Are Arterial Calcifications a Marker of Remodeling in Vertebrobasilar Territory?

Slaven Pikija, MD; Jožef Magdič, MD; Alenka Knific, MD

**Background and Purpose**—Intracranial atherosclerosis is responsible for a substantial proportion of stroke, and vessel calcifications as seen on native computed tomographic scans could be an estimate of its burden. The presence of vertebrobasilar artery calcifications is associated with risk factors.

**Methods**—This study is a retrospective clinical study on 449 consecutive patients with stroke. Native computed tomographic scans were assessed for the presence of calcification in the intracranial segment of vertebrobasilar artery, and the area of each vessel was calculated from 2 perpendicular diameters. A comprehensive assessment of standard risk factors was recorded.

**Results**—A total of 245 (54.6%) patients had visible calcifications in vertebrobasilar artery. Calcifications were positively associated with advanced age (odds ratio, 1.04; 95% confidence interval, 1.02–1.06; \( P < 0.001 \)), larger total vessel area (odds ratio, 1.01; 95% confidence interval, 1.00–1.01; \( P < 0.001 \)), and history of previous transient ischemic attack/stroke (odds ratio, 1.82; 95% confidence interval, 1.08–3.07; \( P = 0.024 \)).

**Conclusions**—Higher prevalence of calcifications in vertebrobasilar artery territory of patients with stroke is associated with advanced age, larger arterial area, and history of previous transient ischemic attack/stroke. *(Stroke. 2014;45:874-876.)*

**Key Words:** basilar artery  ■  intracranial atherosclerosis  ■  stroke  ■  vertebral artery

Intracranial atherosclerosis occurs frequently with advanced age and is highly prevalent in stroke population.1,2 Calcifications on the vessel wall are a marker of advanced albeit a stable atherosclerotic disease and can be easily evaluated in the intracranial (V4) segment of vertebral arteries (VAs) and in the basilar artery.3 Vertebrobasilar artery (VBA) calcifications are highly prevalent in strokes, and more elaborated calcifications are associated with the male sex and diabetes mellitus and present more frequently in the dominant artery.4 Arteries change their shape because of atherosclerosis in the process known as arterial remodeling. Positive remodeling leads to a compensatory increase in focal vessel size, and negative remodeling narrows a vessel.5,6 The former is associated with neurological symptoms in middle cerebral artery stenosis and is also more prevalent in the BA than the latter.7,8 It is unknown whether calcifications are associated with vessel area diameter in VBA territory, and if they are, what risk factors are associated with them. Data could give us a better estimate of risk factors to plan effective preventive measures.

**Subject and Methods**

Detailed methodology has been reported previously.4 During a 12-month period, native brain computed tomographic scans were assessed in 449 consecutive hospitalized patients with an ischemic stroke. Hounsfield unit cutoff for the presence of calcifications was set at 90 HU. In those with VBA calcifications, 2 vessel diameters were measured outside of calcifications. Vessel area was calculated for each vessel as the product of 2 perpendicular diameters and \( \Pi \). Total vessel area (TVA) in square millimeters was calculated as the sum of left VA, right VA, and basilar arterial areas. Also, searching through medical history, a telephone interview with the subject and family/caregiver was conducted to gather more data. The presence of calcifications in VBA, sex, history of transient ischemic attack, and previous strokes were univariately associated (\( P < 0.100 \)) with TVA and entered into the multivariate regression model. STATA SE 11.2 was used for statistical analysis.

**Results**

A total of 245 (54.6%) patients had visible VBA calcifications. For demographics, see Table 1. Vessel area could not be calculated in 8 (1.8%) patients because of technical issues. Left VA was dominant in both samples, and right VA was the smallest. Basilar artery and left VA were almost equal in area. Larger right VA, left VA, and basilar arterial areas were univariately associated with the presence of VBA calcifications (Figure). In the multivariate analysis, larger TVA was independently associated with the presence of calcifications (95% confidence interval, 14.94–39.21; \( P < 0.001 \)) and male sex (95% confidence interval, 6.88–31.41; \( P = 0.002 \)), whereas age and previous transient ischemic attack/stroke were not associated with TVA. Significantly more women had calcifications. Cerebral angiography (computed tomography, digital subtraction, and MRI angiography) was available in 98 (21.8%) patients. There was no association between stenosis and occlusion with calcifications.
In the multivariate model (adjusting for age and sex), larger TVA (both as continuous or a binary variable; TVA \(<242.0\) or TVA \(\geq242.0\) mm\(^2\)) and transient ischemic attack/stroke history were associated with higher odds for calcifications, whereas positive smoking history versus never smoked was associated with lower odds for calcifications (Table 2). Another independent effect was for age (higher age–higher odds; Table 2). Lacunar strokes were more frequent than other stroke types (16.6% versus 8.0%) in the subgroup with no calcifications in the VBA territory, although difference was not statistically significant (6/36 versus 4/50; \(P=0.215\)).

Conclusions

Arterial atherosclerosis changes the morphology of an affected vessel with a process that eventually leads to vessel remodeling.\(^5\),\(^7\) Previous reports showed that age was positively associated with VBA diameter; however, we could not replicate this finding.\(^10\) We have shown that independent of age the presence of calcifications is associated with larger arterial areas. We can conclude that atherosclerotic process continues along the vessel and possibly produces positive arterial remodeling distally from the calcified plaque. However, there is a possibility that atherosclerosis and consequently calcifications tend to occur in larger arteries. Patients with calcifications were more symptomatic in the past. Contradictory to previous reports, positive smoking history lowers the odds for calcifications but this could be biased because of the retrospective nature of our study.

Shortcomings of our study are its retrospective nature, the measurement of arterial diameter with a nonperfect method because no data on eventual stenosis in sufficient number of patients (only 22% have available angiography) could be gathered, and rather modest sample size. Moreover, VBAs of patients (only 22% have available angiography) could be more symptomatic in the past. Contradictory to previous reports, positive smoking history lowers the odds for calcifications but this could be biased because of the retrospective nature of our study.

In conclusion, calcifications in VBAs of patients with stroke are associated with advanced age, larger arterial area, and previous transient ischemic attack/stroke. Further investigation into the possible arterial remodeling associated with calcifications is required.

Disclosures

None.

References

Figure. Vertebrobasilar arteries area (in square millimeter) with total vessel area grouped by the presence of calcifications. Basilar a. indicates basilar artery; calc., calcifications present; no calc., no calcifications; and VA, vertebral artery.


### Table 2. Independent Association of TVA as Continuous (Model 1) and Binary Variable (Model 2) and VBAC

<table>
<thead>
<tr>
<th>Effects</th>
<th>OR (95% CI)</th>
<th>P Value</th>
<th>OR (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>TVA, mm²</td>
<td>1.01 (1.00–1.01)</td>
<td>0.000</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>TVA &gt;242.0 mm²</td>
<td>...</td>
<td>...</td>
<td>2.46 (1.48–4.09)</td>
<td>0.001</td>
</tr>
<tr>
<td>Age, y</td>
<td>1.04 (1.02–1.06)</td>
<td>0.000</td>
<td>1.03 (1.01–1.06)</td>
<td>0.000</td>
</tr>
<tr>
<td>Sex (male)</td>
<td>1.08 (0.68–1.73)</td>
<td>0.737</td>
<td>1.05 (0.66–1.67)</td>
<td>0.844</td>
</tr>
<tr>
<td>TIA/stroke history</td>
<td>1.82 (1.08–3.07)</td>
<td>0.024</td>
<td>2.06 (1.23–3.46)</td>
<td>0.006</td>
</tr>
<tr>
<td>Atrial fibrillation</td>
<td>1.82 (0.99–3.34)</td>
<td>0.054</td>
<td>1.64 (0.90–2.99)</td>
<td>0.107</td>
</tr>
<tr>
<td>Known hyperlipidemia</td>
<td>1.63 (0.98–2.73)</td>
<td>0.062</td>
<td>1.52 (0.91–2.54)</td>
<td>0.107</td>
</tr>
<tr>
<td>Never smoked vs smoking</td>
<td>0.56 (0.33–0.93)</td>
<td>0.027</td>
<td>0.58 (0.35–0.97)</td>
<td>0.038</td>
</tr>
<tr>
<td>Unknown history of smoking</td>
<td>1.73 (0.98–3.07)</td>
<td>0.060</td>
<td>1.71 (0.97–3.00)</td>
<td>0.062</td>
</tr>
</tbody>
</table>

Outcome variable: presence of VBAC. CI indicates confidence interval; OR, odds ratio; TIA, transient ischemic attack; TVA, total vessel area; and VBAC, vertebrobasilar artery calcification.
Are Arterial Calcifications a Marker of Remodeling in Vertebrobasilar Territory?
Slaven Pikija, Jozef Magdic and Alenka Knific

Stroke. 2014;45:874-876; originally published online January 14, 2014;
doi: 10.1161/STROKEAHA.113.003518
Stroke is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2014 American Heart Association, Inc. All rights reserved.
Print ISSN: 0039-2499. Online ISSN: 1524-4628

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://stroke.ahajournals.org/content/45/3/874

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Stroke can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Stroke is online at:
http://stroke.ahajournals.org//subscriptions/