Vertebrobasilar Vasospasm after Aneurysmal Subarachnoid Hemorrhage: Review

Abstract
In the present review we outline the clinical data, diagnosis and prognosis of vertebrobasilar (VB) vasospasm (VS) after subarachnoid hemorrhage (SAH). Aneurysmal SAH is associated with high rates of morbidity and mortality. Although a major advancement has been made in recent years in diagnosis and treatment of aneurysmal SAH, 30% of the patients who survived the initial bleeding show further deterioration as a result of delayed cerebral ischemia (DCI) that traditionally was associated with large arteries lasting vasospasm (VS). The diagnosis of cerebral VS is based on clinical presentation, transcranial Doppler (TCD) evaluation and perfusion imagines as significant arterial narrowing is associated with reduced cerebral perfusion in the affected territories, DCI and cerebral infarcts. Although cerebral VS in the anterior circulation was intensely studied, little is known about VS in the posterior circulation. The incidence of posterior circulation VS and basilar artery (BA) VS is lower than the incidence reported for the anterior circulation, however it is associated with worst outcome. The diagnosis of posterior circulation and BA-VS is mainly based on measurement of TCD intracranial/extracranial (IC/EC) flow velocities FVs ratio that have been correlated with arterial narrowing on computerized tomography (CT) angiography, cerebral hypoperfusion and outcome. Within the past decade, there has been very little scientific activity to follow up on the research outlined above although TCD grading criteria for BA- VS are in widely used on daily clinical practice for the diagnosis of posterior circulation VS. The purpose of the present review is to increase clinician awareness and knowledge of posterior circulation VS after aneurysmal SAH and other intracranial pathology as for it major impact on outcome of patients with cerebral VS.

Keywords: Vasospasm; Subarachnoid hemorrhage; Transcranial Doppler; Basilar artery; Cerebral Blood flow; Outcome

Abbreviations: VB: Vertebrobasilar; VS: Vasospasm; SAH: Subarachnoid Hemorrhage; DCI: Delayed Cerebral Ischemia; TCD: Transcranial Doppler; BA: Basilar Artery; CT: Computerized Tomography

Introduction
Aneurysmal subarachnoid hemorrhage (SAH) affects 5-10 per 100,000 individuals per year¹ and is associated with high rates of morbidity and mortality [1-4]. Main contributor to poor outcomes after SAH are the early cerebral injury (ECI) caused by the immediate increase in intracranial pressure, decreased cerebral perfusion pressure and global ischemia [1,5-9] and delayed cerebral ischemia (DCI) which affects 30% of the SAH survivors leading to neurological deficit, cognitive decline [4,6,9-13] and death [14]. This ischemia is historically though to results from a long-lasting narrowing of the large-capacity cerebral arteries. Kassell et al. [15] published statistics that roughly hold to this day, whereby 40-70% of aSAH patients having survived the acute phase demonstrated angiographic VS, 20-30% manifested delayed neurologic deficits (DID), and 7% having died as a consequence there of. Another seminal study by Broderick et al. [16] have discerned a mortality rate of 45%, attributed 2 of 36 (6%) total deaths to VS, even though 44% of all patients manifested DCI. In 1994, Dorsch & King [17] published a review based on over 30,000 clinical cases that established an incidence of angiographic vasospasm at 43.3% overall and DID occurring at a rate of 32.5%. Of those who experienced DID, 34% sustained permanent neurological deficits and 30% died, such that VS was considered the cause of death in roughly 10% of aSAH patients.

Cerebral VS after aneurysmal SAH develops as soon as 3 to 4 days after the initial bleeding, with maximal narrowing occurring between days 5 and 14, gradually resolving by the third or fourth week [18-20]. Symptomatic VS presents through focal neurological signs such as hemiparesis, aphasia, apraxia, neglect, or cranial nerve deficits; alternately it can manifest in a decreased level of consciousness, typically fluctuating and with gradual onset [13]. Its clinical features are functionally determined by the involved ischemic territory. Unlike anterior circulation VS which have been studied and reported very intensively, vertebrobasilar (VB) VS has rarely been studied clinically. Therefore, many clinicians may not be well guided in the monitoring and treatment of VB-VS. The purpose of this review is to highlight the prevalence, diagnostic criteria and clinical importance of Basilar artery (BA) VS after aneurysmal SAH. In the present review we outline the clinical
data, diagnosis and prognosis of vertebrobasilar vasospasm. The purpose of the present study is to increase clinician awareness and knowledge of posterior circulation VS after aneurysmal SAH and other intracranial pathology as it major role in in outcome of patients with cerebral VS.

**Vertebrobasilar Vasospasm**

In contrast to the more robust scientific interest in and concentration on CVS of the anterior circulation, research on the diagnosis, clinical features and pathophysiologic characteristics of posterior circulation VS was belated, largely owing to the unique methodologic difficulties and obscurities involved in the investigation thereof. In 1964 Crompton [21] reported bilateral VS in the posterior communicating arteries in one of his cases of basilar tip aneurysms. In 1968, Wilkins et al. [22] had noted VS in the event of ruptured VB aneurysm, however the affected arteries were in the anterior circulation. In 1977, Saito et al. [23] discovered VS of the VB system owing to aneurysmal SAH, albeit rare among its cohort Saitos group [23] subsequently argued that VS of the VB system resulting from aneurysmal SAH presented with negligible neurological deficit relative to vasospasm of the anterior circulation [24]. Yet in 1978, Marshall et al. [25] reported on four patients who presented with significant head trauma and developed neurological deficits suggestive of primary brainstem or cerebellar dysfunction without an understanding of the underlying cause. The intracranial pressure had been normal in four of the patients and mildly elevated in two, indicating that the clinical presentation could not be explained on the basis of secondary compression of the brainstem and thus pointing towards an alternate etiology that was then clarified on angiography namely, VB-VS.

Research on the use of transcranial Doppler (TCD) for the diagnosis of VS took off in the 1980s. The landmark paper by Aaslid et al. [26] in 1982, recorded normal flow velocities (FVs) by means of TCD, did note the detection of Doppler shift from the BA, yet a follow-up paper two years later on the sonographic diagnosis of VS neglected the VB system [27]. However, as research on the use of TCD for assessment of intracranial arteries broke further ground, more attention was paid the posterior circulation. Lindegaard et al. [28] in a study that illuminated the inverse relationship between residual lumen diameter and FVs, provided recordings of flow volumes in both angiographically normal as well as stenotic vessels including those of the BA. Moreover, featured in this paper was a particular case of VS isolated to the BA, that is to say, not affecting the vertebral arteries or the PCA. Another prominent study analyzing the comparative accuracies of angiography and TCD in the detection of vasospasm in both the anterior and posterior circulations highlighted an illustrative case of increased FVs in the BA of a patient ten days after aneurysmal SAH [28]. Indeed other contemporaneous evaluations of the clinical applicability of TCD had included data on the posterior circulation; nevertheless, the scientific focus on the anterior circulation continued to predominate, so that VS of the VB system remained essentially uncharted territory. Although the criteria and technical parameters for insonation of the posterior circulation had been established years before [29,30], Sloan et al. [31] in 1994 were the first to ascertain the sensitivity and specificity of TCD for capturing VS in both the basilar and vertebral arteries.

In addition to confirming a direct correlation between severity of stenosis grade and mean FVs in the VB system, as previously had been proven with regard to the circle of Willis, they found that defining angiographic VS in mild to moderate cases by convention of FVs above 60 cm/s (nearly twice the normal value) resulted in a sensitivity and specificity for the vertebral arteries of 44% and 87.5% respectively, and 76.9% and 79.3% for the BA, respectively. However, they observed that when the diagnostic criterion was elevated to ≥ 80 cm/s for the vertebral artery, and ≥ 95 cm/s for the BA, all false-positive results were eliminated, consequently providing a much improved specificity and a positive predictive value of 100%. Since the sensitivity of the test thereby was compromised, and having attributed a high false positive rate to factors such as increased collateral flow and hyperemia, Sloan et al. [31] stressed the necessity of devising a posterior circulation FV ratio analogous to the “Lindegaard ratio,” as described above, and so opened the door to further research to lay the foundation for accurate TCD evaluation of VB vasospasm. Though Lee et al. [32] attempted to improve TCD diagnosis of vasospasm by aid of an “initial slope index” (ISI) that previously had been proposed as an alternative to the Lindegaard’s Index (by accounting for anatomical variations in the internal carotid arteries) [33], its ability to compensate for elevated FVs in the BA was undermined by its exclusion of cerebral blood flow within the posterior circulation. However, Soustiel et al. [34] effectively solved this problem by formulating a novel intracranial/extracranial (IC/EC) FVs ratio for the posterior circulation. Of note, the BA/IVA and IVA/EC FV ratios effectively were unchanged in SAH patients without evidence of VS on computed tomography (CT) angiography in comparison to healthy subjects, whereas the BA/extracranial (EC) vertebral artery (VA) FVs ratio showed a 58.8% increase in patients with a stenotic BA diameter <3 mm, constituting a statistically significant and indeed virtually linear correlation with vasospasm severity; similar findings with respect to the vertebral arteries were achieved. This correlation was even further improved by replacing the BA diameter with its expression as a percentage of the average EC-VA diameter, thereby minimizing the anatomical variations in the size of the VAs that are liable to distort results of TCD measurements of FVs in the VAs.

**TCD Criteria for Posterior Circulation CVS**

In comparative analysis between CT angiography and TCD results Soutiel et al. [34] reported showed that the BA/EC-VA FVs ratio was 2 in all patients with BA vasospasm (sensitivity 100%), with a ratio of 3 implicating severe angiographic BA vasospasm (50% diameter reduction). And so, just as Lindegaard et al. [28] had done for the anterior circulation, Soustiel et al. [34] innovated the use of an intracranial(IC)/EC FVs ratio that significantly improved the accuracy of TCD in the diagnosis of BA-VS, and by doing so reduced the number of false-positive results. Concerns about the accuracy of this new IC/EC index in light of certain methodologic irregularities, were put to rest by later analysis that elaborated on the biostatistical parameters for TCD diagnosis of BA-VS. Sviri et al. [35] evaluated Forty-three patients with aneurysmal SAH who underwent cerebral angiography during the acute phase of vasospasm (days 4-12 after the hemorrhage). BA narrowing was measured and compared to a baseline angiogram.

done within 48 hours from the initial hemorrhage. TCD was
done within 6 hours prior to angiography and both BA and EC-
VA mean FVs were measured: The BA/EC vertebral arteries FVs’s
ratio was found to be in significant correlation with the degree of
basilar artery narrowing (p<0.0001, r = 0.7792). A ratio higher
than 2.0 was found in 28 of 31 patients with BA-VS. This ratio was
associated with 90% sensitivity, 50% specificity and 85% positive
predictive value (PPV). A ratio higher than 2.5 was found in 20
of 21 patients with BA narrowing of more than 25%. A ratio higher
than 3.0 was associated with 100% sensitivity for BA narrowing of
more than 40%; those TCD criteria (Table 1) for BA-VS remain the
most relevant and widely accepted guidelines for TCD diagnosis
for spasm within the posterior cerebral circulation [36].

Table 1: TCD Criteria for severity of basilar artery vasospasm; Basilar
artery mean flow velocities (BA- MFVs); extracranial/intracranial (EC/IC).

<table>
<thead>
<tr>
<th>BA Vasospasm Severity</th>
<th>BA- MFVs (cm/sec)</th>
<th>EC/IC Ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>&lt; 70</td>
<td>&lt; 2.0</td>
</tr>
<tr>
<td>Mild (&lt;20% narrowing)</td>
<td>70-79</td>
<td>&gt; 2.0</td>
</tr>
<tr>
<td>Moderate (20-39 % narrowing)</td>
<td>&gt; 80</td>
<td>2.0-3.0</td>
</tr>
<tr>
<td>Significant (&gt;40 % narrowing)</td>
<td>&gt; 80</td>
<td>&gt; 3</td>
</tr>
</tbody>
</table>

Vertebrobasilar Vasospasm, Cerebral Hypoperfusion and Outcome after Aneurysmal Subarachnoid Hemorrhage

With regard to the clinical outcomes of vasospasm of the
posterior circulation, Lee et al. [32] had demonstrated with TCD
measurements of blood flow in a group of patients with VS in
the VB system (nearly all of whom had concomitant VS in the
middle cerebral artery), thus affected in both the anterior and
posterior circulations VS ended up with drastically worse clinical
outcomes than those patients without TCD-detected VS in MCA
only (p=0.013). Furthermore, in a study that revealed an overall
incidence of VB-VS of 23.8% detected on TCD (that corresponded
with Sloani’s finding of 30.9%) Soustiel et al. [37] made a host
of significant novel clinical observations, including that DCI,
particularly with regard to brainstem impairment, was nearly
time more frequent in patients with TCD evidence for VB-
VS than in those without. VB- VS was significantly more frequent in
association with traumatic SAH and FVs in the VB system closely
related with the severity of the SAH (especially in trauma,
perhaps owing to the frequent involvement of the midbrain and
the brainstem). Moreover, Soustiel et al. [37] noted that, whereas
FVs in the anterior cerebral vessels do not correlate with the
distribution of subarachnoid blood, in the VB system FVs were
significantly elevated in patients with posterior basal cistern
hemorrhage. In another report, Soustiel et al. [38] revealed that
severe BA VS was associated with permanent neurological deficit
or death in 85.3% of a patient cohort. Ultimately, in concert with
the findings of Lee et al. [32], the Soustiel group [38] clarified that
FVs in the BA have unique clinical significance, whereby VS of
the posterior circulation was associated with poor functional
outcomes, suggesting that BA-VS may result in secondary insult to the brainstem. Indeed, subsequent research on the
hemodynamics of BA-VS designed to explore that very thesis

provides the basis for current knowledge on the neuroanatomic
determinants of clinical outcomes associated with spasm in the
VB system. In similar fashion to previous efforts that shed light
on the correlation between regional hypoperfusion and DCI in the
anterior circulation [39], Svir et al. [40,41] ascertained a causal
link between basilar artery vasospasm and hypoperfusion to the
brainstem and other areas supplied by the posterior circulation.
By assessing a cohort of aneurysmal SAH patients with TCDs,
baseline and follow-up (99mTc) ECD-SPECT imaging of the territories of the posterior circulation, and
 correlating the results to clinical evaluations of neurological status
per the Glasgow Coma Score and Fisher’s grading scale, it was
found that 79.3% of cases of delayed brainstem hypoperfusion had TCD measurements consistent with BA VS. Moreover, severe
hypoperfusion was discerned in all of the patients presenting with
BA mean FVs exceeding 115 cm/s, thus providing a diagnostic
threshold to identify patients at high risk for brainstem ischemia.
In essence, delayed brainstem ischemia was found to be associated
with higher bleeding intensity and elevated BA FVs, delayed ischemic neurological deficits, and so worse overall outcomes,
which they posited could be secondary to significant compromise
in flow through the perforating arteries emerging from the basilar
artery at a 90° angle that serve as the main source of blood flow
to the brainstem. In an additional research of Svir et al. [42] BA
narrowing ≥25% was found in 23 of 65 patients, and delayed
brainstem (BS) hypoperfusion, as estimated by ECD-SPECT, was
found in 16. Fourteen of 23 patients with BA narrowing ≥25%
experienced BS hypoperfusion, whereas only 2 of 42 patients
with ≥25% BA narrowing experienced BS ischemia. Stepwise
correlation regression after adjusting for age with Hunt and Hess
grade, Fisher grade, hydrocephalus, and aneurysmal location
as co-variables revealed BA narrowing ≥25% and delayed BS
hypoperfusion to be significantly and independently associated
with unfavorable 3-month outcome (P=0.0001; odds ratio, 10.1;
95% CI, 2.5 to 40.8; and P=0.007; odds ratio, 13.8, 95% CI, 2.18
to 91.9, respectively) and was an independent prognostic factor
highly associated with an unfavorable outcome in aneurysmal SAH
patients with clinically suspected severe VS, further suggesting
that endovascular therapy intervention should be considered in
the event of significant spasm in the VB system [41,42].

Conclusion

The incidence of VS after aSAH is high and is associated
with increased morbidity and mortality rate. VS usually affect
the anterior circulation and peaking on days 5-14 after the
hemorrhage. The diagnosis of VS is based on clinical presentation,
TCD evaluation and perfusion imagines. The incidence of posterior
circulation VS and BA-VS are lower than the incidence in the
anterior circulation, however it is associated with worst
outcome. The diagnosis of posterior circulation and BA VS is
mainly based on measurement of TCD IC/EC FVs ratio that have
been correlated with arterial narrowing on CT angiography,
cerebellar hypoperfusion and outcome. Within the past decade,
there has been very little scientific activity to follow up on the
research outlined above. However, TCD grading criteria for BA VS
are in widely used on daily clinical practice for the diagnosis of BA
vasospasm.

DOI: 10.15406/jnslk.2018.08.00278
Acknowledgement

None.

Conflict of Interest

None.

References


