Stroke Risk After Posterior Circulation Stroke/Transient Ischemic Attack and its Relationship to Site of Vertebrobasilar Stenosis
Pooled Data Analysis From Prospective Studies

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**Background and Purpose**—Recent prospective studies have shown vertebrobasilar (VB) stenosis predicts stroke risk in posterior circulation stroke and transient ischemic attack. It is unclear whether this association is independent of other risk factors, and whether intracranial or extracranial stenosis confers different risks.

**Methods**—A pooled individual patient analysis of data from 2 prospective studies was performed in 359 patients presenting with VB transient ischemic attack or stroke. Contrast-enhanced magnetic resonance angiography, or computed tomography angiogram, and clinical follow-up were available in 323 patients. Risk of stroke was calculated from any VB transient ischemic attack/stroke in the month before the presenting episode (first event) and from the presenting event. A systematic review of similar prospective studies was performed.

**Results**—Ninety-day risk of stroke from the first event was 24.6% in patients with VB stenosis versus 7.2% in those without (odds ratio, 4.2; 95% confidence interval, 2.1–8.6; \( P < 0.0001 \)). Risk was higher (33%) with intracranial (odds ratio, 6.5; 2.8–15.0; \( P < 0.0001 \)) than extracranial stenosis (16.2%; odds ratio, 2.5; 0.9–6.8; \( P = 0.06 \)). Risk from the presenting event was 9.6% in patients with stenosis versus 2.8% in those without (odds ratio, 3.7; 1.2–11.0; \( P = 0.012 \)), and again the risk was higher with intracranial stenosis. Cox regression showed the risk associated with VB stenosis was independent of other cardiovascular risk factors. The systematic review identified only 1 other report, which included only 6 patients.

**Conclusions**—Symptomatic VB stenosis, particularly intracranial stenosis, is a strong independent predictor of stroke recurrence. The high early risk of stroke provides a strong rationale for randomized trials to determine whether stenting can reduce risk. (Stroke. 2013;44:598-604.)

**Key Words:** posterior circulation • prognosis • stroke • systematic review • TIA • vertebrobasilar

Vertebrobasilar (VB), or posterior circulation, stroke accounts for 20% of all strokes, but its investigation and treatment have received less attention than carotid stroke. Although it was previously thought that recurrent stroke risk was lower than that for carotid stroke, this has been shown not to be the case when the high early risk of recurrent stroke is captured. This finding was confirmed in 2 recent prospective studies: 1 population-based (Oxford Vascular Study, OXVASC) and 1 hospital register–based study (St. George’s Study). Both showed VB stenosis was a major predictor of recurrent stroke, particularly in the first month. These findings suggest that more intensive medical therapy, and possibly revascularization with stenting, should be considered for VB transient ischemic attack (TIA) or stroke, in the same way as carotid endarterectomy has become routine for symptomatic carotid artery stenosis. However, although both studies found an increased risk of stroke associated with VB stenosis, neither alone had the power to determine the relationship between the site of stenosis and recurrent stroke risk nor to determine whether the increased risk was independent of other cardiovascular risk factors. We performed a pooled analysis using individual patient data from both studies to answer these questions. We also performed a systematic review to identify any additional data relating the presence of recently symptomatic VB stenosis to recurrent stroke risk.

**Methods**

**Pooled Individual Patient Data Analysis**
A pooled analysis was performed on individual patient data from 2 prospective studies recruiting consecutive patients.
St. George Study
Two hundred and sixteen consecutive patients presenting with posterior circulation ischemic stroke or TIA were recruited to a comprehensive stroke service in South London, United Kingdom, from November 2004 to May 2008. In 8 patients, radiographic appearances of vertebral dissection were identified and because of the different pathophysiology of this subtype these patients were excluded, leaving 208 patients. Clinical details including history, examination, and investigations were collected prospectively on a standard proforma as part of a prospective stroke register. In addition, any history of TIA or minor stroke in the 30 days before hospital admission was recorded. Cases in whom symptoms lasted <24 hours, but in whom there was an acute infarct on diffusion-weighted imaging, were classified as stroke. A diagnosis of posterior circulation event was made by a consultant neurologist on the basis of clinical and structural brain imaging findings. All patients had brain computerized tomography (CT), and in 180 (83%) patients structural brain magnetic resonance imaging, including diffusion-weighted imaging, was performed.

Hypertension was defined as antihypertensive drugs at time of stroke or persistent elevation of blood pressure with systolic ≥140 mm Hg or diastolic ≥90 mm Hg at least 1 week after stroke. Diabetes mellitus was defined as previous diagnosis or 2 random blood glucose readings of >11.1 mmol/L or fasting blood glucose >7.0 mmol/L. Hypercholesterolaemia was defined as serum total cholesterol >5.2 mmol/L, or current treatment with lipid lowering therapy, including diffusion-weighted imaging, was performed.

Neuroradiology Evaluation
In St. George study, 186 of the 208 patients had VB imaging with either contrast-enhanced magnetic resonance angiography (CE-MRA) or CT angiography (CTA). The first line vascular imaging modality was CTA. CTA was used when MRA was contraindicated or unavailable. Imaging modalities in the 186 patients were CE-MRA alone, 157; CTA alone, 29; CE-MRA and CTA, 38. In addition, where intracranial views were suboptimal, time of flight MRA was performed (in 32). In 22 patients, imaging was not performed because of contraindications to contrast (5), patient were too ill or died (12), and lack of consent (5). All angiographic images were reviewed by a consultant neuroradiologist to determine the presence of VB stenosis, and lack of consent. VB stenosis was taken as the closest measurable section of nondiseased vertebral artery (or basilar artery), that is, analogous to the North American Symptomatic Carotid Endarterectomy Trial (NASCET) method of measurement of carotid stenosis or to the Warfarin-Aspirin Symptomatic Intracranial Disease (WASID) method of measuring intracranial VB stenosis.5,6

All scans were reviewed by a neuroradiologist. Stenosis was defined and measured as for the St. George Study.

Site of Stenosis
In both groups of patients, site of stenosis was defined according to location in the VB arterial tree according to standard terminology: (1) extracranial – V1 (extracranial preforaminal artery), V2 (extracranial foraminar artery), and V3 (extracranial postforaminal artery); (2) intracranial – V4 (intracranial vertebral artery) and basilar artery. For our analysis, stenoses were divided into extracranial (V1–3) or intracranial (V4 and basilar) stenosis.

Follow-up and Outcomes
In both studies, patients were prospectively followed up and 90-day rates of recurrent stroke and TIA were recorded. If a recurrent event was suspected, patients underwent brain CT or magnetic resonance imaging. Our primary end point was clinical stroke in the VB territory.

Analysis
We determined the relationship between stenosis and recurrent events with reference to both the first TIA or stroke, and the presenting stroke or TIA. In both studies, the presenting event was the event that led directly to the patient seeking medical attention. However, we also calculated risk from the first event (ie, including events for which patients might not have sought medical attention). The first event was the same as the presenting event, when the first event lead to medical attention. However, in cases where there was a previous event within 30 days that event was used as the first event, if in the opinion of the neurologist the description was convincing for a TIA or stroke. Statistical analysis was performed using SPSS version 16 (SPSS Inc). Values were expressed in real numbers (%) or mean values±SD. Cumulative event-free rates for the time to a recurrent stroke were estimated by Kaplan–Meier survival analysis with patients stratified by the presence or absence of VB stenosis, intracranial stenosis, or extracranial stenosis. Risk ratios with 95% confidence interval were calculated by χ² analysis. Cox-regression analysis was performed to determine whether any associations were independent of risk factors using the following risk factors as covariates: age, sex, diabetes mellitus, hypercholesterolemia, hypertension, current smoking. Hazard ratios with 95% confidence interval were determined.

Systematic Review
Search Strategy
Articles which reported follow-up data on patients presenting with posterior circulation stroke, or TIA, or stroke, and in which the presence or absence of VB stenosis and its relationship to outcome could be determined, were identified. A search was performed in pubmed for the period 1966 to March 5, 2012, using the following search terms: (posterior circulation or vertebrobasilar or basilar or vertebral) and (stroke or TIA), and (recurrence or recurrent or early risk or outcome) and (stenosis). The search was limited to human studies and those in English. In addition, reference lists were searched, including those of a systematic review published in 2003.1

Inclusion Criteria
Studies were included if they fulfilled the following criteria: (1) prospective or retrospective cohort ≥5 subjects; (2)
patients had history of stroke or TIA; (3) data available on the presence or absence of VB stenosis; (4) outcome data on recurrent stroke available. Studies where subjects underwent neurointerventional or other surgical intervention were excluded.

Abstracts were screened by 1 researcher (G.G.). Studies potentially meeting inclusion criteria were analyzed by 2 researchers (G.G., H.S.M.). The following information was extracted: (1) number of patients; (2) population- or hospital-based; (3) recruitment of consecutive subjects; (4) prospective or retrospective study; (5) imaging modality used for VB stenosis assessment; (6) risk of recurrent stroke, stratified for the presence of VB stenosis if the study included both groups.

Results

Pooled Analysis

Demographic characteristics of the 2 study groups and main imaging results are shown in Table 1. In the combined population, imaging of the VB circulation with CE-MRA or CTA was obtained in 327 patients (91.1%). VB stenosis was detected in 73 (22.3%); 37 extracranial, and 36 intracranial.

In the pooled population, follow-up to 90 days or recurrent stroke or death was available in 354 of 359 patients (96.6%). Overall, 323 patients (90.0%) had both VB imaging and complete follow-up. Results reported below relate to patients with complete follow-up and VB imaging only.

Taking the first event as the index event 66 patients (20.4%) had a recurrent VB event: 36 strokes and 30 TIAs. Taking the index event as the presenting event, 29 (9.0%) had a recurrent VB event: 36 strokes and 30 TIAs. Taking the first event as the index case, the risk of recurrent stroke was not higher in patients with extracranial stenosis (odds ratio, 2.0; 0.9–6.8; P=0.06). Taking the presenting event as the index case, the risk of recurrent stroke was not higher in patients with extracranial stenosis (odds ratio, 2.0; 0.4–9.9; P=0.39). Results in Table 3 show that the association between extracranial VB stenosis and recurrent stroke remained little altered after controlling for other risk factors.

Systematic Review

Two hundred and fifty-seven abstracts were identified. Sixty-six potentially met inclusion criteria and after reading full-text articles, only 1, apart from the St. George’s and OXVASC studies already included in the analysis, met inclusion criteria for providing comparative data in patients with and without VB stenosis. This study included 6 patients who had intra-arterial angiography to exclude stenosis, from a larger trial of aspirin versus heparin in early stroke prevention in patients with TIA within 7 days of symptom onset. Recurrent stroke occurred in 2 of 4 individuals with stenosis and none of 2 without stenosis; data relating the site of stenosis to recurrent stroke risk were not available. A further small study

### Table 1. Baseline Characteristics and Demographics in Patients

<table>
<thead>
<tr>
<th>Details of Stenoses Detected on Imaging</th>
<th>OXVASC (N=141)</th>
<th>St. George (N=186)</th>
<th>Pooled (N=327)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years±SD</td>
<td>69±12.4</td>
<td>69±13.5</td>
<td>70±13.2</td>
</tr>
<tr>
<td>Men</td>
<td>77 (54.6%)</td>
<td>117 (62.9%)</td>
<td>194 (59.3%)</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>20 (14.2%)</td>
<td>55 (29.6%)</td>
<td>75 (22.9%)</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>47 (33.3%)</td>
<td>121 (65.0%)</td>
<td>168 (51.4%)</td>
</tr>
<tr>
<td>Hypertension</td>
<td>81 (57.4%)</td>
<td>134 (72.0%)</td>
<td>215 (65.7%)</td>
</tr>
<tr>
<td>Current smoker</td>
<td>19 (13.5%)</td>
<td>28 (15.0%)</td>
<td>47 (14.4%)</td>
</tr>
<tr>
<td>Ex smoker</td>
<td>63 (44.7%)</td>
<td>76 (40.8%)</td>
<td>139 (42.5%)</td>
</tr>
<tr>
<td>History of previous stroke</td>
<td>6 (4.2%)</td>
<td>28 (15.0%)</td>
<td>34 (10.4%)</td>
</tr>
<tr>
<td>Previous myocardial infarction</td>
<td>9 (6.4%)</td>
<td>30 (16.1%)</td>
<td>39 (11.9%)</td>
</tr>
</tbody>
</table>

### Table 2. Risk of Recurrent Stroke Related to the Presence and Site of Stenosis

<table>
<thead>
<tr>
<th>Stenosis</th>
<th>From First Event</th>
<th>From Presenting Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>Any stenosis</td>
<td>4.2 2.1–8.7 &lt;0.0001</td>
<td>3.7 1.3–11.0 &lt;0.012</td>
</tr>
<tr>
<td>Extracranial stenosis</td>
<td>2.5 0.9–6.8 0.06</td>
<td>2.0 0.4–10.0 0.39</td>
</tr>
<tr>
<td>Intracranial stenosis</td>
<td>6.5 2.8–15.1 &lt;0.0001</td>
<td>5.6 1.7–18.9 &lt;0.0001</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; and OR, odds ratio. ORs are comparisons against patients with no stenosis.
reported the risk of stroke in patients with or without VB stenosis, but data on duration of follow-up were incomplete and it was a highly selected subset of patients, all presenting with intranuclear ophthalmoplegia. In addition, 14 studies were identified, which only included patients with VB stenosis, without a control group with no stenosis. Two studies reported the risk of stroke in patients with extracranial vertebral artery stenosis only (see the online-only Data Supplement references I and II), 8 in intracranial VB stenosis9 (see the online-only Data Supplement references III through IX), and in 7 the risk relating to site of stenosis was unclear2,3,7,8 (see the online-only Data Supplement references X through XII). No studies provided direct comparative data on the risk of extracranial versus intracranial stenosis in the same study population. There were a number of publications from the same populations, particularly for the WASID study, and only the publication with the most complete data is shown.

Details of the stroke risk in those that specified site of stenosis are shown in Table 4. These reported markedly different rates of recurrent stroke rate, which may reflect differences in study design including time to recruitment from qualifying event (which was not documented for a number of studies), and retrospective versus prospective design. However, overall, there was a tendency for higher rates of stroke in intracranial stenosis.

Discussion

This pooled individual patient analysis of 2 prospective studies2,3 demonstrates that VB stenosis is associated with a high risk of recurrent stroke, and this risk is particularly high in the first few weeks after TIA or stroke. Our results add to existing data in 2 ways. First, they demonstrate that this association is independent of conventional risk factors. Second, they show intracranial stenosis is associated with a higher risk of early recurrence as high as 33% in the first 90 days after the first event.

The novelty of this data is demonstrated by our systematic review that identified only 1 other study, which allowed the relationship between the presence and absence of stenosis to be related to recurrent stroke risk with relevant data in only 6 patients.7 Its results were consistent with our data showing a high early recurrent stroke risk in symptomatic VB stenosis.

Other studies reported stroke risk in intracranial or extracranial stenosis but not in both groups within the same cohort. These estimates varied widely but tended to be lower than those found in our prospective study. This is likely to reflect the fact that most patients were recruited outside the initial first 2-week period, the period over which we have shown the highest risk, a fact supported by 1 small study, which found most recurrent strokes occurred within the first 2 weeks.9

Table 3. Results of Cox Regression Identifying Independent Predictors of Recurrent Vertebrobasilar Stroke Risk

<table>
<thead>
<tr>
<th>Factor</th>
<th>P Value</th>
<th>HR</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intracranial stenosis</td>
<td>0.011</td>
<td>4.8</td>
<td>1.4–16.0</td>
</tr>
<tr>
<td>Extracranial stenosis</td>
<td>0.632</td>
<td>1.5</td>
<td>0.3–7.6</td>
</tr>
<tr>
<td>Sex</td>
<td>0.154</td>
<td>3.1</td>
<td>0.7–14.4</td>
</tr>
<tr>
<td>Hypertension</td>
<td>0.324</td>
<td>2.0</td>
<td>0.5–8.2</td>
</tr>
<tr>
<td>Hypercholesterolaemia</td>
<td>0.149</td>
<td>0.4</td>
<td>0.1–1.4</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>0.996</td>
<td>1.0</td>
<td>0.3–3.5</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.131</td>
<td>1.8</td>
<td>0.8–3.9</td>
</tr>
<tr>
<td>Previous stroke</td>
<td>0.145</td>
<td>2.8</td>
<td>0.7–10.8</td>
</tr>
</tbody>
</table>

CI indicates confidence interval; and HR, hazards ratio.

Figure 1. Kaplan–Meier curves showing risk of recurrent stroke from the first event. Solid line, patients with no stenosis; dashed line, patients with extracranial stenosis; and dotted line, patients with intracranial stenosis.
The degree, and temporal profile, of the increased risk we found in patients with both extra- and intracranial vertebral stenosis is very similar to that seen in symptomatic carotid stenosis. For symptomatic carotid stenosis, endarterectomy has been shown to be beneficial, and because of the high early recurrent risk, for maximum effectiveness and surgery needs to be performed soon after TIA or minor stroke. Our results suggest that the atherosclerotic vertebral plaque acts in

Figure 2. Kaplan–Meier curves showing risk of recurrent stroke from the presenting event. Solid line, patients with no stenosis; dashed line, patients with extracranial stenosis; and dotted line, patients with intracranial stenosis.

Table 4. Risk of Recurrent Stroke in Patients With Symptomatic Extra and Intracranial Vertebrobasilar Stenosis

<table>
<thead>
<tr>
<th>Study (Cohort or First Author and Reference)</th>
<th>N</th>
<th>Sample Type</th>
<th>Pros/Retro</th>
<th>Mean Duration Follow-up, months</th>
<th>Time Since Last Stroke/TIA to Recruitment</th>
<th>Degree of Stenosis</th>
<th>Artery Stenosed</th>
<th>Imaging Modality</th>
<th>Stroke Risk</th>
<th>Annual Stroke Risk</th>
</tr>
</thead>
<tbody>
<tr>
<td>Extracranial stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Karameshev(S2)</td>
<td>29</td>
<td>consecutive selected</td>
<td>pros</td>
<td>33</td>
<td>&lt;48 hours</td>
<td>&gt;70% vertebral</td>
<td>CTA, MRA, DSA</td>
<td>3/29 (10.3%)</td>
<td>3.7%</td>
<td></td>
</tr>
<tr>
<td>CAVATA(S1)</td>
<td>8</td>
<td>non-consecutive selected</td>
<td>pros</td>
<td>57</td>
<td>&lt;6 months mean 92 days</td>
<td>&gt;50% vertebral</td>
<td>DSA</td>
<td>0</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>Intracranial stenosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>WASID(S3)</td>
<td>107</td>
<td>non-consecutive selected</td>
<td>pros</td>
<td>20</td>
<td>&gt;7 days to &lt;30 days</td>
<td>&gt;50% vertebral</td>
<td>DSA</td>
<td>23/107 (21.5%)</td>
<td>12.8%</td>
<td></td>
</tr>
<tr>
<td>WASID(S3)</td>
<td>112</td>
<td>non-consecutive selected</td>
<td>pros</td>
<td>20</td>
<td>&gt;7 days to &lt;30 days</td>
<td>&gt;50% basilar</td>
<td>DSA</td>
<td>16/112 (14.3%)</td>
<td>8.6%</td>
<td></td>
</tr>
<tr>
<td>GESICA(S4)</td>
<td>23</td>
<td>selected</td>
<td>pros</td>
<td>23.4</td>
<td>Mean 1.2 months</td>
<td>&gt;50% vertebral</td>
<td>CTA, MRA, DSA</td>
<td>6/23 (26%)</td>
<td>13.3%</td>
<td></td>
</tr>
<tr>
<td>GESICA(S4)</td>
<td>26</td>
<td>selected</td>
<td>pros</td>
<td>23.4</td>
<td>Mean 1.2 months</td>
<td>&gt;50% basilar</td>
<td>CTA, MRA, DSA</td>
<td>15/26 (57.7%)</td>
<td>29.6%</td>
<td></td>
</tr>
<tr>
<td>Woolfenden(S9)</td>
<td>26 (out of 28)</td>
<td>non-consecutive selected</td>
<td>retro</td>
<td>22.5</td>
<td>time 0</td>
<td>&gt;50% basilar</td>
<td>DSA, MRA, TCD</td>
<td>4/26 (15.4%)</td>
<td>8.2%</td>
<td></td>
</tr>
<tr>
<td>Moufarrij(S5)</td>
<td>44</td>
<td>non-consecutive selected</td>
<td>retro</td>
<td>72</td>
<td>unknown</td>
<td>&gt;50% vertebral and basilar</td>
<td>DSA</td>
<td>5/44 (11.4%)</td>
<td>1.9%</td>
<td></td>
</tr>
<tr>
<td>Shin(S8)</td>
<td>41</td>
<td>non-consecutive selected</td>
<td>pros</td>
<td>31.4</td>
<td>unknown</td>
<td>&gt;50% vertebral</td>
<td>DSA, MRA</td>
<td>6/41 (14.6%)</td>
<td>5.6%</td>
<td></td>
</tr>
<tr>
<td>Pessin(S6)</td>
<td>9</td>
<td>non-consecutive selected</td>
<td>retro</td>
<td>24</td>
<td>time 0</td>
<td>&gt;50% basilar</td>
<td>DSA</td>
<td>1/9 (11%)</td>
<td>5.5%</td>
<td></td>
</tr>
<tr>
<td>Quereshi(S7)</td>
<td>102 (out of 128)</td>
<td>non-consecutive selected</td>
<td>retro</td>
<td>15</td>
<td>unknown</td>
<td>&gt;50% vertebral and basilar</td>
<td>DSA, MRA</td>
<td>8/102 (7.8%)</td>
<td>6.3%</td>
<td></td>
</tr>
<tr>
<td>Osman Kozak</td>
<td>4</td>
<td>consecutive</td>
<td>retro</td>
<td>16 (for larger group)*</td>
<td>0</td>
<td>&gt;50% vertebral</td>
<td>DSA</td>
<td>1/4 (25%)</td>
<td>…*</td>
<td></td>
</tr>
<tr>
<td>Osman Kozak</td>
<td>4</td>
<td>consecutive</td>
<td>retro</td>
<td>16 (for larger group)*</td>
<td>0</td>
<td>&gt;50% basilar</td>
<td>DSA</td>
<td>3/5 (60%)</td>
<td>…*</td>
<td></td>
</tr>
</tbody>
</table>

CTA indicates computed tomography angiogram; DSA, digital subtraction angiography; MRA, magnetic resonance angiography; TCD, transcranial doppler ultrasound; and TIA, transient ischemic attack.

*Mean follow-up not possible to calculate as mean follow-up for a larger group with all intracranial stenosis. However, most events occurred early: days 1, 3, and 243 for basilar stenosis and day 14 for vertebral stenosis. The references for I through IX can be found in the online-only Data Supplement.
a similar fashion and that urgent intervention is also required if the recurrent stroke risk is to be reduced. The pattern of high early recurrent stroke risk, which rapidly declines despite persisting stenosis, would be consistent with thromboembolism on an unstable atherosclerotic plaque being an important mechanism for both extra- and intracranial stenosis.

Such an intervention could be medical or interventional. Studies using the surrogate end point of asymptomatic embolic signals detected on transcranial Doppler ultrasound have shown dual antiplatelet therapy with aspirin, and clopidogrel is more effective at reducing asymptomatic embolization in carotid stenosis than aspirin alone. More intensive antiplatelet regimes may also be useful for vertebral stenosis. The high early recurrence risk in symptomatic vertebral stenosis also justifies studies to evaluate neuroradiological intervention with stenting in stroke prevention.

There are numerous case reports of vertebral stenting but no data from sufficiently powered randomized control trials. Systematic reviews of available data have suggested that the periprocedural risk associated with vertebral stenting is lower for extracranial compared with intracranial stenosis. However, our results demonstrate that the natural history of intracranial stenosis is more severe. This suggests that patients with intracranial stenosis may particularly benefit from intervention, even if it is associated with a higher procedural risk. The recent Stenting and Aggressive Medical Management for Preventing Recurrent stroke in Intracranial Stenosis (SAMMPRIS) trial found that, for intracranial stenosis as a whole, best medical treatment was better than stenting. However, there were few patients with VB stenosis, only 13% of the total, and intracranial vertebral stenosis may have a lower operative risk than stenting of basilar and other intracranial stenosis. Therefore, whether stenting results in clinical benefit in extra- and intracranial vertebral stenosis can only be answered by randomized clinical trials, and 2 feasibility studies are currently underway (Vertebral Ischaeemia Stenting Trial [VIST], www.controlled-trials.com/ISRCTN95212240/ VIST; and Vertebral Artery Stenting Trial [VAST], www.controlled-trials.com/ISRCTN29597900).

Our study has a number of strengths. It included results from the only 2 published prospective studies recruiting consecutive patients with posterior circulation stroke and performing noninvasive imaging to allow detect of the presence and site of VB stenosis. Previous studies have largely used ultrasound and this has low sensitivity for the presence of vertebral stenosis. In contrast, CE-MRA and CTA are sensitive to detection of vertebral stenosis when compared with the gold standard of intra-arterial angiography. Both studies involved a similar protocol, and in both studies there was a high proportion of patients imaged and receiving prospective follow-up.

The presenting event was the event that led directly to the patient seeking medical attention; risks quoted from this event are relevant to clinicians seeing patients in practice. We also analyzed risk from the first event (ie, including events for which patients might not have sought medical attention) because a high proportion of patients with VB TIA and minor stroke ignore the event and do not seek medical attention until they go on to have a subsequent stroke. This risk of recurrence from the first event is useful because it gives an estimate of the true natural history of the disease that is, the risk that we might see if patients could be persuaded to seek medical attention immediately. It is partly an overestimate of risk, however, because we would have identified those patients who went on to have a stroke, but not patients who had a TIA and never sought medical attention and did not have a stroke. On the contrary, we will underestimate risk because we will underascertain preceding TIAs in those patients with major VB stroke in whom we could not take a history for recently preceding events. Overall, the true natural history of VB stenosis is somewhere between the presenting event risk and the first event risk. It can never be estimated with complete reliability, but it is important that both risks are presented so that the upper and lower limits of the true risk can be appreciated.

A limitation of the study is that both studies used a cutoff of >50% to identify stenosis and data were not available on different cutoffs, such as >70% stenosis. However, noninvasive measurement of stenosis is less accurate for vertebral arteries than carotid arteries because of their smaller caliber and therefore this cutoff is not inappropriate. Future studies with higher resolution MRA and CTA may give more information on the relationship between degree of stenosis and risk. Another limitation is that both studies did not collect information on treatment post presentation and its relationship to recurrence. If treatment patterns differed for extra- and intracranial stenosis, this could produce bias. However, protocols for treatment of both conditions were similar over the study time period in both institutions.

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References


Stroke Risk After Posterior Circulation Stroke/Transient Ischemic Attack and its Relationship to Site of Vertebrobasilar Stenosis: Pooled Data Analysis From Prospective Studies
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