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Color Doppler ultrasonography findings of vertebral arteries: A correlation with 64-slice CTA

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Ethics Committee Approval
The study was approved by the Ethical Committee of Ankara Research and Training Hospital (2010/385-3162).
All procedures in this study involving human participants were performed in accordance with the 1964 Helsinki Declaration and its later amendments.

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No conflict of interest was declared by the authors.

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Abstract

Background/Aim: Although normal Color Doppler US (CDU) findings of the carotid system were described by many studies, normal findings of the vertebral system have not been studied extensively. This study aimed to evaluate vertebral artery CDU hemodynamic and morphologic findings in patients with normal vertebral arteries (VAs) on 64-slice Computed Tomography Angiography (CTA) and investigate the correlation between RDUS and CTA in evaluating the VA anatomy.
Methods: In this retrospective cohort analysis, the patients referred to our radiology department for CTA who had normal VA anatomy underwent a CDU for visualization of the orifice and segments (V1-V2) of the VA. Peak systolic velocity (PSV), and end-diastolic velocity (EDV) were measured in V1 while PSV, EDV were measured and resistive index and FV were calculated in V2. The presence of hypoplasia and dominance were noted.
Results: A total of 77 patients who had normal vertebral arteries on CTA were included in this study. CDU findings were highly consistent with multislice CTA findings regarding the measurement of VA diameter (ICC=0.856, ICC=0.830), hypoplasia (kappa=0.488), and dominance (kappa=0.752). No consistency was found between the two modalities in the visualization of the orifice and V1 segment of the VAs on both sides. CTA was able to show the orifice and the V1 segment in all cases, while the success rate was lower in CDU, especially in terms of visualizing the orifice of VA. VA FV was not significantly different between the patients with and without vertebrobasilar insufficiency (P=0.300).
Conclusion: CDU findings were consistent with 64-slice CTA findings in VA diameter measurement and the diagnosis of hypoplasia and dominance. However, CTA is more successful than RDUS in evaluating the vertebral artery orifice and V1 segment, the most common sites of atherosclerotic involvement. There was no significant difference between the patients with and without VBI symptoms in evaluating FV.

Keywords: Vertebral artery, Doppler ultrasound, Computed tomography angiography, Vertebrobasilar insufficiency

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Introduction

Vertebral arteries (VA) were not paid as much attention as the carotid arteries, possibly due to their anatomic location, which limits their surgical accessibility. However, in the last decade, the treatment of the VA has improved, partly resulting from advances in balloon angioplasty or stenting techniques as well as improvements in new generation ultrasound imaging [1, 2].

Intra-arterial digital subtraction angiography (DSA) is still the standard of choice in radiological diagnosis and assessment of vascular lesions located above the aortic arch and proximal to the cranium. Nevertheless, DSA has its complications, such as neurological, non-neurological (4%), and persistent neurological deficits (0.07-0.5%) [3-5]. Thus, DSA does not seem to be suitable as a screening tool [6]. Color Doppler ultrasonography (CDU) and computed tomography angiography (CTA) are used as alternative imaging modalities to DSA [7]. Since CDU is repeatable, easy to perform, and cost-effective, it has been widely used in the diagnosis of obstructive diseases of the cerebral vessels [2, 8]. CTA has increasingly been used in the diagnosis of VA pathologies and anatomical variations as it provides important information regarding the structure and pathology of V3 and V4 segments, which are poorly viewed by CDU [9].

The diagnosis of vertebrobasilar insufficiency (VBI) is a clinical challenge because its manifestations are subjective and difficult to quantify [2]. While some authors suggest that symptoms are caused by thromboembolism, others advocate that it results from a hemodynamic phenomenon due to the reduction of net blood flow velocity in VAs [10]. Clinically, it frequently presents with symptoms such as vertigo, dysarthria, and sometimes ataxia, and hemiparesis [11]. Flow volume (FV) is an important parameter for the evaluation of brain perfusion and a noninvasive assessment of FV, which is possible with the CDU.

The purpose of this study was to evaluate diameter, flow volume (FV), and mean velocities of the normal VA verified by computed tomography angiography (CTA) and determine a threshold value for the FV.

Materials and methods

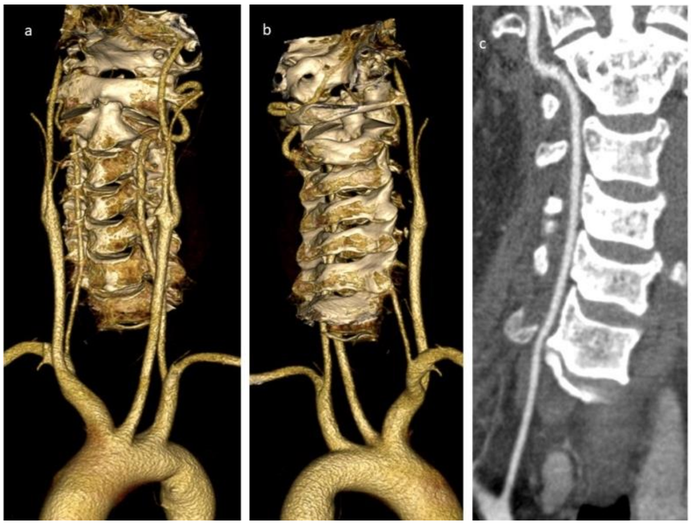
Between August 2009 and October 2010, 135 consecutive patients with a suspected transient ischemic attack, cerebrovascular disease, or VBI were referred to our Radiology Department for CTA to evaluate the vertebral arteries. Patients with bilateral normal vertebral arteries were included in the study. Normal VA was defined as one with homogenous contrast filling and no vessel wall abnormalities, stenosis/occlusion in the CTA.

Twenty-nine patients were excluded from the study because of the presence of vertebral artery stenosis or occlusion. Twenty-five patients with higher than 50% stenosis in the anterior circulation and four patients with bilateral severe ICA hypoplasia were excluded since these conditions might affect VA flow parameters. Four patients in whom CDU was not completed due to non-cooperation were also excluded. The final study group of this retrospective cohort study included a total of 77 patients. Power analysis revealed a minimum number of patients of $n = 70$ to obtain a power of 95 % for an alpha significance level of 0.05.

The study was conducted per the Strobe Cohort guideline. Of the forty cases, all had clinical signs of VBI (such as vertigo, drop attacks, tinnitus, and ataxia).

CTA was performed using a 64-slice CT scanner (Aqullion 64, Toshiba, Tokyo, Japan) with the following parameters: mAs:440, kV:120, slice thickness:3 mm, 512x512, FOV:320 mm, pitch 0.641 for all patients. Before the procedure, a 20 Gauge venous line was introduced into the antecubital vein and 75 ml of 350 mg/ml non-ionic contrast media was injected through the cannula followed by 20 ml of physiologic saline flushing. The area between the aortic arch and the Willis polygon was screened caudo-cranially. Optimal timing for scanning was decided manually by starting the image acquisition as soon as the contrast medium arrived in the internal carotid artery (ICA) at the level of 1-2 cervical vertebrae. Subsequently, CTA raw data were transformed to a remote workstation (Vitrea 2; Vital Images Inc., Minnetonka, Minn. USA) to achieve further processing of the images (Figures 1 a, b, c).

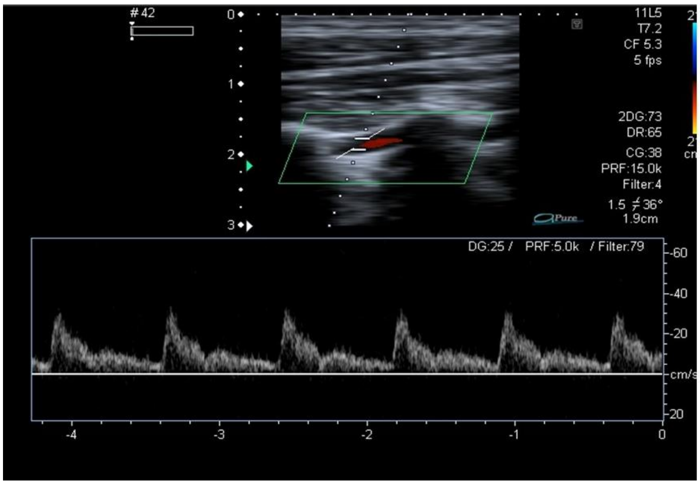
Figure 1: a, b, c: Normal CTA, 3D VR (volume rendering) AP, PA oblique and coronal CPR (curved planer reformate) images of vertebral artery



CDU was performed by an experienced sonographer with more than 4 years of experience using a device with adequate standards (SA-660A; Toshiba, Tokyo, Japan) equipped with a 6-7.5 Mhz linear transducer. Patients were in the supine position; their necks were slightly extended, and their faces were positioned opposite the examined side. First, the orifice of the VA and V1 and V2 segments were evaluated. Next, the orifice of the VA and V1 were visualized in B-mode. Then, flow dynamics were measured in color and spectral modes. Peak systolic velocity (PSV) and end-diastolic velocity (EDV) were measured through the V1 segment where its course is most parallel to the cervical axis.

V2 lumen measurements were performed at the C5-C6 level between the two intimal layers vertically to the longitudinal axis of VA. The presence of hypoplasia and dominance were noted. PSV, EDV, resistive index (RI), and FV were calculated. The viewability of the orifice of the VA and V1 was noted. Spectral sampling interval was placed centrally to the vessel and Doppler angle to lie between 30-60 degrees. All measurements were performed three times and mean values were calculated (Figure 2). CDU examination and CTA interpretation were performed by two different radiologists who were blinded to each other's results.

Figure 2: Normal Doppler spectral pattern of vertebral artery



VA hypoplasia was defined as the presence of an artery lumen diameter of less than 2 mm. RI was calculated using the following formula: PSV- EDV/PSV. All analyses were performed for both vertebral arteries in each patient. The diameter was expressed as mm, flow rates as cm/sec, and blood flow volume as ml/min.

Ethics approval

The study was approved by the Ethics Committee of Ankara Research and Training Hospital (2010/ 385-3162) and conducted following the principles of the Helsinki Declaration.

Statistical analysis

All statistical analyses were performed using SPSS ver. 15.0 (SPSS Inc., Chicago, IL, USA)

Continuous variables were expressed as mean (standard deviation) and categorical variables, as percentages. Independent samples t-test and Mann Whitney test were used for comparison of CDU parameters between genders. Independent samples t-test was used for comparison of CDU parameters between subjects with and without VBI. For assessment of the consistency between CTA and CDU findings, the kappa test was used for dominance and hypoplasia, the ICC test (intra-class correlation coefficient test) was used for diameter, and the McNemar test was used for viewability of the orifice of the VA and V1. Differences were considered significant when $P<0.05$.

Results

A total of 34 males (44.2%) and 43 (55.8%) females with a mean age of 53.6 (13.5) years (range: 19-87 years) were included in this study.

In CDU, the mean diameter of the VA was 3.4 (0.6) (range 1.8-5.0) mm on the right and 3.7 (0.7) (range 2.1-6) mm on the left, whereas in CTA, the mean diameter of the VA was 3.6 (0.6) mm on the right and 3.7(0.7) mm on the left. Diameter measurements in CDU were significantly consistent with those in CTA (ICC=0.856, ICC=0.830). Evaluation of dominance by CDU and CTA are presented in Table 1. CDU findings were significantly consistent with those of CTA (kappa=0.752).

Table 1: Number and percentage of right, left dominance, or co-dominance number according to CDU and CTA

	Right (n, %)	Left (n, %)	Codominant (n, %)
CDUS	30 (38.9%)	43 (55.8%)	3 (5.1%)
CTA	34 (42.8%)	42 (54.5%)	1 (2.5%)

CDU: Color Doppler ultrasonography, CTA: computed tomography angiography

Hypoplasia of the vertebral artery was present in one case (1.2%) according to CDU and in three cases (3.8%) according to CTA. CDU and CTA findings were significantly consistent (kappa=0.488). In CDU, the mean diameter of the right VA and FV of the left VA were significantly higher in males compared to females ($P=0.007$, $P=0.028$).

For the right and left VAs, the CDU findings were not consistent with those of CTA concerning the viewability of the orifice of the VA ($P=0$ for both right and left) and V1 segment ($P=0.01$, $P=0.06$ for right and left respectively).

The orifice of the VA and the V1 segment could be visualized by CTA in all cases, whereas the success of CDU was lower (Tables 2, 3). Table 4 shows the level and percentage of the entrance of the VAs to the transverse foramina. Table 5 shows the diameter, FV, and CDU velocity parameters in right and left vertebral arteries. One patient (1.3%) had left VA originating from the arcus aorta and two patients had duplicated left V1 VA. Neither variation was detected by CDU.

Table 2: Visualization rates of the VA orifice by CDU and CTA

Side	Number of patients visualized on CDU	CDU percent	Number of patients visualized on CTA	CTA percent
Right	53	68.8%	77	100%
Left	41	53.2%	77	100%

CDU: Color Doppler ultrasonography, CTA: computed tomography angiography, VA: vertebral artery

Table 3: Visualization rates of the V1 for right and left VA by CDU and CTA

Side	Number of cases visualized on CDU	Percent	Number of patients visualized on CTA	CTA percent
Right	66	85.7%	77	100%
Left	65	84.7%	77	100%

CDU: Color Doppler ultrasonography, CTA: computed tomography angiography, VA: vertebral artery

Table 4: Entrance level of VA to transverse foramina

	Number of cases	%
C6	144	93.5%
C5	9	5.8%
C4	1	0.6%
Total	154	100%

VA: vertebral artery

Table 5: Diameter, flow volume, and Doppler velocity parameters of normal VA on CTA on the right and left sides

	Right	Left
Diameter	3.4 (0.6) (1.8-5.0)	3.7 (0.7) (2.1-6.0)
Flow volume	78.6 (49.4) (10-310)	97.6 (53.6) (20-260)
V2 PSV	24.3 (10.9) (8.0-83.0)	24.2 (9.4) (6.0-63.0)
V2 EDV	8.9 (3.8) (3.0-24.0)	8.9 (3.6) (4-25)
RI	0.63 (0.070) (0.46-0.83)	0.63 (0.080) (0.43-0.81)
V1 PSV	29.2 (11.1) (13.0-65.0)	30.5 (9.2) (10.0-53.0)
V1 EDV	10.5 (6.7) (4.0-46.0)	11.0 (3.9) (4.0-21.0)
V2/V1 PSV	0.88 (0.38) (0.36-2.86)	0.85 (0.44) (0.24-3.50)
V2/V1 EDV	0.99 (0.54) (0.22-3.29)	0.90 (0.45) (0.28-3.57)

VA: vertebral artery, CTA: computed tomography angiography, PSV: peak systolic velocity; EDV: end-diastolic velocity, RI: resistive index

There were 40 cases (51.9%) with VBI symptoms (such as vertigo, drop attacks, tinnitus, and ataxia) while symptoms were associated with the anterior system (the patients which were evaluated for carotid artery stenosis) in 37 of cases (48.1%).

No significant difference was found between the patients with and without VBI symptoms regarding the FV ($P=0.300$).

Discussion

DSA is still the gold standard for the assessment of vertebrobasilar system pathologies. However, its elevated cost and possible complications have led to the development of novel non-invasive imaging techniques as screening tools. Being the first-line assessment tool of the VA, CDU has several advantages: It is a non-invasive, bedside tool that is cost-effective, and easy to perform. Its disadvantages in the assessment of VA cannot be standardized since the method is highly user-dependent and VA itself causes potential challenges due to its anatomic properties [12-15]. CDU provides a rough assessment regarding the hemodynamics of VA and posterior cerebral circulation. However, ipsilateral posterior circulation is evaluated indirectly. Therefore, a substantial number of pathologies may be overlooked [2, 12].

Multidimensional CTA technology has marked an era in CTA and allowed the visualization of the whole carotid and VA vascularity, including intracranial segments. CTA is preferred in the diagnosis of VA diseases for two reasons. First, atherosclerotic changes in the origin of the vessel may be easily visualized. Second, it allows the evaluation of the vessel wall adjacent to the lumen [10]. On the other hand, ionizing radiation and nephrotoxic contrast medium use are among the major disadvantages of CTA.

Although there have been several studies providing knowledge and normal values regarding the VA, few studies have sought to determine whether there is a correlation between CTA and CDU findings in the diagnosis of VA disease. Pucher et al. [16] reported that CDU was moderately correlated with CTA and had significant clinical limitations.

In our study, CDU findings were consistent with those of CTA regarding the right and left VA diameter measurements, determination of hypoplasia, and dominance (ICC=0.842, ICC=0,799 kappa=0.788, kappa=0.7693). To the best of our knowledge, such a relationship has not yet been investigated in the literature.

In our study, the left VA was the dominant side in 54-55% of the cases. Zwiebel et al. [17] reported that left VA dominance was more common than right VA dominance (73%). However, there have been other studies reporting co-dominance of VAs or right VA dominance [18, 19].

The reported thresholds for VA hypoplasia range between 2 mm-3 mm [18-21]. The frequency of VA hypoplasia in a healthy population ranges between 2-9%. In our study, 2 mm was accepted as the threshold for VA hypoplasia. We found that hypoplasia was present in 1.2% and 3.8% of patients according to CDU and CTA evaluation, respectively. The frequency of hypoplasia in CTA was consistent with that reported in the literature.

In our study, in CDU, the diameter of the right VA was significantly larger and FV was significantly higher in males compared to females. While some studies report that total VA FV is lower in females compared to males, other studies suggest otherwise [22].

Atherosclerosis is the most common VA pathology throughout its pre-cranial course and most seen in the first segment, particularly in the orifice. Thus, accurate visualization of the origin is crucial. Left VA lies deeper than the subclavian artery in contrast to the right VA and its origin is located more medially. In addition, although the VA rarely originates directly from the aortic arch on the right side, its origin is on the arch in up to 8% of cases on the left side [23, 24]. Therefore, visualization of the left VA origin may be harder compared to the right side [25]. In our study, the CDU visualization rate of the right VA orifice was higher than left (68.8% and 53.2% for the right and left, respectively). In previous studies, the visualization rate of the orifice was highly variable and ranged between 60-94% on the right side and 59-76% on the left side [1, 9, 18, 19, 26-28]. However, CTA visualization of the orifice of both VA and V1 segments was achieved in all cases, suggesting the superiority of CTA.

Normal hemodynamic features of VA were defined in several studies and different results were reported [18-20, 29-31]. Sheel et al. [32] reported that the VA flow rate was above 40 in healthy individuals. However, Benedict and Jackson [10] suggested that a flow rate of 20 cm/sec was normal and <20 cm/sec was insufficient. In our study, the mean PSV of V2 was 23.7 (8.8) and the mean EDV was 8.7(3.5) in the right VA, while they were 23.0 (7.3) and 8.5 (2.9) on the left VA, respectively. In our study, PSV values were lower than the literature, while EDV values were similar.

The threshold value for insufficiency is 200 ml/min in some studies. Benedict et al. reported that flow volumes were below 200 ml/min in patients with VBI. Kafadar et al. [6] reported that they found a flow volume of <200 ml/min in 55% of their patients. In the study of Kızılkılıç et al. [2], the FV of the VAs were below 200 mL/min in 81.7% of the patients who did not have clinical manifestations of VBI and in 71% of the patients who did. We found that FV did not significantly differ between patients with or without clinical signs of VBI, similar to these authors. This result supports the claim that FV should not be regarded as the sole criterion for diagnosis of VBI since clinical symptoms of VBI might emerge even when the VA FV is within the normal range [2, 8]. Therefore, additional parameters should also be added to the routine CDU examination of patients with a clinical suspicion for VBI. However, in contrast to the carotid system, a CDU examination of the vertebral arteries has not been standardized because threshold values for velocity have not been well defined in large prospective studies, although studies that report thresholds for significant stenosis exist [16, 33].

Limitations

The main limitation of our study was that although our patients had normal vertebral arteries on CTA, they were not completely healthy and had neurological complaints. Second, we did not assess interobserver variability for the study. We performed 3 measurements to decrease measurement mistakes and the mean was calculated.

To the best of our knowledge, there has been no study investigating whether CDU findings were consistent with those of CTA for visualization of the VA orifice and V1 segment, diameter measurements, determination of hypoplasia, and dominance, which constitutes the strength of our study.

Conclusion

Our study provides important data regarding the morphologic and hemodynamic characteristics of 154 vertebral arteries of 77 patients with normal VA anatomies on CTA. We think that our results would contribute to the identification of normal ranges of VA in the Turkish population and help to make a more reliable diagnosis of VA pathologies.

CDU findings are consistent with those of CTA for the determination of VA diameter and identification of hypoplasia or dominance. However, CDU has significant limitations in visualizing the orifice of the VA, which is the most common site of atherosclerosis. CTA enables visualization of the vertebral artery through its entire course including its orifice and V4 segment (which is impossible to visualize with CDU); hence, it is superior to the CDU in revealing anatomical details, variations, and anomalies as well as pathological processes.

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