur.1 Approximately one third of these murmurs are localized mid-carotid bifurcation bruits, and about three fourths of the persons with localized bruit have not had cerebral or retinal ischemic symptoms.

When the clinician auscultates a localized or diffuse carotid bruit, the question of whether to perform further noninvasive or invasive diagnostic procedures or to treat the patient with antiplatelet or anticoagulant agents or carotid endarterectomy is raised. The purpose of this study was to provide a prospective analysis of the predictive value of diffuse and localized carotid bruit in a sample of patients compared with a population-based age- and sex-matched control group without carotid bruit in regard to subsequent transient ischemic attack (TIA), ischemic and hemorrhagic stroke, and death.

Two studies2,3 recently delineated the predictive value of asymptomatic carotid stenosis as defined by noninvasive cerebrovascular procedures (oculoplethysmography2 and carotid ultrasonography3). These studies indicated a significantly increased stroke risk for patients with asymptomatic carotid bruit and underlying high-grade internal carotid system stenosis ($\geq 75\%$ area stenosis) but an only slightly increased risk of stroke in patients with lesser degrees of stenosis. However, one of these studies was retrospective,2 and neither study included a population-based control group. Two population-based studies4,5 have addressed the predictive value of asymptomatic carotid bruit, but neither study delineated the predictive value of diffuse versus localized carotid bruit.

Subjects and Methods

From 1976 to 1980, we recruited 566 patients with asymptomatic carotid bruit (245 men and 321 women, mean age 65 years) who were seen at the Mayo Clinic. These patients were recruited from a referral practice and were initially seen as outpatients throughout the Mayo Clinic and were then referred to one of the investigators for examination and enrollment in the study. Each patient was interviewed and examined, and most patients had an ophthalmologic examination and measurement of retinal artery pressures.
vascular history, and a neurovascular examination were interviewed and examined by one of the investigators, consisting of blood pressure and pulse measurements.

The age and sex distributions of the asymptomatic bruit cohort are noted in Table 1. The population-based cohort was based on a sample of the population of Olmsted County, Minnesota, with the aim of evaluating approximately 1% of the population aged 45–54 years, 2.5% of the population aged 55–64 years, and 3.5% of the population aged ≥65 years. The individuals were randomly selected from a 10% sample of the population of Olmsted County aged >45 years, without regard to preexisting or current illness. The persons were initially contacted by telephone, and the project was explained to them. Those who refused or who were unwilling to be examined for any reason (including infirmity) were replaced by random selection of others in the same age and sex group. Those who agreed to participate were interviewed and examined by one of the investigators. Among the 509 persons who agreed to participate and were evaluated, 32 had prior TIA or stroke and 49 without prior TIA or stroke had cervical bruit and were included in the asymptomatic bruit cohort. The remaining 428 made up the population-based cohort without bruit are noted in Table 1.

All persons in each cohort were given a standardized examination including a health inventory, with particular attention to cerebrovascular and cardiovascular history, and a neurovascular examination consisting of blood pressure and pulse measurements and auscultation of the heart, neck, and orbits with the subject in the sitting and lying positions. Cervical bruits were characterized by their location, duration, and intensity and then further categorized as being 1) venous in origin, 2) supraclavicular, 3) transmitted to the carotid arteries, or 4) carotid artery bruits, a) localized to the mid–carotid bifurcation area or b) diffuse, over the entire cervical distribution of the carotid artery. Patients with only venous bruit were excluded from the present study.

Patients in both cohorts were followed by means of a standardized follow-up questionnaire that was mailed to the patient every 6 months. For a few patients, the questionnaire was completed by telephone interview.

All patients were followed for a total of 5 years or until death. The follow-up questionnaire solicited information relevant to any stroke-like symptoms the patient experienced, including transient symptoms. The patients were also asked to list other medical problems and all medications taken since their last follow-up.

When the report of a possible cerebral or retinal ischemic event was unclear, one of the investigators either examined the patient or spoke by telephone with the patient or the patient’s physician, or both, to document the end point (TIA or amaurosis fugax, ischemic or hemorrhagic stroke). In cases of deceased patients, the cause of death was determined by contacting the local physician or obtaining medical records, or both, including death certificates and autopsy information when available.

The occurrence and severity of end points was independently verified by at least two investigators based on review of all of the available data. The rates of survival, stroke, and stroke or TIA for both the asymptomatic carotid bruit cohort and the population-based cohort were estimated by the Kaplan-Meier life table method, beginning at the time of the initial identification of the patients for the study.

All persons in each cohort were given a standardized examination including a health inventory, with particular attention to cerebrovascular and cardiovascular history, and a neurovascular examination consisting of blood pressure and pulse measurements and auscultation of the heart, neck, and orbits with the subject in the sitting and lying positions. Cervical bruits were characterized by their location, duration, and intensity and then further categorized as being 1) venous in origin, 2) supraclavicular, 3) transmitted to the carotid arteries, or 4) carotid artery bruits, a) localized to the mid–carotid bifurcation area or b) diffuse, over the entire cervical distribution of the carotid artery. Patients with only venous bruit were excluded from the present study.

Patients in both cohorts were followed by means of a standardized follow-up questionnaire that was mailed to the patient every 6 months. For a few patients, the questionnaire was completed by telephone interview.

All patients were followed for a total of 5 years or until death. The follow-up questionnaire solicited information relevant to any stroke-like symptoms the patient experienced, including transient symptoms. The patients were also asked to list other medical problems and all medications taken since their last follow-up.

When the report of a possible cerebral or retinal ischemic event was unclear, one of the investigators either examined the patient or spoke by telephone with the patient or the patient’s physician, or both, to document the end point (TIA or amaurosis fugax, ischemic or hemorrhagic stroke). In cases of deceased patients, the cause of death was determined by contacting the local physician or obtaining medical records, or both, including death certificates and autopsy information when available.

The occurrence and severity of end points was independently verified by at least two investigators based on review of all of the available data. The rates of survival, stroke, and stroke or TIA for both the asymptomatic carotid bruit cohort and the population-based cohort were estimated by the Kaplan-Meier life table method, beginning at the time of initial identification of the patients for the study.

Death, stroke, and either stroke or TIA were treated as end points in separate life table analyses. Amaurosis fugax was considered as a TIA. When stroke or TIA was the end point and when a patient died during follow-up from a cause other than an end point, the patient was withdrawn from the sample under observation.

### Table 1. Age and Sex Distributions of Individuals in Both Cohorts

<table>
<thead>
<tr>
<th>Age (yr)</th>
<th>Asymptomatic bruit cohort</th>
<th>Population-based cohort without bruit</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M</td>
<td>F</td>
</tr>
<tr>
<td>45–54</td>
<td>22</td>
<td>36</td>
</tr>
<tr>
<td>55–64</td>
<td>83</td>
<td>114</td>
</tr>
<tr>
<td>65–74</td>
<td>105</td>
<td>134</td>
</tr>
<tr>
<td>≥75</td>
<td>35</td>
<td>37</td>
</tr>
<tr>
<td>Total</td>
<td>245</td>
<td>321</td>
</tr>
</tbody>
</table>

Data are number of individuals. M, male; F, female.

However, the vast majority of these patients had no other invasive or noninvasive cerebrovascular testing performed. The age and sex distributions of the asymptomatic bruit cohort are noted in Table 1.

All persons in each cohort were given a standardized examination including a health inventory, with particular attention to cerebrovascular and cardiovascular history, and a neurovascular examination consisting of blood pressure and pulse measurements and auscultation of the heart, neck, and orbits with the subject in the sitting and lying positions. Cervical bruits were characterized by their location, duration, and intensity and then further categorized as being 1) venous in origin, 2) supraclavicular, 3) transmitted to the carotid arteries, or 4) carotid artery bruits, a) localized to the mid–carotid bifurcation area or b) diffuse, over the entire cervical distribution of the carotid artery. Patients with only venous bruit were excluded from the present study.

Patients in both cohorts were followed by means of a standardized follow-up questionnaire that was mailed to the patient every 6 months. For a few patients, the questionnaire was completed by telephone interview.

All patients were followed for a total of 5 years or until death. The follow-up questionnaire solicited information relevant to any stroke-like symptoms the patient experienced, including transient symptoms. The patients were also asked to list other medical problems and all medications taken since their last follow-up.

When the report of a possible cerebral or retinal ischemic event was unclear, one of the investigators either examined the patient or spoke by telephone with the patient or the patient’s physician, or both, to document the end point (TIA or amaurosis fugax, ischemic or hemorrhagic stroke). In cases of deceased patients, the cause of death was determined by contacting the local physician or obtaining medical records, or both, including death certificates and autopsy information when available.

The occurrence and severity of end points was independently verified by at least two investigators based on review of all of the available data. The rates of survival, stroke, and stroke or TIA for both the asymptomatic carotid bruit cohort and the population-based cohort were estimated by the Kaplan-Meier life table method, beginning at the time of initial identification of the patients for the study.

Death, stroke, and either stroke or TIA were treated as end points in separate life table analyses. Amaurosis fugax was considered as a TIA. When stroke or TIA was the end point and when a patient died during follow-up from a cause other than an end point, the patient was withdrawn from the sample under observation.

### Table 2. Locations and Grades of Bruits Among Asymptomatic Carotid Bruit Cohort

<table>
<thead>
<tr>
<th>Grade of bruit</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Location of bruit</td>
<td>R base</td>
<td>40</td>
<td>62</td>
<td>24</td>
<td>15</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>R carotid</td>
<td>103</td>
<td>123</td>
<td>86</td>
<td>47</td>
<td>10</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>R orbit</td>
<td>7</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>L base</td>
<td>33</td>
<td>44</td>
<td>39</td>
<td>20</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>L carotid</td>
<td>100</td>
<td>132</td>
<td>103</td>
<td>53</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td>L orbit</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Data are number of bruits. R, right; L, left.
TABLE 3. Associated Medical Conditions in Both Cohorts

<table>
<thead>
<tr>
<th>Condition</th>
<th>Asymptomatic carotid bruit cohort (n=566)</th>
<th>Asymptomatic bruit from population-based cohort (n=49)</th>
<th>Population-based cohort without bruit (n=428)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypertension</td>
<td>41</td>
<td>25</td>
<td>29</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>13</td>
<td>20</td>
<td>13</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>15</td>
<td>18</td>
<td>19</td>
</tr>
<tr>
<td>Prior myocardal infarction</td>
<td>12</td>
<td>14</td>
<td>10</td>
</tr>
<tr>
<td>Angina pectoris</td>
<td>15</td>
<td>14</td>
<td>12</td>
</tr>
<tr>
<td>Cigarette smoking</td>
<td>Never</td>
<td>45</td>
<td>42</td>
</tr>
<tr>
<td></td>
<td>Ever</td>
<td>59</td>
<td>55</td>
</tr>
</tbody>
</table>

Data are percent of n.

To assess the relative impact of several independent variables on the risk of focal cerebral ischemic events or death, a Cox proportional-hazards analysis was used. The following independent variables were assessed: age; sex; diffuse versus localized bruit; systolic versus systolic and diastolic bruit; and presence versus absence of symptomatic peripheral vascular disease, diabetes mellitus, hyperlipidemia, history of myocardial infarction, angina, congestive heart failure, hypertension, abnormal retinal artery pressure measurements, and history of cigarette smoking.

Focal cerebral ischemic events were localized to either the carotid or the vertebrobasilar systems in accordance with previously published criteria. The diagnosis of congestive heart failure was based on clinical history and examination, including the opinion of a cardiologist or general internist. The diagnosis of diabetes mellitus was established according to previously published criteria. Hypertension was defined as a blood pressure of ≥160/95 mm Hg. The diagnosis of symptomatic peripheral vascular disease was based on clinical history and examination, including the opinion of a cardiologist or general internist; the vast majority of such patients had intermittent claudication. Cigarette smoking was recorded in terms of total pack-years of smoking.

Results

Of the 566 patients with asymptomatic bruit, 449 had carotid bifurcation bruit, 123 on the right, 159 on the left, and 167 bilateral. Ninety-five percent of these bruits were systolic only, and the other 5% had both systolic and diastolic components. One hundred seventeen patients had supraclavicular diffuse or transmitted bruit without carotid bifurcation bruit. Twenty-one orbital bruits were documented in this cohort, all of which were systolic in character. The bruits were graded on a scale of 1 to 6 to define loudness (Table 2).

Prevalence of bruit and other characteristics of the population-based cohort have been described previously. Associated medical conditions in the two cohorts are shown in Table 3.

The distribution of focal cerebrovascular symptoms (infarction or TIA) is listed in Table 4. Among the 566 patients with asymptomatic carotid bruit, 63 had unilateral or bilateral carotid system cerebral ischemic symptoms (21 had TIA and 32 had cerebral infarction). The ischemic symptoms were ipsilateral to the carotid bruit in 55 patients.

Among the population-based cohort, 17 of 428 patients had cerebral ischemic symptoms during follow-up (five had TIA and 12 had cerebral infarction). The arterial distribution of the focal ischemic symptoms is noted in Table 4. Among the 12 patients with cerebral infarction, one had antecedent TIA in an uncertain distribution. None had antecedent TIA clearly in the distribution of the subsequent infarct.

The probabilities of survival free of stroke are shown for both cohorts and are compared with expected rates for the entire Rochester, Minnesota, population in Figure 1. The cumulative probability of stroke (given survival) among the asymptomatic carotid bruit cohort was 7.5% in 5 years (1.5%/yr) compared with 2.4% in 5 years (0.5%/yr) for the population-based cohort. The cumulative probability of stroke or TIA (whichever was first) was 12% in 5 years (2.4%/yr) in the asymptomatic bruit cohort and 3.4% in 5 years (0.7%/yr) in the population-based cohort. Among patients in the asymptomatic bruit cohort, there was no difference in the probability of cerebral ischemic events for patients with diffuse compared with localized carotid bruit (p=0.11).

In the asymptomatic bruit cohort, 419 of 566 patients had retinal artery pressure measurements. Among these, 343 patients had normal studies, 72 had unilateral abnormalities, and four had bilateral abnormalities based on previously defined criteria. Among the 76 patients with abnormal studies, 16 (21%) had carotid system focal ischemic events, 15 of which were ipsilateral to the abnormal retinal artery pressure. In the population-based cohort, 412 patients had retinal artery pressure measurements, including 402 patients with normal studies, seven with unilateral abnormalities, and three with bilateral abnormalities. Among the 10 patients with
abnormal studies, only one had subsequent cerebral ischemic symptoms.

The probability of survival at 5 years was 84% in the asymptomatic bruit cohort, which was nearly identical to the expected survival of an age- and sex-matched West-North-Central white population (Figure 2, left). The probability of survival in the population-based cohort without bruit was 93%, which was much better than that expected for an age- and sex-matched population (Figure 2, right).

In the asymptomatic bruit cohort, 103 patients died (nine of cerebral infarction). In the population-based cohort, 36 patients died (four of cerebral infarction) during follow-up. The leading cause of death for both cohorts was cardiovascular (46 in the asymptomatic bruit cohort and 14 in the population-based cohort).

In the Cox proportional-hazards analysis outlined above for the asymptomatic bruit cohort, significant (p<0.05) independent predictors of future ischemic stroke were history of myocardial infarction (p=0.0034), particularly recent myocardial infarction (p<0.001), followed by abnormality of retinal artery pressure (p=0.0067), presence of signs and symptoms of peripheral vascular disease (p=0.02), and history of congestive heart failure (p=0.035).

The 49 patients with asymptomatic carotid bruit originally identified from the Olmsted County population were similar to the entire cohort of patients with asymptomatic carotid bruit in regard to survival and the probability of stroke or TIA.

**Discussion**

Patients with asymptomatic carotid bruit are approximately three times more likely to have ischemic stroke than an age- and sex-matched population sample known not to have carotid bruit. Meissner et al documented the increased risk for patients with pressure-significant carotid system lesions, with or without underlying bruit, defined by abnormal oculoplethysmographic studies and patients with localized carotid bruit and normal oculoplethysmographic studies. The methodology for the present study differed from that of the previous study in that the present study involved a prospective follow-up and the follow-up was carried out at 6-month intervals as opposed to a retrospective design with one follow-up at the end of the period in the previous study. The present design would be expected to identify more TIsAs and perhaps more strokes as well, particularly if the stroke deficit resolved entirely or was minimal. Therefore, ischemic stroke rates are used for comparison between the two studies.

Figure 3 demonstrates the probability of stroke (given survival) over 4 years for all of these groups and
indicates that the presence of a pressure-significant lesion as defined by oculoplethysmography is a better predictor of a future cerebral ischemic event than the presence of a bruit alone. The probabilities are quoted for 4 years because uniform complete information for all groups was available for this period.

There was no difference in the predictive value of localized versus diffuse carotid bruit, and this finding is consistent with recent data concerning the correlation between clinical auscultation and findings on cerebral angiography. These data indicate that either a diffuse or a localized carotid bruit is approximately 85% predictive of an underlying moderate to high-grade carotid stenosis in patients with cerebral ischemic symptoms.

The patients in the population-based cohort had a better prognosis with respect to stroke and a much better survival rate than the general population, and this was probably the result of a combination of several factors. First, the patients were contacted by telephone and agreed to participate and were willing and well enough to come in for an examination, thus excluding very ill or disabled persons and including persons who were probably healthier than the general population. Another source of improved prognosis in the population-based cohort was the exclusion of 49 patients with carotid bruit who were added to the asymptomatic carotid bruit cohort for purposes of follow-up. When these 49 patients were included in the population-based cohort, the stroke rate increased slightly (from 0.5% to 0.7%/yr), but the mortality rate (1.6%/yr) was still considerably better than the expected rate (3.3%/yr).

The relatively minor increase in stroke rate produced by adding the patients with carotid bruit to the population-based cohort without bruit, plus the 85% predictive value of bruit for underlying moderate to severe stenosis, suggests that moderate to severe carotid atherosclerosis may account for <25% of first stroke in the population.

With a subsequent stroke rate in this aggregate bruit cohort of approximately 1.5%/yr and an ipsilateral subsequent stroke rate of approximately 1%/yr, it does not seem justifiable to perform arteriography or carotid endarterectomy on all patients with bruit. However, it does seem justified to further characterize the magnitude of the underlying lesion with noninvasive studies such as oculoplethysmography and duplex scanning to identify patients at higher risk who may have a much better chance of benefiting from corrective surgery.

References

Key Words • bruit • cerebral ischemia • epidemiology • risk factors
Prospective comparison of a cohort with asymptomatic carotid bruit and a population-based cohort without carotid bruit.
D O Wiebers, J P Whisnant, B A Sandok and W M O'Fallon

Stroke. 1990;21:984-988
doi: 10.1161/01.STR.21.7.984

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://stroke.ahajournals.org/content/21/7/984