Evaluation of the clinical utility of a carotid bruit

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Summary

Background: Uncertainty exists over whether listening for carotid bruits as part of the clinical examination is informative in terms of predicting the presence or severity of carotid stenosis.

Aim: We sought to undertake a comprehensive meta-analysis and meta-regression of all studies to date that have assessed the relationship between a carotid bruit and severity of degree of stenosis.

Methods: Electronic databases were used to identify all published studies in humans evaluating the association between bruit and stenosis published until and including October 2011. Pooled sensitivity, specificity and diagnostic odds ratio (DOR) were calculated for each stenosis group. Summary receiver operating characteristic (SROC) curve analysis was performed in studies assessing clinically relevant (i.e. >70%) stenosis. Meta-regression was performed in all studies, using random effects.

Results: We identified 26 studies evaluating the association between carotid bruit and stenosis, in 15117 arteries. For clinically relevant stenosis (i.e. >70%), we found pooled sensitivity 0.53 [95% confidence interval (CI): 0.5–0.55], specificity 0.83 (95% CI: 0.82–0.84) and DOR 4.32 (95% CI: 2.78–6.66). SROC curve analysis gave an area under the curve of 0.73. Meta-regression analysis showed a (non-significant) ($P=0.067$) inverse relationship between carotid bruit and stenosis.

Conclusion: The carotid bruit is of moderate value for detecting clinically relevant carotid stenosis. It gives high specificity but low sensitivity. The likelihood of a carotid bruit does not increase at increasing degrees of stenosis.

Introduction

Over the past 5 decades, there has been much debate about the clinical significance of carotid bruits\textsuperscript{1–17} with some studies reporting bruits in \textsuperscript{~4%} of the normal population.\textsuperscript{9,18,19}

Several large studies have shown that high degrees of carotid stenoses are a major risk factor for stroke in symptomatic\textsuperscript{20,21} and asymptomatic\textsuperscript{22} patients. However, a wide range of sensitivity (24–84%) and specificity (40–98%) exists for carotid bruits predicting stenosis.\textsuperscript{12} Furthermore, in high degrees of stenosis or occluded vessels, bruits may be absent due to reduced or non-existent flow.\textsuperscript{10,23} The association of bruit and generalized atheroma is further evidenced by the predictive value of bruits in myocardial infarction.\textsuperscript{13} In a recent meta-analysis, patients with bruit were found to be at a 4-fold increased risk of stroke;\textsuperscript{14} however, the relationship between bruit and increasing levels of stenosis has yet to be defined.

We sought to undertake a comprehensive meta-analysis of all studies to date to assess the clinical utility of a carotid bruit. We also performed a meta-regression analysis to test the a priori hypothesis that the likelihood of a carotid bruit increases with increasing levels of stenosis.

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Methods

Data sources

Electronic searches using PubMed, Google Scholar, Yahoo and EMBASE were used to identify all published studies in humans evaluating the association between bruit and stenosis and bruit and stroke published until and including October 2011. Letters and abstracts were included in the searches. The medical subject headings and text words used for the search were "stenosis", "stroke", "transient ischaemic attack" and "bruit" with a and/or as a Boolean operator. Search results were limited to human, and all languages were searched. The references of all identified publications were hand searched for additional studies and the PubMed option related articles was used to examine all relevant articles.

Study selection

Selection criteria included all studies where the degree of carotid stenosis was measured and the presence or absence of carotid bruit was assessed. Studies were selected where stenosis was diagnosed using appropriate imaging, i.e. Doppler ultrasound, Doppler spectrum analysis, carotid angiography, digital subtraction angiography or oculoplethysmography. All patient populations were included such as patients presenting to neurology or vascular outpatients, patients with coronary artery disease, peripheral vascular disease and patients scheduled to undergo coronary artery bypass grafting. Studies were excluded if no control or comparable group was present or if the appropriate data were not available. For studies with more than one publication describing results among the same or overlapping groups of patients or controls, only the largest of the available published data sets was included.

Study quality

We assessed study quality using the Effective Public Health Practice Project Quality Assessment tool. Six characteristics were assessed: selection bias, study design, confounders, blinding, data collection methods, withdrawals and drop-outs. Studies were graded strong, moderate or weak. The PRISMA guidelines were followed (http://www.prisma-statement.org/).

Statistical analyses

Data were analysed using Meta-DiSc and Comprehensive Meta Analysis version 2.2.023 (Biostat, http://www.biostat.org). Pooled sensitivity, specificity and diagnostic odds ratio (DOR) were calculated for each stenosis group using (DerSimonian and Laird) random effects models. Sensitivity analysis was also performed. Summary receiver operating characteristic (SROC) curve (DerSimonian Laird model) analysis was performed in studies assessing clinically relevant stenosis (i.e. >70, 75 and 80% stenosis). Sub-group analyses were performed for studies defining symptomatic and asymptomatic bruits. Meta-regression, using random effects (method of moments estimator), was performed to determine the association between the presence of a carotid bruit and the degree of stenosis.

Tests for heterogeneity were performed for each meta-analysis with significance set at $P \leq 0.05$. Publication bias was assessed using funnel plots, while the Egger regression asymmetry test was conducted for each category with two or more publications. Meta-regression was performed using random effect (method of moments estimator) model.

Results

A total of 10,328 studies were identified in our primary search. After reviewing 94 abstracts, 41 manuscripts were reviewed and 15 were excluded (Figure 1). Twenty-six studies evaluating the association between carotid bruit and stenosis met our inclusion criteria. Out of 26 articles, study quality was graded moderate in 4 and...
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weak in 22. However, this was due to the fact that 24 studies were observational and only three reported blinding (Supplementary Table 1).

The meta-analysis relating carotid bruits to stenosis included 15 117 arteries (3502 with bruits and 11 615 without bruits) in 26 studies (both arteries were not assessed in all studies). The degree of stenosis was classified into six groups depending on the percentage luminal diameter at which stenosis was defined as 25–30% stenosis (four studies), 50% stenosis (12 studies), 60% stenosis (seven studies), 70% (six studies), 75% (three studies) and 80% (three studies) (Figure 1).

Pooled DOR, pooled sensitivity and pooled specificity values for each stenosis group are listed in Table 1. Sensitivity analysis was carried out by removing those studies graded moderate for a stenosis level of 50 and 60%. No studies assessing other levels of stenosis were graded moderate, therefore sensitivity analysis was not carried out in these groups. DOR was significant in all groups except at stenosis >80% (95% CI: 0.64–6.14). There was significant heterogeneity between studies in all stenosis groups. For clinically relevant stenosis (i.e. >70, 75 and 80%) (n = 12), we found pooled sensitivity of 0.53 (95% CI: 0.5–0.55) (Figure 2), pooled specificity of 0.83 (95% CI: 0.82–0.84) (Figure 3) and pooled DOR of 4.31 (95% CI: 2.78–6.66) (Figure 4). There was no overlap between studies. SROC curve analysis gave an area under the curve of 0.73 (Figure 5) suggesting listening for carotid bruits of moderate value in assessing stenosis. Sub-group for clinically significant asymptomatic stenosis (n = 3) showed pooled sensitivity 0.59 (95% CI: 0.53–0.65), pooled specificity 0.85 (95% CI: 0.83–0.87) and pooled DOR 7.95 (95% CI: 5.83–5.24). A sub-group analysis for clinically significant asymptomatic bruits was not performed, as study number was insufficient (n = 2).

Meta-regression analysis shows an inverse relationship between carotid bruit and stenosis (Figure 6). However, this was not statistically significant [correlation co-efficient (cc) = -0.00914, P = 0.07]. Sub-group analyses of asymptomatic and symptomatic bruits were not significant (asymptomatic: cc = -0.0453, P = 0.08, symptomatic: cc = -0.0076, P = 0.48).

Table 1 Pooled sensitivity, specificity and DOR at varying levels of stenosis

<table>
<thead>
<tr>
<th>Stenosis (%)</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>DOR</th>
<th>CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>0.492</td>
<td>0.9</td>
<td>6.2</td>
<td>2.55–15.03</td>
</tr>
<tr>
<td>50</td>
<td>0.558</td>
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<td>5.934</td>
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</tr>
<tr>
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CR, clinically relevant stenosis: 70, 75 and 80%; DOR: diagnostic odds ratio; CI: confidence interval.

Discussion

We show that listening for carotid bruits is of moderate value when assessing stenosis. Its relatively good specificity suggests that the absence of a bruit is useful in ruling out stenosis but the presence of a bruit does not necessarily imply that stenosis is present. Furthermore, we found a statistically significant diagnostic odd ratio of carotid bruit as a test for carotid stenosis at all levels apart from stenoses >80%. This may be due to the absence of bruits as a consequent to reduced flow intraluminal turbulence at increasing levels of stenosis.10,23 Meta-regression analysis showed an inverse relationship between bruit and stenosis; however, this was not statistically significant (P = 0.07).

Prompt surgical intervention following detection of clinically relevant stenosis has been shown to improve outcome. There is therefore a time-sensitive need to determine the severity of clinically relevant stenosis as quickly as possible following a cerebral event. Our study suggests carotid bruit as a predictor of degree of stenosis has a relatively high specificity in all groups except a clinically relevant stenosis of >80%.

The European Carotid Surgery Trial (ECST)21 found that carotid endarterectomy is indicated in carotid stenosis of >80%, whereas the North American Sympathetic Endarterectomy Trial (NASCET)20 found benefit at 70–99% stenosis. For the purpose of this meta-analysis, we define clinically relevant carotid stenosis as stenosis groups 70, 75 and 80%. However, two recent Cochrane reviews assessing the benefit of carotid endarterectomy in symptomatic and asymptomatic carotid stenosis suggest that there may be benefit in treating patients with 50% stenosis and above. In a symptomatic carotid stenosis review, Rothwell et al. concludes that endarterectomy is of some benefit for patients with 50–69% stenosis, whereas it is highly beneficial in patients with 70–99% stenosis.44 For asymptomatic stenosis, Chambers et al.45 states that there was no difference of treatment effect between 60–69%, 70–79%, 80–89% and 90–99% stenosis groups,

**Table 1**

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Sensitivity analysis.
Figure 2. Graph showing SROC curve analysis for clinically relevant stenosis. *Each study is represented by a red dot with size corresponding to weighting. Area under the curve (AUC) is 0.73 and (Q*) Q-index is 0.67 suggesting listening for carotid bruits of moderate value in assessing stenosis. Standard error of AUC SE and standard error of Q-index are low SE(Q*) at 0.03 and 0.02, respectively. *Clinically relevant stenosis: 70, 75 and 80%.

Figure 3. Graph showing Pooled DOR for clinically relevant stenosis. Each study is represented by a red dot with size corresponding to weighting. Pooled DOR is 4.31 showing value in auscultating for carotid bruits. Cochran-Q test shows significant heterogeneity. I-square shows a high percentage of variation across studies due to heterogeneity. Tau-squared shows between study variance.
Figure 4. Graph showing pooled specificity for clinically relevant stenosis. Each study is represented by a red dot with size corresponding to weighting. Pooled specificity of 83% shows that those without carotid bruits are unlikely to have stenosis. Chi-square shows significant heterogeneity. I-square shows a high percentage of variation across studies due to heterogeneity.

Figure 5. Graph showing pooled sensitivity for clinically relevant stenosis. Each study is represented by a red dot with size corresponding to weighting. Pooled sensitivity of 53% shows that the presence of a carotid bruit is not sensitive to carotid stenosis. Chi-square shows significant heterogeneity. I-square shows a high percentage of variation across studies due to heterogeneity.

Figure 6. Weighted linear regression of log odds ratio of bruit against % carotid stenosis. Meta-regression showing a (non-significant) inverse relationship between carotid bruit and stenosis.
although their analysis was underpowered. A study by Rothwell et al. assessed the risk of stroke in asymptomatic carotid artery stenosis for patients on best medical therapy. This showed that for those with $\geq 50\%$ stenosis, the risk of stroke was low.\textsuperscript{46} Although still a matter of debate, there is little evidence for carotid endarterectomy in asymptomatic carotid stenosis.\textsuperscript{47}

Our study has a number of limitations, which need to be taken into consideration. A wide range of imaging methods were used to detect and measure carotid artery stenosis, but only one study reported using NASCET or ESCT criteria to define stenosis.\textsuperscript{32} Rothwell et al.\textsuperscript{48} has previously highlighted the difficulty of performing a meta-analysis of studies with poor methodologies and design where carotid stenosis has been measured. Study quality was reported as weak in 22 of 26 studies. However, this was mainly due to the fact that most studies were observational or failed to report blinding. As with any meta-analysis its interpretation must be made within the context of these limitations, including study selection, publication bias and variability in the methodological quality of the included studies. Although publication bias was quantified by us, it cannot be completely excluded.

Carotid bruits are associated with an increased risk of TIA and stroke\textsuperscript{14} and are a prognostic indicator of cardiovascular death and myocardial infarction.\textsuperscript{13} Therefore, the detection of a carotid bruit should prompt implementation of cardiovascular risk reduction strategies.

Our findings suggest that routine examination for carotid bruits in clinical practice is of moderate use in identifying the presence of carotid stenosis. However, the absence of a bruit does not reliably exclude disease particularly at higher levels of stenosis. Therefore, duplex ultrasound scanning of the carotid arteries must be performed in symptomatic patients. We also show that increasing severity of stenosis does not increase the likelihood of a carotid bruit.

Supplementary Data
Supplementary Data is available at NAR QJMED Online.

Acknowledgements
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