Carotid artery ultrasonographic assessment in patients from the Fremantle Diabetes Study Phase II with carotid bruits detected by electronic auscultation


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Carotid artery ultrasonographic assessment in patients from the Fremantle Diabetes Study

Phase II with carotid bruits detected by electronic auscultation

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Running head: Electronic auscultation for carotid bruits

Key words: Carotid bruit, diabetes, electronic auscultation, Doppler ultrasound, intima-medial thickness
Abstract

Background: Electronic auscultation appears superior to acoustic auscultation for identifying hemodynamic abnormalities. The aim of this study was to determine whether carotid bruits detected by electronic stethoscope in patients with diabetes are associated with stenoses and increased carotid intima-medial thickness (CIMT).

Methods: Fifty Fremantle Diabetes Study patients (mean±SD age 73.7±10.0 years, 38.0% males) with a bruit found by electronic auscultation and 50 age- and sex-matched patients with normal carotid sounds were studied. The degree of stenosis and CIMT were assessed from duplex ultrasonography.

Results: Patients with a bruit were more likely to have stenosis ≥50% and CIMT >1.0 mm than those without (odds ratios (95% confidence intervals) 14.0 (1.8-106.5) and 5.3 (1.8-15.3), respectively, both \( P=0.001 \)). For the six patients with stenosis ≥70%, five had a bruit and one (with a known total occlusion) did not (5.0 (0.6-42.8), \( P=0.22 \)). The sensitivity and specificity of carotid bruit for stenoses ≥50% and ≥70% were 88% and 58%, and 83% and 52%, respectively. The equivalent negative and positive predictive values were 96% and 30%, and 98% and 10%, respectively.

Conclusions: Electronic recording of carotid sounds for later interpretation is convenient and reliable. Most patients with stenoses had an overlying bruit. Most bruits were false positives, but ultrasonography is justified to document extent of disease; CIMT measurement will identify increased vascular risk in most of these patients. The absence of a bruit was rarely a false negative finding, suggesting that these patients can usually be reassured that they do not have hemodynamically important stenosis.
Introduction

A carotid bruit detected by conventional acoustic auscultation is associated with a 2-4 fold increased risk of transient ischemic attack, stroke and death in general population studies.\(^1\) Diabetes further increases the risk of both a bruit\(^2\) and the subsequent risk of stroke.\(^3\) Meta-analysis suggests that the sensitivity and specificity of a bruit for a \(\geq 70\%\) carotid stenosis detected by ultrasonography, angiography and/or oculoplethysmography are only 53\% and 83\%, respectively.\(^4\) Nevertheless, current guidelines state that it is reasonable to perform duplex ultrasonography in patients with or without diabetes who have a carotid bruit to determine whether a hemodynamically significant stenosis is present.\(^5\) Ultrasonography remains a non-invasive way of identifying which patients should benefit from optimal medical management including anti-platelet therapy and perhaps further imaging with a view to revascularization.\(^6,\,7\) In addition, ultrasonographic measurement of the carotid intima-medial thickness (CIMT) can provide indirect evidence of co-existent coronary artery and/or peripheral vascular disease,\(^8-10\) further reinforcing the need for optimized cardiovascular risk factor management.

Carotid auscultation using an acoustic stethoscope is a simple tool that requires application of the correct technique in a noise-free environment by a skilled operator who instantaneously interprets what is heard, including differentiation of a bruit from a transmitted cardiac murmur. When these conditions cannot be met, the opportunity for potentially valuable screening is lost. The electronic stethoscope has, however, emerged as a way in which a trained non-expert operator can obtain a permanent auscultatory record for later expert interpretation. These digital recordings are of better quality than those obtained using acoustic stethoscopes.\(^11,\,12\) This technology has been applied successfully in clinically challenging situations such as in aviation.
The sensitivity and specificity of carotid bruits ascertained by electronic auscultation for ultrasonographically identified carotid stenosis and increased CIMT have not been examined previously. We hypothesized that the use of an electronic stethoscope by a trained non-expert operator with subsequent evaluation by an experienced clinician would improve the diagnosis of carotid atherosclerosis in patients with diabetes.

**Subjects and Methods**

*Patients*

We studied participants in the Fremantle Diabetes Study Phase II (FDS2), a community-based prospective observational study conducted in an urban region of approximately 153,000 people. A detailed description of FDS2 identification/recruitment procedures, sample characteristics, classification of diabetes type and details of non-recruited patients has been published previously. The FDS2 protocol was approved by the Human Research Ethics Committee of the Southern Metropolitan Area Health Service, and all subjects gave informed consent before participation.

Of 1,732 FDS2 subjects recruited between 2008 and 2011, 361 had died or withdrawn by early 2013. Of the 1,371 available for participation in the present sub-study, 84 (6.1%) were identified as having a carotid bruit by electronic auscultation at prior FDS2 assessments. Each of these patients and one age- and gender-matched FDS2 subject without a bruit were invited to undergo carotid Doppler ultrasonography. We did not exclude patients who reported a history/symptoms of cerebrovascular disease or those with prior carotid imaging, but did exclude those who had
undergone carotid revascularization subsequent to identification of the bruit.

Clinical assessment

At FDS2 baseline assessment and subsequent biennial reviews, a comprehensive history of diabetes and co-morbidities was recorded, a physical examination was performed by a trained nurse, and fasting blood and urine samples were taken for analyses in a single nationally-accredited laboratory. Each patient underwent standardized screening for carotid bruits by electronic auscultation. A Littmann 3000 stethoscope (3M, North Ryde, New South Wales, Australia) was applied to six areas (upper and lower carotid bilaterally, and aortic and pulmonary areas) and a recording of ≥5 beats was taken at each site with the patient holding his/her breath in deep inspiration. The recordings were subsequently analyzed by one of two study physicians (BAS or TMED) utilizing the Littmann Sound Analysis Software (version 2.0.C). A carotid bruit was considered present if there was a clearly audible systolic bruit in the upper and/or lower carotid region and no infra-clavicular murmur. Where interpretation was unclear, the recording was assessed by the alternate study physician and a consensus reached. Other chronic complications were ascertained using standard criteria.

Ultrasonography

Carotid duplex ultrasonography was performed using a iU22 System (Philips Healthcare, North Ryde, New South Wales, Australia) under Australasian Society for Ultrasound in Medicine guidelines. Images were assessed by two experienced sonographers and two radiologists and categorized as i) 0% stenosis with normal waveform/image; ii) <15% diameter reduction assessed from deceleration with a spectral broadening and peak systolic velocity (PSV) <125
cm/sec; iii) 16-49% diameter reduction with a pansystolic spectral broadening (PSB) and PSV <125 cm/sec; iv) 50-69% diameter reduction with PSB, PSV >125 cm/sec and end diastolic velocity (EDV) <110 cm/sec or ratio of internal carotid artery PSV to common carotid artery PSV (ICA/CCA) >2; v) 70-79% diameter reduction with PSB and PSV >270 cm/sec or EDV >110 cm/sec or ICA/CCA >4; vi) 80-99% diameter reduction and criteria as in v) plus EDV >140 cm/sec; vii) occluded with no flow terminal thump.

Bilateral measurements of the anterior, lateral and posterior bifurcation CIMT were made as per the American Society of Echocardiography (ASE) consensus statement\textsuperscript{18} using a 12.5 mHz linear array transducer. Pre-processing configurations (log gain compensation 60 dB, image persistence) were kept constant. Using antero-oblique insonation, far-wall CIMT was adjusted bilaterally at the carotid bifurcation and 1.0 cm proximally from the flow divider by visualizing the double lines of the carotid artery on the near and the far wall of the common carotid artery. Optimized transducer depth (usually 4.0 cm) was adjusted to avoid slice thickness artefacts. The images were captured during systole at the R-waves over 3-4 cardiac cycles. Three edge-to-edge measurements were taken of the far-wall with a CIMT over ≥1 cm lengths without the zoom function. The presence of carotid plaque was defined as focal wall thickening ≥50% greater than that of the surrounding vessel wall or as a focal region with IMT >1.5 mm protruding into the lumen and distinct from the adjacent boundary.\textsuperscript{18} Plaques ranged from hard (calcified) to soft (echogenic without calcification).\textsuperscript{17}

\textit{Carotid intima-medial thickness threshold and percentile distribution}

A fixed CIMT threshold of ≥1.0 mm is considered an adverse cardiovascular indicator.\textsuperscript{19, 20} In
the ASE consensus statement,\textsuperscript{18} the nomogram of the CIMT percentile distribution is taken from the Carotid Atherosclerosis Progression Study\textsuperscript{21} which classifies CIMT values in percentile distribution by age, sex and race/ethnicity. Those in $\geq 75^{\text{th}}$, 25-75\textsuperscript{th} and $\leq 25^{\text{th}}$ percentile ranges are considered at increased, average and lower risk, respectively.

\textit{Screening for Heart Attack Prevention and Education (SHAPE) guidelines}

Under SHAPE guidelines,\textsuperscript{22} patients are categorized as lower, moderate, moderately high, high and very high risk based on age and carotid ultrasound findings. A positive atherosclerotic test is defined as CIMT (worse side) $\geq 50^{\text{th}}$ percentile or presence of plaque (focal wall thickening $\geq 50\%$ greater than that of the surrounding vessel wall or a focal region with CIMT $> 1.5 \text{ mm}$ protruding into the lumen and distinct from the adjacent boundary\textsuperscript{17}). All $\geq 75$ year-olds are assumed high risk unless they have a carotid stenosis $\geq 50\%$ which, with a positive test, indicates very high risk. High risk patients have a positive test, $< 50\%$ carotid stenosis, and a CIMT $\geq 1 \text{ mm}$, a CIMT $\geq 75^{\text{th}}$ percentile or carotid plaque. Moderately high risk patients have a positive test, a CIMT $< 1.0 \text{ mm}$ and $< 75^{\text{th}}$ percentile with no plaque. Moderate risk patients have a negative test and cardiovascular risk factors. Those at lower risk have a negative test and no risk factors.

\textit{Statistical analysis}

Data are presented as proportions, mean$\pm$SD, geometric mean (SD range), or for those not conforming to a normal or log-normal distribution, median [interquartile range (IQR)]. For independent samples, two-way comparisons of proportions were by Fisher’s exact test while the Students $t$-test was used for normally distributed variables. For comparisons between individually matched cases and controls, McNemar’s and McNemar-Bowker’s tests as well as
matched odds ratios (OR) with 95% confidence intervals (CI) were used for proportions, paired t-tests for normally distributed variables, and the Wilcoxon signed-rank test for non-normally distributed variables. A two-sided \( P<0.05 \) was considered significant.

**Results**

*Patient characteristics*

Of the 84 patients with a carotid bruit, 50 underwent carotid Doppler ultrasonography, one was ineligible (recent carotid endarterectomy), three declined, and 30 did not respond to the invitation to participate. Compared with these latter 33 patients, the 50 recruits were not significantly different in age or sex distribution (\( P \geq 0.54 \)), but had a significantly shorter median diabetes duration (11.9 [7.7-20.7] vs 19.1 [11.2-29.6] years, \( P=0.021 \)). At the time of ultrasonography, the 50 cases and 50 controls had similar proportions of type 1 and 2 diabetes and similar diabetes duration (see Table 1). The cases had a lower diastolic but similar systolic blood pressure to the controls, consistent with a wider pulse pressure, and their serum HDL-cholesterol concentrations were higher.

The carotid ultrasound parameters and SHAPE categories are summarized in Table 2. Compared to those without a bruit, patients with a bruit were significantly more likely to have carotid stenosis \( \geq 50\% \) and \( >2.5 \) times more likely to have a CIMT \( >1.0 \) mm (OR 95% CI) 14.0 (1.8-106.5) and 5.3 (1.8-15.3), respectively, \( P=0.001 \) in each case), and they were also more likely to fall within the very high SHAPE vascular risk category (\( P=0.018 \)). For the small numbers detected as having a high grade carotid stenosis (\( \geq 70\% \)), those with a bruit were more likely to fall into this category but this did not reach statistical significance (5.0 (0.6-42.8), \( P=0.22 \)). Three
patients in this category, two in the bruit group and the one case in the non-bruit group who also had a history of coronary artery disease and peripheral vascular disease, were aware that they had a completely occluded internal carotid artery on one side prior to the ultrasound. Arterial tortuosity was graded semi-quantitatively as minimal, moderate or marked, and those with a carotid bruit were more likely to have at least minimal tortuosity (2.0 (0.9-4.7), \(P=0.15\)) and at least moderate tortuosity (3.3 (0.9-12.1), \(P=0.09\)). None of the cases or controls with at least minimal and with at least moderate tortuosity had a carotid stenosis \(\geq 70\%\).

The sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) of a carotid bruit for each parameter are detailed in Table 3. The sensitivity of an electronically detected carotid bruit for a stenosis of \(\geq 70\%\) was 83\% with a modest specificity of 52\%. For a stenosis of \(\geq 50\%\), the specificity and sensitivity were both higher but the NPV was \(>96\%\) in both cases. For CIMT \(>1.0\) mm, CIMT \(\geq 75\)th percentile, and the presence of plaque, sensitivity and specificity ranged between 60\% and 75\%. After exclusion of eight case/control pairs that included at least one patient who had reported a history of carotid artery disease or prior ultrasonographic assessment prompted by symptoms, the sensitivity of a bruit for a stenosis of \(\geq 50\%\) or \(\geq 70\%\) increased to 100\% but with wider 95\% confidence intervals (see Table 3).

**Discussion**

The present data show that carotid bruits identified by an electronic stethoscope in community-based patients with diabetes have high sensitivity (>83\%) and NPV (>96\%) for both moderate (\(\geq 50\%\)) and high grade (\(\geq 70\%\)) carotid stenoses detected subsequently by carotid duplex ultrasonography. Given that the PPV was low (\(\leq 30\%\)), these observations suggest that most of
the patients with carotid stenoses had an overlying bruit but that most bruits were false positives, and that the absence of a bruit was rarely a false negative finding. The practical implications of these observations are that i) electronic recording of carotid sounds by a trained operator for later transmission and interpretation appears reliable when expert acoustic auscultation is unavailable, ii) patients with diabetes who have no carotid bruit detected in this way can usually be reassured that they do not have hemodynamically important carotid atherosclerosis, iii) patients with diabetes and a carotid bruit will usually not have a significant (≥70%) stenosis but, consistent with current guidelines,\textsuperscript{5} duplex ultrasonography should still be recommended to more objectively document the extent of disease, and iv) measurement of the CIMT patients with diabetes and a carotid bruit will identify increased vascular risk in most of these patients regardless of the presence of stenosis.

A recent meta-analysis of studies examining the utility of carotid bruits ascertained using an acoustic stethoscope for clinically significant carotid stenoses (>70%) generated a pooled sensitivity of 53% and a specificity of 83%.\textsuperscript{4} The higher sensitivity and lower specificity found in the present study could be due to several factors. First, the better acoustic quality obtained using the electronic stethoscope\textsuperscript{11,12} may have meant that more bruits were detected. This includes softer bruits both associated with reduced flow in severely stenosed vessels\textsuperscript{24} thus increasing sensitivity, and as a manifestation of low grade stenoses or vascular tortuosity which would attenuate specificity and PPV. Indeed, the prevalence of bruits detected by acoustic stethoscope in the first phase of the FDS (FDS1) between 1993 and 1996 was lower at 4.5\%\textsuperscript{3} compared with 6.1\% in the present study. Second, we employed relatively rigorous methodology in an attempt to eliminate the confounding influence of transmitted cardiac murmurs\textsuperscript{24} that would
potentially reduce sensitivity. Infra-clavicular auscultation was not performed in a number of studies\textsuperscript{7, 25, 26} and, in another, ascertainment of bruits was based solely on the referring physician’s assessment.\textsuperscript{27}

The cost-effectiveness of screening for asymptomatic carotid artery stenosis using duplex ultrasonography has not been assessed through a randomized clinical trial. It remains contentious and dependent on key variables such as the stenotic threshold for intervention (which has been set at 50\%, 60\% and 70\%), the prevalence of stenosis in the target population (which can be increased, for example, by including only older men), and treatment outcomes (especially when assessment and intervention are not carried out in centers of excellence).\textsuperscript{28-30} Indeed the sensitivity and specificity of duplex ultrasonography itself compared with angiography are variable in published studies,\textsuperscript{31-33} but typically $\geq 90\%$ for a stenosis $\geq 70\%$.\textsuperscript{29} Although a formal health economic evaluation would be required, our data suggest that pre-screening with electronic auscultation could improve cost-effectiveness, especially since specificity and NPV were both $>96\%$ in our asymptomatic patients.

There is evidence that carotid bruits are more predictive of cardiovascular than cerebrovascular disease outcomes including death.\textsuperscript{10, 34} CIMT is a proven indicator of cardiovascular risk and can refine assessment of patients at intermediate risk.\textsuperscript{18} Our data demonstrate that the presence of a carotid bruit increases the likelihood of a CIMT $\geq 1$ mm three-fold. There were also 50\% more patients with carotid plaques in the group with detectable carotid bruits. A recently published editorial suggested that a combination of CIMT $\geq 1$ mm and carotid plaque might improve coronary risk prediction more than either parameter alone,\textsuperscript{35} and the SHAPE guidelines
incorporate these variables independently.\textsuperscript{22} Indeed, almost one third of our patients with bruits were in the very high SHAPE vascular risk category compared with only 4\% of those without bruits. Thus, observations and measures other than degree of carotid stenosis can inform management since patients assessed at very high risk are recommended to have a stricter serum LDL cholesterol target (<1.8 mmol/L) than other categories and to be considered for investigation of myocardial ischemia such as through an exercise stress test.\textsuperscript{22} Indeed, most of our patients, including those with a CIMT ≥1 mm and/or a carotid bruit, had a serum LDL cholesterol ≥1.8 mmol/L despite the fact that the majority were taking lipid-modifying agents (largely statins), suggesting that therapeutic intensification may be possible. The apparently paradoxical higher serum HDL cholesterol concentrations in those with carotid bruits is most likely a chance finding.

There was a trend to increased carotid artery tortuosity in the patients with carotid bruits, especially for at least moderate degrees of this vascular anomaly which was independent of the presence of high grade (≥70\%) stenosis. Mild tortuosity is a relatively common asymptomatic finding,\textsuperscript{36} but there is debate as to the significance of more severe tortuosity. It has been associated with atherosclerosis and its risk factors including hypertension,\textsuperscript{36} and it predicts subsequent intra-procedural complications in patients undergoing carotid artery stenting,\textsuperscript{37} but its prognostic value for cerebrovascular events is uncertain.\textsuperscript{38} In the present study, at least moderately severe tortuosity was present in one in five patients with carotid bruit and may have explained why a bruit was readily detected by electronic auscultation in these subjects.

Our study had limitations. We recruited only 100 patients but our sample size was restricted by
the prevalence of bruits in the large FDS2 cohort. Nevertheless, FDS2 patients appear representative of people with diabetes in a large urban Australian community, while the similarities in demographic variables between those with carotid bruits who participated in the present sub-study and the 33 who did not suggests that there was no significant recruitment bias. We did not perform simultaneous acoustic auscultation as our aim was to assess use of the electronic stethoscope against reference ultrasonography. It is likely, however, that electronic capture of carotid sounds is more reliable based on the greater prevalence of bruits in FDS2 vs FDS1 6.1% vs 4.5% and other studies directly comparing the two methods.

The present study suggests that electronic auscultation is more accurate than a conventional acoustic stethoscope for the detection of carotid bruits in patients with diabetes, while offering the convenience of later interpretation if a skilled operator is not available when the patient is assessed. The presence of a bruit identified in this way should prompt i) intensified cardiovascular risk factor management and ii) consideration of ultrasonography and perhaps other imaging with a view to revascularization depending on symptoms and factors such as age and co-morbidities. The absence of a bruit does not exclude a hemodynamically significant stenosis but there may be other indications of cerebrovascular disease. For example, in our patient without a bruit who had an occluded carotid artery, there was a history of cerebrovascular symptoms and evidence of established vascular disease at other sites which is itself collateral evidence of significant carotid stenosis risk. The cost of the electronic stethoscope and software used in the present study is approximately twice that of a high quality acoustic model, suggesting that it is affordable technology even in basic healthcare settings.
Competing interests

The authors declare that they have no competing interests.

Acknowledgements

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operating room: a prospective randomized blinded trial comparing electronic and


Table 1. Characteristics of the patients by classified by carotid bruit status.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Carotid bruit detected</th>
<th>No carotid bruit detected</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>50</td>
<td>50</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>73.7±10.0</td>
<td>73.8±10.1</td>
<td>0.95</td>
</tr>
<tr>
<td>Sex (% male)</td>
<td>38.0</td>
<td>38.0</td>
<td>1.00</td>
</tr>
<tr>
<td>Type 2 diabetes (%)</td>
<td>90.0</td>
<td>96.0</td>
<td>0.38</td>
</tr>
<tr>
<td>Diabetes duration (years)</td>
<td>12.9 [8.0-21.0]</td>
<td>13.5 [8.3-20.1]</td>
<td>0.86</td>
</tr>
<tr>
<td>HbA1c (%)</td>
<td>6.7 [6.3-7.3]</td>
<td>7.1 [6.4-7.6]</td>
<td>0.17</td>
</tr>
<tr>
<td>HbA1c (mmol/mol)</td>
<td>50 [45-56]</td>
<td>54 [46-60]</td>
<td>0.17</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>29.1±4.7</td>
<td>30.6±5.4</td>
<td>0.14</td>
</tr>
<tr>
<td>Supine systolic blood pressure (mm Hg)</td>
<td>149±21</td>
<td>143±21</td>
<td>0.20</td>
</tr>
<tr>
<td>Supine diastolic blood pressure (mm Hg)</td>
<td>73±12</td>
<td>78±11</td>
<td>0.010</td>
</tr>
<tr>
<td>Antihypertensive therapy (%)</td>
<td>90.0</td>
<td>88.0</td>
<td>1.00</td>
</tr>
<tr>
<td>Total serum cholesterol (mmol/L)</td>
<td>4.3 ± 1.0</td>
<td>4.3±0.9</td>
<td>0.87</td>
</tr>
<tr>
<td>Serum HDL-cholesterol (mmol/L)</td>
<td>1.31±0.33</td>
<td>1.17±0.28</td>
<td>0.037</td>
</tr>
<tr>
<td>Serum LDL-cholesterol (mmol/L)</td>
<td>2.4±0.9</td>
<td>2.3±0.7</td>
<td>0.62</td>
</tr>
<tr>
<td>Serum triglycerides (mmol/L)</td>
<td>1.4 (0.9-2.1)</td>
<td>1.6 (0.9-2.8)</td>
<td>0.08</td>
</tr>
<tr>
<td>Lipid-modifying therapy (%)</td>
<td>76.0</td>
<td>76.0</td>
<td>1.00</td>
</tr>
<tr>
<td>Aspirin therapy (%)</td>
<td>44.0</td>
<td>44.0</td>
<td>1.00</td>
</tr>
<tr>
<td>Urinary albumin:creatinine (mg/mmol)</td>
<td>2.4 (0.7-8.3)</td>
<td>3.4 (1.0-11.4)</td>
<td>0.14</td>
</tr>
<tr>
<td>Estimated glomerular filtration rate &lt;60 ml/min/1.73m² (%)</td>
<td>28.0</td>
<td>38.0</td>
<td>0.33</td>
</tr>
<tr>
<td>Self-reported ischemic heart disease (%)</td>
<td>28.0</td>
<td>30.0</td>
<td>1.00</td>
</tr>
<tr>
<td>Self-reported stroke/transient ischemic attack (%)</td>
<td>6.0</td>
<td>12.0</td>
<td>0.51</td>
</tr>
<tr>
<td>Self-reported carotid artery disease/prior ultrasound (%)</td>
<td>14.0</td>
<td>4.0</td>
<td>0.13</td>
</tr>
</tbody>
</table>
**Table 2.** Ultrasonographic findings and SHAPE categories in the two patient groups.

<table>
<thead>
<tr>
<th>Carotid stenosis ≥50%</th>
<th>Carotid bruit detected</th>
<th>No carotid bruit detected</th>
<th>Matched odds ratio (95% CI)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>15 (30.0)</td>
<td>2 (4.0)</td>
<td>14.0 (1.8-106.5)</td>
<td>0.001</td>
</tr>
<tr>
<td>Carotid stenosis ≥70%</td>
<td>5 (10.0)</td>
<td>1 (2.0)</td>
<td>5.0 (0.6-42.8)</td>
<td>0.22</td>
</tr>
<tr>
<td>Hard or mixed plaque</td>
<td>39 (78.0)</td>
<td>26 (52.0)</td>
<td>4.3 (1.4-12.6)</td>
<td>0.007</td>
</tr>
<tr>
<td>CIMT &gt;1.0 mm</td>
<td>26 (52.0)</td>
<td>9 (18.0)</td>
<td>5.3 (1.8-15.3)</td>
<td>0.001</td>
</tr>
<tr>
<td>CIMT ≥75th percentile()</td>
<td>30 (66.7)</td>
<td>20 (44.4)</td>
<td>3.0 (1.1-8.3)</td>
<td>0.041</td>
</tr>
</tbody>
</table>

SHAPE categories:
- Lower/moderate 1 (2.0) 2 (4.0)
- Moderately high 1 (2.0) 3 (6.0) 0.018
- High 33 (66.0) 43 (86.0)
- Very high 15 (30.0) 2 (4.0)

\(\text{n}=45\) for case-control pairs both of whom were within the <85 year age range utilized by the SHAPE guidelines
Table 3: Sensitivity, specificity, positive predictive value and negative predictive value and [95% confidence intervals] of carotid bruits for stenosis, CIMT and plaque. Data for 42 case/control pairs, both of whom had no prior symptoms of carotid arterial disease, are also shown.

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>CIMT ≥1.0 mm</strong></td>
<td>74 [56-87]</td>
<td>63 [50-74]</td>
<td>52 [38-66]</td>
<td>82 [68-91]</td>
</tr>
<tr>
<td><strong>CIMT ≥75th percentile</strong></td>
<td>60 [45-73]</td>
<td>63 [46-77]</td>
<td>67 [51-80]</td>
<td>56 [40-70]</td>
</tr>
<tr>
<td><strong>Hard/mixed plaque</strong></td>
<td>60 [47-72]</td>
<td>69 [51-83]</td>
<td>78 [64-88]</td>
<td>48 [34-62]</td>
</tr>
</tbody>
</table>

Asymptomatic cases/controls

<table>
<thead>
<tr>
<th></th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>Positive predictive value</th>
<th>Negative predictive value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Carotid stenosis ≥50%</strong></td>
<td>100 [63-100]</td>
<td>56 [44-67]</td>
<td>21 [11-37]</td>
<td>100 [90-100]</td>
</tr>
<tr>
<td><strong>Carotid stenosis ≥70%</strong></td>
<td>100 [20-100]</td>
<td>51 [40-62]</td>
<td>5 [1-17]</td>
<td>95 [90-100]</td>
</tr>
</tbody>
</table>