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Journal of the Neurological Sciences 260 (2007) 183–187

Journal of the Neurological Sciences

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Transcranial Doppler ultrasonographic evaluation of vertebral artery hypoplasia and aplasia

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Received 17 March 2007; received in revised form 18 March 2007; accepted 23 April 2007
Available online 29 June 2007

Abstract

Background and purpose: Evaluation of vertebral artery (VA) with transcranial Doppler ultrasonography (TCD) is difficult due to anatomical variations of hypoplasia (HP) or aplasia (AP). TCD findings of HP or AP of VA are rarely known. Comparing with magnetic resonance angiography (MRA), we tried to evaluate characteristic findings of HP or AP of VA using TCD.
Methods: Consecutive healthy patients who underwent TCD and MRA were included. VA was classified as normal (NL), hypoplasia (HP), and aplasia (AP) according to MRA. TCD parameters of mean flow velocity (MFV), pulsatility index (PI), vertebral/basilar artery flow velocity ratio (VA/BA FVR), and asymmetry index (AI) of VA were compared between three groups.
Results: Four hundred and ten patients were included, and 298 patients (72.7%) were classified as NL, 98 (23.9%) as HP and 14 (3.4%) as AP. MFV, PI and VA/BA FVR of ipsilateral VA were not different between groups. However, MFV of contralateral VA and AI were significantly increased in HP and AP groups ($p<0.001$). AI was significantly different between the three groups (17.7% and 30.5%, $p<0.001$). Sensitivity and specificity for HP or AP were 20.5% and 90.9%, if AI over 40% were adopted as diagnostic criteria.
Conclusion: MFV of VA should be interpreted with caution for its frequent anatomical variations. Increased MFV of unilateral VA may indicate not only as ipsilateral stenosis, but also as contralateral HP or AP. AI over 40% is specific to predict unilateral HP or AP with clinical correlation.

Keywords: Transcranial Doppler (TCD); Vertebral artery; Hypoplasia; Aplasia; Stenosis; Magnetic resonance angiography (MRA)

1. Introduction

Transcranial Doppler (TCD) is useful to assess stenosis or occlusion of intracranial arteries. However, the evaluation of vertebral artery (VA) has some limitations because of its common anatomical variations. The diameter of VA is often larger in the left side according to angiographic or sonographic studies [1–3]. The frequency of hypoplasia (HP) or aplasia (AP) has been reported from 2% to 15% in healthy controls, although this variability may be due to the methodological difference or various definitions of HP and AP [4,5]. Sonographic findings of HP or AP of VA are rarely known. Although one duplex study with angiography has reported high-resistance (70%) or low-resistance flow (20%) pattern from 10 patients with HP, the number of observed patients was small and descriptions of sonographic finding were not enough for conclusion [6]. In addition, there have never been comparative studies using TCD with MRA for HP or AP, which are occasionally observed in the clinical situation, although a few TCD studies were reported regarding stenosis of VA [6–8]. Therefore, we tried to reveal the characteristic TCD findings for vertebral HP or AP.

2. Materials and methods

Consecutive patients who underwent TCD and MRA with informed consent were included (Jan 2004 to Apr 2005). Patients with acute stroke, symptoms of vertebrobasilar ischemia or focal stenosis of VA defined on MRA were

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doi:10.1016/j.jns.2007.05.001

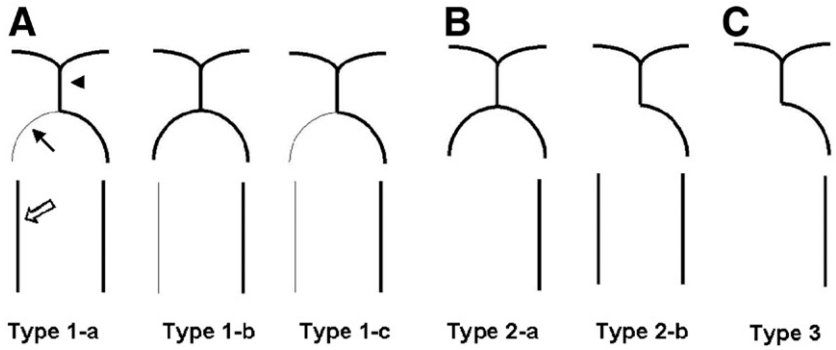

Fig. 1. Schematic representation of MRA criteria for hypoplasia (HP) and aplasia (AP) of intracranial (VAi; black arrow) or extracranial vertebral artery (VAe; arrow with black lining). Basilar artery is indicated as a black arrow head. (A). Type 1 denotes HPs showing VAi or VAe with the diameter less than 50% of the contralateral side. (B). Type 2 represents HP having invisible VAi or VAe. (C). Type 3 denotes AP with both VAi and VAe not visible.

excluded. MRA was performed by a 1.0-T superconducting magnet with three-dimensional time-of-flight (3D TOF) methods and analyzed blindly to the TCD results. VA was classified as normal (NL), hypoplasia (HP), and aplasia (AP) according to our MRA criteria, where HP was defined as VA with diameter less than 50% of the contralateral side and the definition of AP was non-visualization of VA in MRA (Fig. 1).

TCD was performed with 2-MHz pulsed Doppler instrument (Pioneer TC-4040, EME, Germany) according to the standard protocol [9]. VA was evaluated between 40

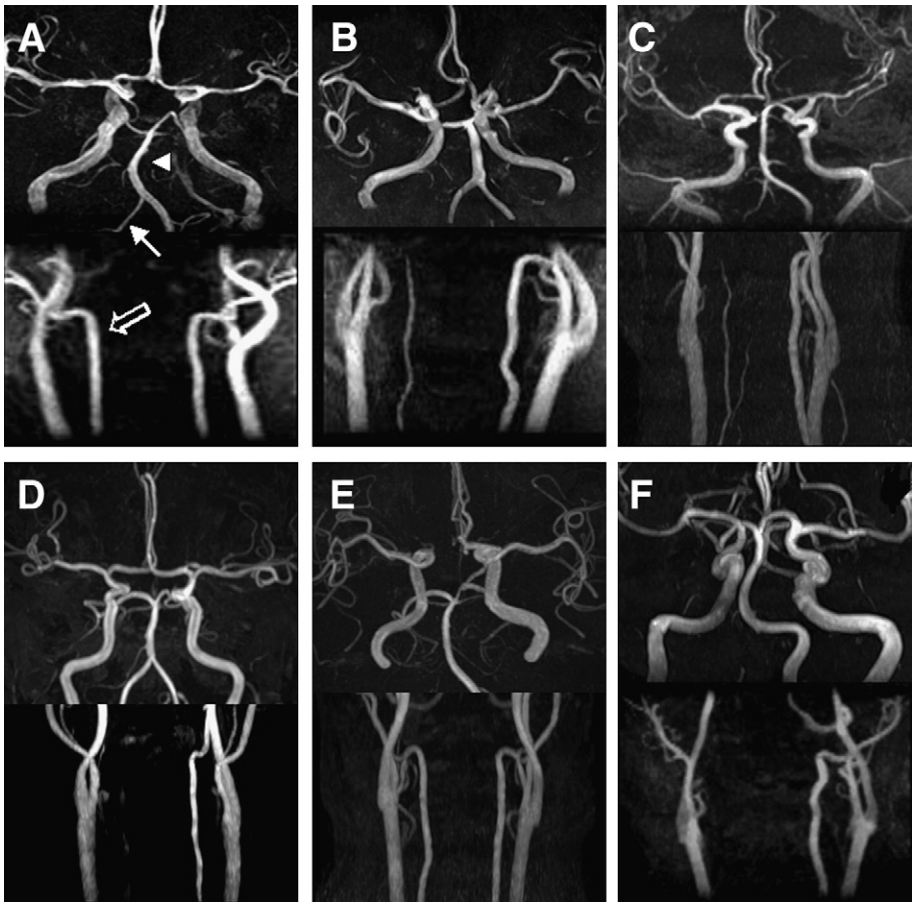

Fig. 2. The details of MRA criteria shown in Fig. 1. MRA was acquired with 3D TOF. Vertebral arteries (VA) are divided into intracranial (white arrow) and extracranial (arrow with white lining) segments and a white head of arrow indicates basilar artery. (HP; hypoplasia, AP; aplasia, VAi; intracranial VA, VAe; extracranial VA). (A). HP type 1-a with hypoplastic VAi and normal VAe. (B). HP type 1-b with normal VAi and hyoplastic VAe. (C). HP type 1-c with hypoplastic VAi and VAe. (D). HP type 2-a showing normal VAi without visualization of VAe. (E). HP type 2-b showing normal VAe without visualization of VAi. (F). AP type 3 with non-visualization of both VAi and VAe.

and 80 mm depth through suboccipital window. Mean flow velocity (MFV), pulsatility index (PI), and flow velocity ratio to basilar artery (VA/BA FVR) were compared between NL, HP, and AP group. Asymmetry index (AI) of VA calculated by $2\times100\times|MFV_{ipsi}-MFV_{contra}|/(MFV_{ipsi}+MFV_{contra})$ (%) was also analyzed (Fig. 2) [10]. Statistical significance was tested by one-way analysis of variances (ANOVA) for MFV, PI, VA/BA FVR, and AI between three groups (SPSS 11.0 for Windows). After post-hoc test (Turkey-*b* method), they were re-evaluated which variables were significant. Using receiver operation characteristic (ROC) curve, sensitivity, specificity, and cut-off value for HP and AP were calculated.

3. Results

Four hundred and ten patients were finally included for analysis (195 men, mean age 55.9±10.7 years). Mean time interval between TCD and MRA was 3.3 days. According to MRA criteria, 298 patients (72.7%) were classified as NL, 98 (23.9%) as HP and 14 (3.4%) as AP. HP was more common on the right side (63.3%, 62/98), while AP was more common on the left side (64.3%, 9/14). HP was similarly observed in men (51%) and women (49%), although the frequency of AP was higher in women (64.3%), compared with men (35.7%). For a side-to-side difference of HP between two sexes, 63.8% of women and 62.7% of men showed right HP. Age, sex, and prevalence of hypertension or diabetes mellitus were not different between three groups (Table 1).

MFV, PI and VA/BA FVR were not different on the affected side between HP, AP and NL groups (Table 2). However, on the non-affected side, MFV was significantly higher on AP and HP groups ($p<0.001$). Also, AI was higher in HP and the highest in AP, which was statistically significant ($p<0.001$). The sensitivity and specificity of AI for HP or AP were 41.1% and 74.5% with the cut-off value of 25%, although there were not significant difference between HP and AP (Fig. 3 and Table 3). When AI was set over 40%, it showed 90.9% specificity for HP or AP.

4. Discussion

We could verify that the interpretation of TCD results from posterior circulation is more complicated for its anatomical variations [4,5]. Generally, MFV is the most commonly used parameter to diagnose stenosis or occlusion in TCD. However, our study showed that MFV criteria are not adequate to evaluate VA due to the occasionally detected vertebral HP or AP (27%). MFV was not significantly decreased in the affected side of hypoplastic and aplastic VAs. Rather, the contralateral VA of HP showed higher MFV and that of AP did the highest MFV, which could imply that HP or AP of unilateral VA in MRA leads to hyperperfusion of contralateral VA with higher MFV. However, these findings were not concordant with our previous study regarding anterior cerebral artery (ACA) HP or AP, where MFV was significantly lower in hypoplastic VA and the lowest in aplastic VA [11]. The reason is uncertain why HP or AP does not result in significant MFV decrement in VA. The hemodynamic difference between posterior and anterior circulations or a technical limitation of MRA may be suggested as explanations. Compared with previous results, the higher frequency of HP or AP in our study also may support the technical demerit of MRA overestimating HP or AP in VA [4,5]. In addition, flow signal was detected in all VAs classified as AP in our study. It could suggest that aplastic VA seen in MRA is not true AP but severe HP so that the contralateral VA to AP has compensatory increased flow, although there is another possibility that flow detected in vertebral AP may belong to other vessels such as posterior inferior cerebellar artery (PICA). Besides contralateral MFV, AI was significantly different between HP, AP and NL, which may result from the elevated MFV of contralateral VA ($p<0.001$), although VA/BA FVR of contralateral VA showed no statistical significance in post-hoc analysis. Therefore, as described above, AI over 40% may be suggested as suitable criteria for HP or AP in clinical

Table 1
Basic demographic data ($n=410$)

	Normal ($n=298$)	Hypoplasia ($n=98$)	Aplasia ($n=14$)	*p*-value
Age, years (mean± S.D.)	55.5±11.3	57.6±9.3	57.7±7.2	0.140
Male sex	139 (46.6)	51 (52.0)	5 (35.7)	0.807
Hypertension	96 (32.2)	12 (12.2)	9 (64.3)	0.261
Diabetes mellitus	22 (7.3)	5 (5.1)	3 (21.4)	0.496

Numbers in parenthesis mean percentage.

Table 2
Mean flow velocity (MFV), pulsatility index (PI), flow velocity ratio (FVR) to BA, and asymmetry index (AI) of vertebral artery in normal, hypoplastic, and aplastic group

	Normal[a] ($n=298$)	Hypoplasia ($n=98$)	Aplasia ($n=14$)	*p*-value[b]
Affected site (Ipsilateral)				
MFV (cm/s)	32.0±10.9	32.6±16.5	34.4±13.1	ns
PI	0.73±0.15	0.77±0.22	0.80±0.20	ns
VA/BA FVR[c]	0.77±0.25	0.78±0.42	0.74±0.34	ns
Non-affected site (Contralateral)				
MFV (cm/s)	31.0±11.5	37.5±19.9	43.3±19.1	<0.001
PI	0.73±0.15	0.75±0.18	0.78±0.17	ns
VA/BA FVR[c]	0.78±0.31	0.89±0.48	0.87±0.28	0.03[d]
AI of the VA (%)	17.7±15.1	24.2±24.1	30.5±27.9	<0.001

ns: non-significant.
[a] Normal group has no affected site; however, we divided two subgroups (right and left) for analysis of variance.
[b] Statistical significances were tested by one-way analysis of variances among groups.
[c] VA/BA FVR indicates the ratio of mean flow velocity of vertebral artery to basilar artery.
[d] After post-hoc test, three groups showed no significant difference.

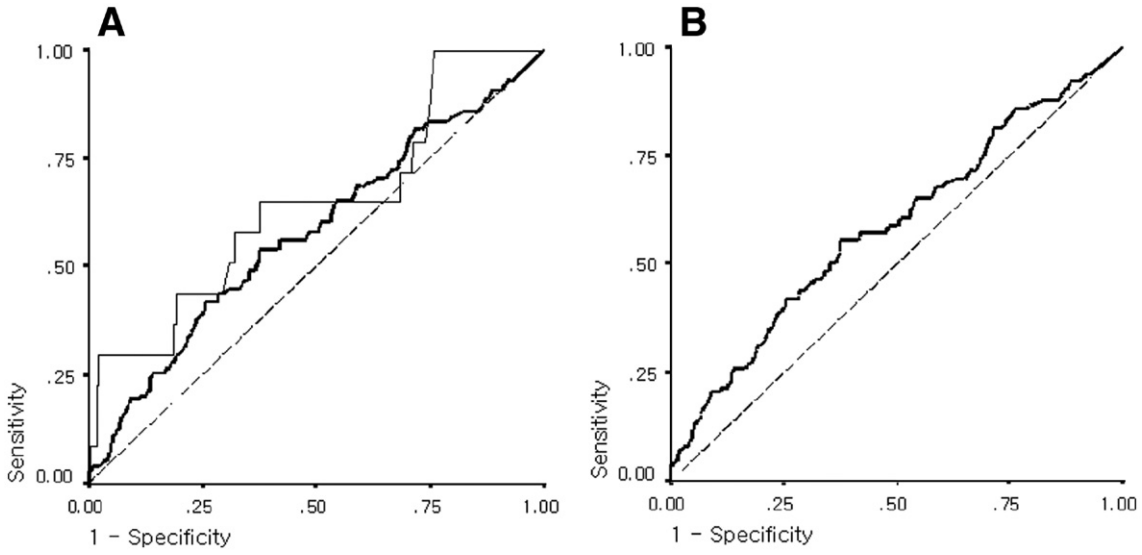

Fig. 3. Receiver operation characteristic (ROC) curves for (A) HP (thick line) and AP (thin line), respectively and for (B) HP or AP. Diagonal segments are produced by ties.

practice for higher specificity (90.9%), although clinical and MRA features have to be supportive.

On the other hand, it is well known that conventional angiography is usually accepted as a gold standard for anatomical variations of cerebral vessels and the direct measurement of VA is much simple and accurate using duplex sonography [4,7]. Our study may have some limitations because MRA used as a diagnostic standard for HP or AP. First, we made our criteria where HP is defined as VA with below 50% of the contralateral diameter, because MRA is not an anatomy-based method to measure the diameter of VA. Some studies denoted that VA with diameters below 2–3 mm is hypoplastic and the normal diameter of VA was reported from about 1 to 5 mm in healthy subjects [4,6,12]. Based on these studies, the diameter of VA defined as HP in our criteria ranges 0.5–2.5 mm, which is considered not far deviated from previous results [4,6,12]. Next, our results could be affected by MRA methodology, because we performed 3D TOF MRA instead of a Gd-enhanced method, which takes less time to get more accurate images of extracranial VAs rather than the former, although it could offer more artifacts by an unskilled technique, especially at the most proximal VA [13,14]. However, there have been no studies for comparing two methods to evaluate VA, so far. Rarely, HP or AP of intracranial or extracranial VA may undistinguishable from severe longitudinal stenosis or occlusion in MRA, although the half- or non-visualization of VA in this study would not imply stenosis or occlusion, because hypoplastic or aplastic VA dose not show the increase of MFV and that all patients were clinically healthy subjects. Finally, much smaller vessels in the posterior circulation (such as PICA) can be undetected in MRA and cannot be distinguished from VA in TCD. However, despite several demerits of MRA, it is necessary to interpret VA HP or AP, which are occasionally observed clinically. Therefore, the most important significance of this study is that we tried to evaluate TCD findings of vertebral HP or AP observed in

Table 3
Sensitivity and specificity of asymmetry index (AI) for the diagnosis of vertebral artery (VA) hypoplasia and aplasia according to TCD criteria

	Hypoplasia (HP)		Aplasia (AP)		HP or AP	
	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)	Sensitivity (%)	Specificity (%)
AI						
>10%	69.4	38.9	64.3	38.9	68.6	38.9
>15%	56.1	52.7	64.3	52.7	57.1	52.0
>20%	49.0	64.8	57.1	64.8	50.0	64.8
>25%	39.8	74.5	42.9	74.8	41.1	74.5
>30%	26.5	81.9	28.6	83.6	26.8	81.9
>35%	22.4	82.6	28.6	87.2	23.2	86.6
>40%	19.4	91.9	28.6	90.9	20.5	90.9

Asymmetry index (AI) of VA was calculated by $2\times100\times|MFV_{ipsi}-MFV_{contra}|/(MFV_{ipsi}+MFV_{contra})$ (%). MFV_{ipsi} and MFV_{contra} indicate ipsilateral and contralateral mean flow velocity of vertebral artery.

MRA, because many clinicians including neurologists perform MRA with TCD at bedside, instead of duplex sonography or conventional angiography.

In conclusion, TCD results with relatively elevated MFV of unilateral VA should be interpreted with caution for the possibility of contralateral vertebral HP or AP as well as ipsilateral stenosis. More importantly, marked asymmetry over 40% may be suggestive of unilateral HP or AP, which may be differentiated from unilateral stenosis with careful examination and clinical correlation. Further studies would help the interpretation of hypoplastic or aplastic VA, comparing TCD or MRA with other anatomy-based methods.

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