Carotid Bruits and Cerebrovascular Disease Risk
A Meta-Analysis

Christopher A. Pickett, MD; Jeffrey L. Jackson, MD, MPH; Brian A. Hemann, MD; J. Edwin Atwood, MD

Background and Purpose—Current guidelines recommend against routine auscultation of carotid arteries, believing that carotid bruits are poor predictors of either underlying carotid stenosis or stroke risk in asymptomatic patients. We investigated whether the presence of a carotid bruit is associated with increased risk for transient ischemic attack, stroke, or death by stroke (stroke death).

Methods—We searched Medline (1966 to December 2009) and EMBASE (1974 to December 2009) with the terms “carotid” and “bruit.” Bibliographies of all retrieved articles were also searched. Articles were included if they prospectively reported the incidence of transient ischemic attack, stroke, or stroke death in asymptomatic adults. Two authors independently reviewed and extracted data.

Results—We included 28 prospective cohort articles that followed a total of 17 913 patients for 67 708 patient-years. Among studies that directly compared patients with and without bruits, the rate ratio for transient ischemic attack was 4.00 (95% CI, 1.8 to 9.0, P < 0.0005, n = 5 studies), stroke was 2.5 (95% CI, 1.8 to 3.5, P < 0.0005, n = 6 studies), and stroke death was 2.7 (95% CI, 1.33 to 5.53, P = 0.002, n = 3 studies). Among the larger pool of studies that provided data on rates, transient ischemic attack rates were 2.6 per 100 patient-years (95% CI, 2.0 to 3.2, P < 0.0005, n = 24 studies) for those with bruits compared with 0.9 per 100 patient-years (95% CI, 0.2 to 1.6, P = 0.02, n = 5 studies) for those without carotid bruits. Stroke rates were 1.6 per 100 patient-years (95% CI, 1.3 to 1.9, P < 0.0005, n = 26 studies) for those with bruits compared with 1.3 per 100 patient-years (95% CI, 0.8 to 1.7, P < 0.0005, n = 6) without carotid bruits, and death rates were 0.32 (95% CI, 0.20 to 0.44, P < 0.0005, n = 13 studies) for those with bruits compared with 0.35 (95% CI, 0.00 to 0.81, P = 0.17, n = 3 studies) for those without carotid bruits.

Conclusion—The presence of a carotid bruit may increase the risk of cerebrovascular disease. (Stroke. 2010;41:2295-2302.)

Key Words: atherosclerosis ▪ carotid bruit ▪ prognosis ▪ stroke ▪ TIA

The physical examination of the patient is a fundamental medical skill and one cornerstone is auscultation. Although auscultation for carotid bruits is inexpensive and simple, auscultating for carotid bruits in asymptomatic patients has fallen out of favor. Both the US Preventive Services Task Force and the Canadian Task Force recommend against routine auscultation of carotid arteries.1,2 In a recent meta-analysis, we found that the presence of a carotid bruit is associated with increased risk for transient ischemic attack, stroke, or death by stroke.3 We concluded that a carotid bruit may be a marker of more generalized atherosclerosis.

Studies that have examined the strength of the relationship between carotid bruits and cerebrovascular events have been mixed. For example, the Systolic Hypertension in the Elderly study found carotid bruits to weakly predict cerebrovascular events with a relative risk of stroke of 1.3,4 whereas the Evans County Study found a strong relationship with a relative risk of 4.1 for the combined event rate of transient ischemic attacks (TIAs) and stroke.5 The uncertainty about the prognostic implications of a carotid bruit and the difficulty in managing asymptomatic carotid stenosis has led some organizations to recommend against routine auscultation for carotid bruits.1,2 Therefore, we conducted a meta-analysis to investigate the association of carotid bruits with cerebrovascular disease. Our study question was, “is there a relationship between the presence of a carotid bruits and the subsequent occurrence of TIA, stroke and death from stroke?”

Methods

Data Sources and Searches
We performed a search of the MEDLINE (1966 to December 2009) and EMBASE (1974 to December 2009) databases using the terms carotid AND bruit. In addition, we searched MEDLINE using the clinical queries PUBMED search engine that is based on a strategy developed by Haynes6: (carotid bruit) AND (incidence[MeSH:noexp] OR mortality[MeSH Terms] OR follow up studies[MeSH:noexp] OR prognosis[Text Word] OR predict*[Text Word] OR course*[Text Word]).

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We augmented our search by reviewing the reference lists of retrieved articles and review articles, personal files of the authors, and reference lists of related articles in the authors’ files. Our medical librarian performed an independent search to ensure completeness. The search was limited to the English language and only published reports were included (Figure 1). Abstracts were included in our search, but none met our inclusion criteria.

**Study Selection**

We attempted to identify all published studies that included prognostic information based on identification of the presence of a carotid bruit. To be included in the analysis, studies had to be on prospective cohorts of asymptomatic adults, English language, and have extractable cerebrovascular outcome data.

**Quality Assessment**

Two reviewers (C.A.P., J.L.J.) independently rated each study’s quality using the rating scheme proposed by Hayden.7 Studies were assessed with 31 questions that assessed quality in 7 domains: (1) description of patient population characteristics; (2) completeness of follow-up; (3) measurement of prognostic factors; (4) measurement of outcomes; (5) measurement and adjustment for potential con-
founders; (6) appropriateness of the analytic methods; and (7) measurement of a carotid bruit. The Spearman rank correlation coefficient for agreement between the 2 raters on overall quality rating for all included studies was 0.84. Disagreements were resolved by consensus.

Data Extraction
Data were abstracted independently by 2 investigators (C.A.P., J.L.J.). From each included study we abstracted study design, year, country, number of included patients, length of follow-up, sex, race, prevalence of diabetes, hypertension, tobacco use, hyperlipidemia, congestive heart failure, atrial fibrillation, point of referral, known coronary or peripheral vascular disease, and the percentage of patients with carotid stenosis >50%. Outcome variables abstracted included the rate of TIA, stroke, and death from stroke. We were unsuccessful in contacting 1 author for data clarification.

Data Synthesis and Analysis
For each study we calculated the rate per patient-year from data provided in each article. Variance for rates was calculated using exact binomial methods. For studies that had direct comparison between patients with and without carotid bruits, rate ratios were calculated. Both rates and relative rates were pooled using a random effects method. Comparison between pooled results for cohorts with and without carotid bruits was performed using meta-regression. Heterogeneity was assessed visually with Galbraith plots as well as the $\chi^2$ test for heterogeneity using the methods of Mantel and Haenszel. Publication bias was assessed visually using funnel plots as well as statistically using the methods of Begg and Egger. In addition, whether statistical or visual heterogeneity was present or not, we performed a sensitivity analysis using stratified analysis and meta-regression to assess the effects of study quality based on the rating in each of the 7 domains (a components approach) and potential confounders (atrial fibrillation, hypertension, diabetes, tobacco use, hyperlipidemia, sex, etc) on our results. All analyses were performed using STATA 112 (STATA Corporation, College Station, Texas).

Results

Search Results and Study Characteristics
We identified 785 potential articles from our literature search. We excluded 757 articles (Figure 1), resulting in 28 articles for analysis. Most articles (n=353) were excluded because review of the title or abstract revealed that the article did not address carotid bruits or did not report outcomes. Among the 28 included studies, 21 were from the United States, from Canada, 33–35 Australia, 38 and Switzerland (Table 1). The mean sample size was 639.8 patients (range, 31 to 4442) who were followed a mean of 3.75 years (range, 1.7 to 7.0 years). In all, a total of 17,913 patients were followed for 67,708 patient-years. This was an older population; the mean age was 64.8 years (range, 60 to 71.6 years). A mean 56.3% of patients were male (range, 25% to 100%). Among the 8 studies that reported ethnicity, patients were predominantly white (mean, 69.5%; range, 12.3% to 100%). Other important potential confounders are provided in Table 2.

Quality Assessment
Studies varied in quality, although most studies had quality problems. Fifty-two percent met our quality rating criteria for an appropriate sampling method; 35% met criteria for adequate follow-up. Only 39% collected information about prognostic factors, 39% collected data on confounders, 65% met criteria for unbiased outcome assessments, 26% used an appropriate analytic approach to the data they reported, and 34% appropriately measured carotid bruits.

Outcomes

Transient Ischemic Attack
Five studies provided head-to-head comparisons of patients with and without carotid bruits (Figure 2). The pooled risk ratio for a TIA in patients with carotid bruit was 4.00 (95% CI, 1.77 to 9.03, $P<0.0005$, heterogeneity $\chi^2=10.0$ [df=4], heterogeneity $P=0.04$, $I^2=60.0\%$). Among the 24 included studies that reported rates of TIA in patients with carotid bruit, the pooled estimate of the annual rate of TIA was 2.6 per 100 patient-years (95% CI, 2.0 to 3.2, $P<0.0005$, heterogeneity $\chi^2=166.5$ [df=23], $I^2=86.2\%$, heterogeneity $P<0.0005$; Figure 3). Five studies reported rates of TIA among patients without bruits: 0.9 per 100 patient-years (95% CI, 0.28 to 1.7, $P=0.02$, heterogeneity $\chi^2=20.3$ [df=4], heterogeneity $P<0.0005$, $I^2=80.3\%$). The difference in the pooled rates of TIA was statistically significant ($P=0.03$).

Table 2. Prevalence of Prognostic Factors and Confounders

<table>
<thead>
<tr>
<th>No. of Studies Reporting</th>
<th>Mean</th>
<th>Range</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>26</td>
<td>64.8 years</td>
</tr>
<tr>
<td>Follow-up</td>
<td>28</td>
<td>3.8 years</td>
</tr>
<tr>
<td>Surgery</td>
<td>17</td>
<td>13.4%</td>
</tr>
<tr>
<td>Carotid intima-media thickness &gt;50%</td>
<td>7</td>
<td>48.7%</td>
</tr>
<tr>
<td>Smoke</td>
<td>14</td>
<td>52.1%</td>
</tr>
<tr>
<td>Hypertension</td>
<td>19</td>
<td>49.5%</td>
</tr>
<tr>
<td>Hyperlipidemia</td>
<td>7</td>
<td>31%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>18</td>
<td>22.1%</td>
</tr>
<tr>
<td>Peripheral vascular disease</td>
<td>8</td>
<td>51%</td>
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<tr>
<td>Coronary artery disease</td>
<td>14</td>
<td>40.2%</td>
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<tr>
<td>Race (white)</td>
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<td>69.5%</td>
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<tr>
<td>Sex (male)</td>
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<td>56.3%</td>
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<tr>
<td>Atrial fibrillation</td>
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<td>1.96%</td>
</tr>
<tr>
<td>Cardiovascular disease</td>
<td>28</td>
<td>0%</td>
</tr>
<tr>
<td>Congestive heart failure</td>
<td>3</td>
<td>4.2%</td>
</tr>
</tbody>
</table>

Figure 2. TIA rate ratios among patients with and without a carotid bruit.
Pooled TIA rates were statistically and visually heterogeneous as were the risk ratios.

**Stroke**

Six studies provided a head-to-head comparison of patients with and without carotid bruits (Figure 4). The pooled risk ratio for stroke in patients with carotid bruit was 2.49 (95% CI, 1.77 to 3.52, P<0.0005, heterogeneity χ²=10.8 [df=5] heterogeneity P=0.06, I²=53.8%). Among 26 studies reporting the rate of stroke in patients with carotid bruit, the pooled estimate of the annual rate of stroke was 1.6 per 100 patient-years (95% CI, 1.3 to 1.9, P<0.0005, heterogeneity χ²=89.9 [df=25] heterogeneity P<0.0005, I²=72.2%; Figure 5). Six studies reported the stroke rate among patients without bruits: 1.3 per 100 patient-years (95% CI, 0.8 to 1.7, P<0.0005, heterogeneity χ²=135.3 [df=4] heterogeneity P<0.0005, I²=97.0%). This difference in rates was not statistically significant (P=0.37). Pooled stroke rates were statistically and visually heterogeneous, although risk ratios were not.

**Death From Stroke**

Three studies provided a head-to-head comparison of patients with and without carotid bruits (Figure 6). The pooled risk ratio for death from stroke in patients with carotid bruit was 2.71 (95% CI, 1.33 to 5.53, P=0.002, heterogeneity χ²=1.04 [df=2] heterogeneity P=0.59, I²=0.0%). Among 13 studies that reported rates of death from stroke in patients with carotid bruits, the pooled estimate of the annual rate of death from stroke was 0.32 per 100 patient-years (95% CI, 0.20 to 0.44, P<0.0005, heterogeneity χ²=7.3 [df=11] heterogeneity P=0.77, I²=0.0%; Figure 7). Among these studies, 3 reported rates of death from stroke among patients without bruits: 0.35 per 100 patient-years (95% CI, 0.00 to 0.81, P=0.17, heterogeneity χ²=19.7 [df=2] heterogeneity P=0.0005, I²=89.8%). This difference in rate was not statistically significant (P=0.96). Neither the risk ratio nor the pooled death from stroke for patients with carotid bruits had statistical or visual evidence of heterogeneity. The pooled rate of death among patients without carotid bruits was heterogeneous.

**Sensitivity Analysis**

Not all studies reported all potential confounding variables. Among included trials, 8 reported the incidence of diabetes, hypertension, hyperlipidemia, and tobacco use; 7 reported the incidence of 3 of these risk factors; 3 provided information on 2 risk factors; and 11 provided no information. Among those studies that provided this information, only patient age was associated with outcomes. Older patients were more likely to have both TIAs (β=0.43, 95% CI, 0.01 to 0.84) and strokes (β=0.09, 95% CI, 0.01 to 0.24). We also performed a components analysis exploring the effect of quality on outcomes. We found that the quality domain, “adequacy of measurement of prognostic factors,” was associated with stroke rates; those studies that met the criteria for this domain had lower stroke rates than those that did not meet the criteria. There was no evidence of publication bias for any outcome assessed.
Cerebrovascular events are a frequent, serious, and disabling medical problem. Worldwide strokes accounted for 5.7 million deaths in 2005. In 2004, the World Health Organization estimated that 15 million people had a stroke and 5 million of those were left permanently disabled. A simple diagnostic test or indicator that can predict the risk of cerebrovascular events would be helpful in allowing clinicians to focus primary preventive efforts to prevent disability and death. Our study suggests that the carotid bruit may be a candidate for such a tool. In this study, we found that the presence of carotid bruits significantly increased the likelihood of cerebrovascular events. Among studies with control groups, the relative risk of TIAs, strokes, and death increased 2- to 4-fold. This increased risk is comparable to several other well-established risk factors such as hyperlipidemia, coronary artery disease, or asymptomatic carotid stenosis.

There are several limitations that temper our enthusiasm. First, it is unclear whether intervening among patients with a carotid bruit would improve outcomes. Several previous studies have shown that although carotid bruits are associated with cerebrovascular events, these strokes often occur on the contralateral side. Surgical intervention for asymptomatic carotid bruits has been studied with mixed results. Important factors for potential benefit for asymptomatic carotid surgery include surgical complication rates, the patient’s sex, and whether or not the patient has complete contralateral carotid obstruction. Whether intensive medical management such as aggressive lipid-lowering or addition of antiplatelet therapy would reduce these rates is uncertain. Cholesterol reduction may reduce stroke risk, whereas aspirin therapy alone may not.

Second, when we pooled rates of TIAs, strokes, and death among all studies, including those without controls, only the rate of TIA events was statistically higher. One must be cautious in interpreting these results because there was considerable heterogeneity among the different study populations included and most studies did not report enough information about important potential prognostic characteristics to evaluate for confounding. Moreover, higher-quality studies contained a cohort with and without carotid bruits. These studies, in which direct comparisons were possible, were methodologically better, and in those comparisons, the prognostic implication of a carotid bruit was stronger. Preventive task force groups currently do not recommend routinely screening with carotid auscultation based both on the clinical uncertainty about the prognostic value of carotid bruits as well as the risks of additional tests and the risks of potential carotid endarterectomy. Our data suggest that the presence of a carotid bruit has significant prognostic implications, although the issue of impact of further testing and therapeutic interventions remain important and need to be taken into account in recommending for or against routine auscultation. Given that we have now found that carotid bruits are associated with a significant increase in the risk of...
cardiac and cerebrovascular events, clinicians who find a bruit should consider aggressive medical modification of patient risk factors.

There are a number of additional limitations to our findings. First, most of the studies did not collect important prognostic information such as the incidence of diabetes, hypertension, or other vascular risk factors, much less adjust for them. Consequently, from our data, it is not possible to determine the independent contribution that carotid bruits have on subsequent risk of cerebrovascular events. It is likely that after adjusting for these independent risk factors, the prognostic implications of a carotid bruit would be smaller. In our opinion, a carotid bruit should not be thought of as an independent “risk factor” for atherosclerotic vascular disease. Instead, it is a marker for the presence of atherosclerotic disease and is a consequence of the cumulative effects of risk factors. To further evaluate the prognostic implications of a carotid bruit heard on examination, the finding needs to be studied prospectively in a large cohort with adjustment of the presence of other well-established vascular risk factors. Second, the number of studies that directly compared outcomes among patients with and without carotid bruits was modest. Among these methodologically stronger studies, the prognostic implication of a carotid bruit was stronger. Third, most of the included studies were from the 1970s and 1980s. It is possible that changes in medical care could influence the prognosis of patients with bruits. Fourth, we limited included articles to English language only. Review of the titles and abstracts of the 32 non-English articles revealed 9 articles (German: 2, Italian: 2, Croatian: 1, Czech: 1, French: 1, Portuguese: 1, Spanish: 1) that might have provided relevant data. Although it is common to include only English language articles in meta-analyses, given the difficulties obtaining accurate medical translations in the various languages, there is literature that suggests that non-English language articles are equally high in quality. Fifth, few studies (34%) specifically defined carotid bruits, and it was unclear whether other causes of a carotid murmur were specifically excluded. Sixth, many of our results were heterogeneous, meaning that there was a considerable difference in results among the included studies. This heterogeneity makes it difficult to know how accurate the pooled outcomes are. The lack of reporting on important confounding variables also made it impossible to explore the specific cause of heterogeneity. We used a random effects model to take into account unexplained heterogeneity and we believe the underlying studies are similar enough to justify pooling. Finally, carotid auscultation is insensitive (sensitivity = 11% to 51%) although specific for the presence of carotid atherosclerosis (specificity = 94% to 99%). However, these test characteristics describe the relationship between detection of a carotid bruit and finding significant stenosis of the carotid artery. We are not attempting to assess degree of stenosis by auscultation, but rather predict risk for future atherosclerotic cerebrovascular outcomes. More relevant to our analysis is the fact that auscultation for carotid bruits has good interrater reliability (κ = 0.67). Independent clinicians tend to agree on whether or not a carotid bruit is present.

**Conclusion**

Patients with a carotid bruit have over 4 times the risk of TIA, over twice the risk of stroke, and an increased risk of death from stroke when compared with defined patient controls without carotid bruits. In lower-quality studies, the pooled rate of TIA in patients with carotid bruit is higher than reported rates among patients without bruits, although not strokes or death. When limited to high-quality studies, the pooled data showed the prognostic implication of a carotid bruit to be stronger. Unfortunately, the implication of this finding is unclear. Given this associated increased risk of cerebrovascular morbidity and mortality, a carotid bruit most likely represents generalized atherosclerosis. Clinical trials have found that aggressive modi-
fication of cardiovascular risk factors reduces subsequent cardiovascular events. It would be tempting to recommend that clinicians auscultate for carotid bruits and, when found, consider aggressive modification of cerebrovascular disease risk factors. Although it is possible that such a strategy may reduce TIA s, strokes, and death, such a conclusion awaits prospective interventional trials, in which the effects of auscultation and aggressive modification of cerebrovascular risk factors such as aggressive cholesterol reduction are compared with standard management.

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We thank the late W. Proctor Harvey, MD, for his inspiration and endless dedication to the one of the fundamental arts of the practice of medicine: the physical examination.

Disclosures

None.

References


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