ELSEVIER

CrossMark

The Spine Journal 15 (2015) 1981–1987

THE SPINE JOURNAL

Clinical Study

Age-related morphologic changes of the vertebral artery in the transverse process. Analysis by multidetector computed tomography angiography

Banu Alicioglu, MD, PhD[a,b,*], Nadir Gulekon, MD, PhD[b], Suha Akpinar, MD[a]

[a]*Department of Radiology, Near East University Medical Faculty, Nicosia / TRNC, Mersin 10 Turkey*
[b]*Department of Anatomy, Gazi University Medical Faculty, Bahriye Üçok Caddesi Ankara/Çankaya, Turkey*

Received 17 November 2014; revised 27 February 2015; accepted 20 April 2015

Abstract

BACKGROUND CONTEXT: The V2 segment of the vertebral artery (VA) ascends and passes through the transverse foramen (TF) of the C6–C1 vertebrae. Atherosclerosis of the VA and degenerative changes in the cervical spine are likely to occur with aging, and subsequent morphologic changes may alter the normal anatomy.
PURPOSE: The aim was to determine the morphologic changes of TF and VA in relation to aging.
STUDY DESIGN/SETTING: This was a retrospective cross-sectional study.
PATIENT SAMPLE: One hundred ten consecutive patients who had undergone computed tomography angiography were included.
METHODS: The subjects were then divided into three groups according to age: Group A, less than 45 years; Group B, from 45 to 65 years; and Group C, older than 65 years. Cases with stenosis and dissection of the VA were excluded from the quantitative analysis. The areas of the VA and TF were measured, and the VA/TF occupation ratio (OR) was calculated accordingly. The presence of VAs tortuosity within the TF was also noted.
RESULTS: The TF was larger in the oldest group, but the difference was not statistically significant. There was also no significant statistical difference among the age groups in terms of the VA and VA/TF ORs ($p>.05$). In the Group C, the rate of overall tortuosity of the VA was 73%, and arterial tortuosity in the TF was 28.6%. In cases with tortuous VA, C6 and C4 TFs were found to be significantly larger.
CONCLUSIONS: Tortuous VAs tend to be associated with enlargement of C6 and C4 TFs. Knowledge of such changes in the anatomy is crucial during instrumentation used for cervical spine surgeries, to prevent serious complications in patients aged older than 65 years. © 2015 Elsevier Inc. All rights reserved.

Keywords: Anatomy; Aging; Cervical spondylosis; Computed tomography angiography; Cervical vertebrae; Vertebral artery

Introduction

Vertebral arteries (VAs) arise as the first branches of subclavian arteries and, after a short soft tissue course, enter the C6 transverse foramen (TF). Vertebral arteries course cranially and longitudinally through the transverse processes of the upper six cervical vertebrae. They then ascend to the C2, making a wide loop between the C2 and the C1. After penetrating dura mater, the VAs unite as a basilar artery. Vertebral artery pathologies cause serious complications in the hindbrain, which is the main supplier of blood [1–3]. In older individuals, arteriosclerosis and progressive degenerative changes, together with alignment disorders in the neighboring cervical vertebrae, can affect the second segment of the VA (V2). Today, the mean age for life expectancy among humans has risen to 75 to 80 years in advanced societies. Consequently, the incidence of surgical interventions has increased. During instrumentation procedures, the greatest danger is tortuosity and/or ecstasia of the

FDA device/drug status: Not applicable.

Author disclosures: ***BA:*** Nothing to disclose. ***NG:*** Nothing to disclose. ***SA:*** Nothing to disclose.

* Corresponding author. Visart Medical Imaging Center, Cinnah cad. No:68 Cankaya, Ankara, Turkey. Tel.: (90) 312 442 2308; fax: (90) 312 439 7308.

E-mail address: alicioglu.b@gmail.com (B. Alicioglu)

http://dx.doi.org/10.1016/j.spinee.2015.04.031
1529-9430/© 2015 Elsevier Inc. All rights reserved.

artery, which can occur along with secondary bony remodeling such as scalloping and thinning of the posterior elements [4,5]. Increased use of screening with computed tomography angiography (CTA) has led to studies of variations in the VA and also of the relationship of these variations to cervical vertebral structures. The aim of this study was to determine the VA and TF areas in relation to aging. Knowledge of changes in the anatomy that are due to aging may change the approaches to surgical cervical spine interventions and reduce complication rates.

Material and methods

This study was approved by the local ethics committee, and written informed consent was obtained from the patients. The carotid-cerebral CTAs that were done in our clinic between October 2011 and January 2013 were analyzed retrospectively. The patients had been sent to our clinic with a prediagnosis of cerebrovascular disease or carotid artery stenosis or suspicion of an aneurysm. None of the patients had a diagnosis of clinical vertebrobasillary insufficiency. The carotid-VA CTAs of 110 cases, including 48 women (43.6%) and 62 men (56.4%), were investigated.

CTA technique

The scans of all the patients were done using 64-channel dual-source computed tomographies (CTs; GE Discovery CT750 HD, Milwaukee, WI, USA). A 20 to 22-G cannula was inserted through the right antecubital vein, and a power injector administered 50 to 65 mL 300 mg/mL iodine contrast (iohexol), followed by 25 to 30 mL saline at a rate of 3.5 to 5.7 mL/s. A bolus tracking method was used, with 6 seconds of delay time, and caudocranial scan direction was obtained with breath holding. The scanning parameters included field of view: 25 cm, 120 kVp with automatic tube current modulation, pitch: 1, and gantry rotation time: 0.4 seconds. Sections starting from the arcus aortae and reaching the vertex were scanned in 6 to 10 seconds. The images were reconstructed by standard algorithm, 0.5-mm slice thicknesses were reconstructed with 0% to 50% overlapping, and submillimetric slices were obtained.

Image processing

Raw data were processed in the Advantage Workstation Volume Share 5 (GE Healthcare, Milwaukee, WI, USA). Analyses of the image measurements were done digitally. Maximum intensity projection, three-dimensional volume rendering, and curved reformatted reconstructions were applied.

Analysis of the images

The pathologies and variations were determined with the consensus of two radiologists. One observer took all the measurements. Variations and acquired abnormalities (atheroma, stenosis, and tortuosity) were recorded. Arterial tortuosity was assessed on maximum intensity projection and three-dimensional volume reconstruction images.

The VAs were displayed on axial sections at the C1–C6 levels within the TF. The images were zoomed for correct measurement. Corresponding window-level widths were applied for VA and TF visualization. The circumferences of the VA and the TF were drawn manually using electronic calipers, and the area was determined automatically (Fig. 1). Vertebral artery/TF occupation ratios (ORs) were then calculated. The VA area could not be measured in cases with severe stenosis or where there was tortuosity of the VA within the TF. For cases where the VA is tortuous within the TF, only the area of the TF was measured.

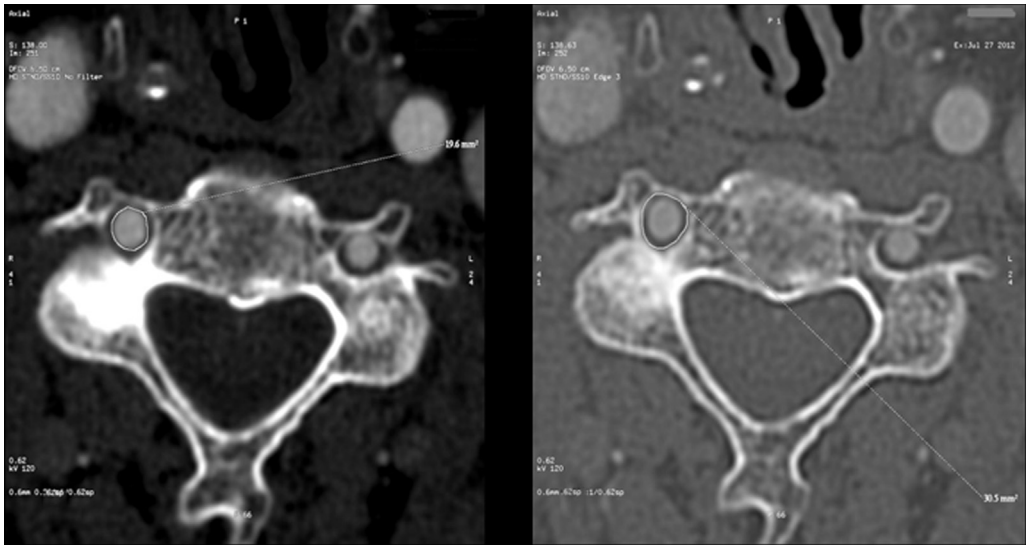


Fig. 1. Area measurements of the VA (Left) and TF (Right) shown at soft tissue and bone window/level settings in the axial plan.

Because of oblique orientation of the VA within the TF at the level of C2, measurements were done from sagittal reformatted images (Fig. 2). Cases with stenosis (15 VAs) and dissection (1 VA) were excluded. In cases with beam hardening artifacts resulting from metallic dental implants, the VA and TF areas could not be measured. When VA is tortuous within the TF, only the TF area was measured.

Statistical analysis

Statistical analysis was performed using SPSS 17.0.0 (SPSS Inc., Chicago, IL, USA) software adapted for Windows. After demographic analysis, the VAs and concordant TFs, the VA/TF OR means, and the standard deviation, minimum and maximum values were determined at each level. Variance between the groups was determined by one-way variance analysis. The Student *t* test was used to compare arterial tortuosity in the different age groups. Interobserver variance was tested by intraclass coefficient correlation. A value of p less than .05 was accepted for statistical significance.

Results

Four VAs (3.6%) had arcus aorta origin, six VAs (5.4%) showed entrance from C5, and one (1.8%) had bilateral entrance from C4. Entrance of the VA from C6 was seen in 102 cases (92%). Hypoplastic VA (area <4 mm^2 was accepted) was seen in three cases.

Measurements from 11 patients who had been randomly selected were taken by a second observer to determine the accuracy and repeatability of the measurements. Intraclass correlation was 90% for the VA area and 85% for the TF area, with a 95% confidence interval. Therefore, the agreement was good.

A total of 94 cases were included in the metric analysis; the mean age was 64.3±15.6 years (minimum, 20; maximum, 96). The cases were divided into three groups according to age: Group A, less than 45 years; Group B, from 45 to 65 years; and Group C, older than 65 years (Table 1).

Table 2 shows the presence of atheroma in the VA and tortuosity of the VA. In 15 cases, the VA/TF OR was not able to be determined because the area of the VA could not be measured because of its tortuosity within the TF (Fig. 3). There was no significant statistical difference among the age groups in terms of the TF areas ($p>.05$; Table 3). The areas of the VA were not statistically different among the age groups ($p>.05$), and the VA/TF ORs were not statistically different among the age groups ($p>.05$).

The correlation between the TF area in terms of VA tortuosity was determined by a Student *t* test (Table 4). The TF area were found to be larger in the presence of VA tortuosity at the C6 and C4 levels ($p<.05$).

When 15 cases with VA that are tortuous within the TF were reanalyzed, there were 5 women and 10 men with mean ages of 70.6±9.3 years old (median 74; minimum 60; and maximum 96). The mean area of the TF at the level of the tortuous VA was 52.64±23 mm^2. The rate of the tortuous VA was 14 of 49 cases (28.6%) in Group C, 1 of 30 cases (3.3%) in Group B, and 0 of 15 in Group A. Figure 4 shows the tortuous course of the VA and spine in a 96-year-old patient.

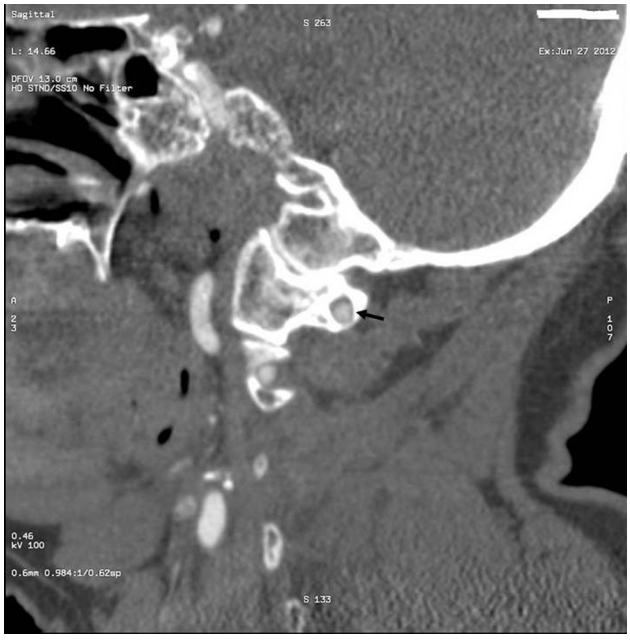


Fig. 2. Display of the VA within the TF (arrow) in sagittal reformatted scan at C2 level.

Discussion

The present study found that the TFs were larger in the older age group than in the younger groups. However, the difference was not statistically significant. Intimal thickening and vascular tortuosity resulting from atherosclerosis are thought to be more likely to change the TF area in the elderly. Although vascular tortuosity was present in 73% of the cases in the older than 65 years group, enlargement of TFs was not consistent in all levels. Nevertheless, tortuous VAs were found to be associated with C6 and C4 TFs. The reason is that vessel tortuosity was not assessed at each TF level. Vascular tortuosity was determined in the presence of tortuosity at any level along the course of the VA. For example, V1 segments or extraforaminal segments of V2 could not directly cause the enlargement of TF. Arterial tortuosity occurring in the TF had a strong correlation with the enlargement of the TF. Enlargement at the C6 level could be explained by the entrance of the VA into the TF at a wider angle compared with that at the superior levels. At C5–C3 and C1, the orientation of the VA in the TF was vertical. Only the TF of the axis differed greatly. It formed an angled canal, which resulted in the lateral deviation of the VA by 45° [6]. However, at C2, the size of the TF did not differ in terms of vascular tortuosity. We found loop

Table 1
Demography of the groups

	Gender						Age		
	Woman		Man		Total				
Groups	n	%	n	%	n	%	Mean±SD	min–max	med
Less than 45 y old (Group A)	10	67	5	37	15	100	37.3±6.9	20–44	40
45–65 y old (Group B)	11	37	19	63	30	100	58.8±4.9	46–66	60
Greater than 65 y old (Group C)	24	49	25	51	49	100	76±7.8	66–96	74
Total	45	48	49	52	94	100	64.3±15.6	20–96	60

SD, standard deviation; min, minimum; max, maximum; med, median.

formations of the VA within the foramen in 15 patients in our study group, but as the area of the VA could not be measured in these patients, they were excluded from the statistical analysis. When these patients were retrospectively analyzed, their mean age was 70.6±9.3, and the average areas of the TFs were 52.64±23 mm^2, whereas those of the TFs were twice the overall average TF areas (26±4.8 mm^2). This finding also supports the theory that tortuosity of the VA may erode the medially located bony structures such as the uncinate process and even the TF [1,6,7]. Erosion that occurs in vertebral bony structures due to loop formation and arterial tortuosity may cause fatal complications in cervical instrumentation surgery in older patients [8]. We expected that loop formation of the VA causes enlargement of the TF and would be expected to occur in the oldest age group. However, because of the low incidence of these cases, we could not reach a statistically significant result. Tortuosity of the arteries occurs as a result of aging, even intraosseous arteries of the vertebrae develop coils causing hemodynamic alterations with aging [9]. The courses of the extraforaminal segments of the V2 are relatively straight and vertical. The progressive medial enlargement of loops of the tortuous VA may cause vertebral body erosion, TF enlargement, and nerve root entrapment [1]. The incidence of medial loop of the VA was found to be between 0.6% and 5.6% [1,6,10]. In our study, the overall incidence was 6.2%, but the incidence increased to 28.6% in patients who were older than 65 years. The variation in the incidence could be due to the heterogeneous age group of the studies and the exclusion from the study groups of patients with eroded vertebral bodies resulting from VA enlargement. The VA loop formations may be projected medially or laterally. Medial loop formation should occur in two ways. In the first type, VA enlarges the TF by progressive medial placement; in the second type, VA moves toward proximal parts of the intervertebral foramen and the nerve exits. The pathophysiology of lateral placement of the loops was explained by the presence of spondylosis [1,10]. Tortuous VA may cause nerve root compression at the proximal neural foramen, and although these patients are usually asymptomatic, radiculopathy may occur after a minor trauma. As there is a high risk of injury during the anterior surgical approach, conservative treatment is usually preferred [8,11].

The areas of the VAs were found to be 10 to 11 mm^2 at all levels on both sides, and the TF areas were measured 20 to 35 mm^2 between the vertebral levels. Constant VA/TF OR compatible with the study by Kim et al. [12] concluded that the VA and TF areas were correlated. The sectional areas were found to be largest at C1 and narrowest at C3–C5. The VA/TF OR was highest at C3–C6 (0.47–0.49) and lowest at C1 (0.34). There are limited publications in the literature that report on studies of the VA/TF OR. A study by Hong et al. [6] found the TF areas to be 24.2±5.7 mm^2, which is similar to our results. However, we did not find any correlation in the VA/TF ORs in the age groups, suggesting that bony remodeling in TFs accompanied arterial enlargement.

There is a methodologic difference between our study and the previous ones. In the earlier studies, either the diameter [1,7,13] or the circle/oval region of interest [12] was used to determine the areas of the VA and the TF. In our study, measurements were taken manually and drawn digitally on a workstation. This method is more accurate, especially when the artery or foramen is in noncircular shape.

Table 2
Distribution of the study groups in terms of atheroma presence in the VA, tortuosity of the VA, and uncovertebral joint degeneration

		Group A (n=15)		Group B (n=30)		Group C (n=49)		
		Absent	Present	Absent	Present	Absent	Present	p*
Atheroma of the VA	n	15/15	0/15	29/30	1/30	25/49	24/49	*.0**
	%	*100*	*0*	*97*	*3*	*51*	*49*	
Tortuosity of the VA	n	14/15	1/15	23/30	7/30	13/49	36/49	*.0**
	%	93	7	77	23	27	73	

p<.05 statistically significant.
Italics, the incidence of atheroma and tortuosity of the VA was significantly high in the group C.
* Pearson chi-square test.



Fig. 3. Axial section. Spiral formation of the left VA (arrow) within the TF, the TF is enlarged. Right VA and TF are normal.

Our study found the VA areas to be constant. However, when we compared these with the previous studies, we found some differences. Because of the frequent variations in the cephalic levels of the TF (C1 and C2), Kim et al. focused on C3–C6 levels. They concluded that while going from C6 to C3, there was a decrease in the area of either the VA or the TF and that TFs that are more involved with VAs are usually larger than TFs with smaller VAs [14]. We also found that TFs diminish slightly when proceeding from C6 to C3; however, the VA areas were the same at all levels. Sanelli et al. [13] have noted that the VA/TF OR changes according to the level and side and between the cases. He found the VA/TF OR to be 8% to 85% in 16 cases where the patients were between 7 and 39 years

Table 3
The TF areas (mm^2) in the age groups

TF level		Age groups		
		Less than 45 y	45–65 y	Greater than 65 y
C6	Right	23.5±6.0	26.0±7.7	29.0±13.1
	Left	24.8±7.1	25.5±8.1	31.3±16.0
C5	Right	21.0±4.7	23.9±5.6	23.9±8.5
	Left	23.9±7.6	25.2±7.5	25.9±11.3
C4	Right	20.1±5.4	21.8±6.0	23.3±8.0
	Left	21.9±6.6	24.2±7.6	25.6±10.7
C3	Right	20.3±6.0	23.6±8.4	23.2±6.5
	Left	22.6±5.2	24.2±7.0	23.1±6.3
C2	Right	26.2±7.5	30.0±8.6	30.7±11.3
	Left	28.4±8.8	34.4±16.4	29.9±11.0
C1	Right	29.5±7.7	35.2±10.5	35.4±8.6
	Left	33.0±9.9	35.7±9.7	35.3±9.8

Note: There was no statistically significant difference among the age groups (p>.05).

Table 4
The correlation analysis of the TF area (mm^2) in terms of the presence of tortuosity of the VA

TF level		VA tortuosity		
		Absent	Present	p
C6	Right	24.9±7.0	29.9±13.8	.025*
	Left	25.0±6.5	32.4±17.0	.005*
C5	Right	22.1±6.1	24.9±9.0	.062
	Left	23.7±6.5	27.1±12.0	.073
C4	Right	21.0±5.1	23.8±8.6	.043*
	Left	22.2±8.1	27.1±11.3	.007*
C3	Right	22.5±7.2	23.3±7.0	.577
	Left	22.6±5.7	24.2±7.0	.209
C2	Right	28.7±11.0	31.0±9.9	.255
	Left	30.5±13.8	31.4±11.4	.695
C1	Right	33.3±9.5	35.6±9.0	.206
	Left	34.1±18.6	36.1±9.6	.298

* TF areas were found significantly higher with the presence of VA tortuosity at C6 and C4 levels.

of age. Variations of the foraminal area were largely dependent on the vertebral levels but less dependent on the right-to-left variation or variations between the individuals [13]. The VA diameters of the genders may also be different: the left VA was found to be larger in diameter in the



Fig. 4. Tortuous and dilated VA (arrows) and severe degenerative changes of the cervical spine in a 96-year-old woman. Both common carotid arteries are also tortuous.

males [7]. Kim et al. [12] declared that the VA diameters are independent from the vascular risk factors (for diabetes mellitus, hypertension, hyperlipidemia, and smoking) but are directly related to the TF. Sanelli et al. [13] concluded that variation in the VA/TF OR is related to the side, level, and case. The VA areas in our study were the same at all levels. Needless to say, it is expected that the dimensions of an artery would stay the same along its course; otherwise, pathologic processes like arterial stenosis or enlargement can occur. In our study, the variations were low and did not show any changes with respect to age. The differences between the results of these studies could be due to the heterogeneity of the age groups (7–39) and the small number of cases [14] involved in our study. Tomasino et al. [14] found that the VA/FT OR was higher on the left side and more frequent among the female population. The lowest OR was at C2 (30.7% in males; 33.6% in females), and the highest OR was at C7 (74.2%). The overall VA/FT OR in our study at all levels and age groups was 45%; in the study by Sanelli et al. [13], it was 34% and in that by Tomasino et al. [14], it was 41.7%. Although there are minor methodologic differences between the study groups, the results are close to each other.

The major limitation of our study was that the VA area could not be measured properly because of its tortuosity or narrowing. The wall thicknesses of the VAs were not taken into consideration for the measurements. There are two reasons for this. First, CTA can only visualize the arterial lumen when contrast material passes through it. The arterial wall was only able to be detected if it was not surrounded by any macroscopic fat, and this was not possible in the all the images. Also, the wall thicknesses of the VAs were in submillimetric ranges, which are below the CTA's spatial resolution sensitivity. Computed tomography angiography is a unique imaging method for displaying the arteries together with the bones.

Clinical implication of the present study could be considered in surgical interventions, which are increasing with the advancing ages of the population. Older patients are likely to have advanced VA atherosclerosis and tortuosity as well as cervical spondylosis along with abnormalities in alignment. During instrumentation procedures, the greatest danger is tortuosity and/or ecstasia of the artery, which can occur along with secondary bony remodeling such as scalloping and thinning of the posterior elements. Those morphologic changes promote accidental injury of the VA during drilling. In addition, the bony structure may be less favorable, complicating identification of the landmarks and making it difficult to apply the screws [4,15]. Therefore, it is necessary to have the correct calculation of the safe trajectory for screw placement. Jost et al. [4] recently proposed virtual determination of the safe trajectory angle on CT scans as the basis for placement of transarticular facet screws in the cervical spine. In this way, knowledge of the axial trajectory angle in combination with an exposure of the lateral edge of the facet joints is helpful in guiding the surgeon. This is relevant for the lower cervical spine where fluoroscopic imaging is limited because of the obscuration of the shoulders. We agree with the previous report proposing that individual virtual determination of the surgical implants in terms of possible tortuosity and/or bony remodeling might increase perioperative VA injuries in the older patients. The incidence of tortuous VA rises to 73% in patients who are older than 65 years. Therefore, neurosurgeons must be alert to this in these patients; the patient's' preoperative cervical spine magnetic resonance imagess or CTs have to be assessed in terms of the course of the VAs, the presence of scalloping of the neighboring spine, or enlargement of the TF that could be a signal for tortuous VA. We propose that patients should have CTAs before cervical spine interventions, to prevent possible complications.

To conclude, the VA and the VA/TF ORs did not alter with aging. Nevertheless, in cases older than 65 years, the incidence of VA tortuosity was 73%. Tortuous VA may enlarge the TF specifically at the TFs of C6 and C4. The TF size was larger in the older group. Although this enlargement was not statistically significant, it is clinically significant because of the increased risk of VA injury during surgical interventions. To prevent mortal complications, the relationship of the VA to the cervical spine should be determined individually before operations are performed in older patients.

Acknowledgment

The authors are very grateful to Dr. Nazan Cobanoglu and Dr. Ozgur Tosun for their statistical assistance.

References

[1] Bruneau M, Cornelius JF, Marneffe V, Triffaux M, George B. Anatomical variations of the V2 segment of the vertebral artery. Neurosurgery 2006;20–4.
[2] Sikka A, Jain A. Bilateral variation in the origin and course of the vertebral artery. Anat Res Int 2012;2012:580765.
[3] Satti SR, Cerniglia CA, Koenigsberg RA. Cervical vertebral artery variations: an anatomic study. AJNR Am J Neuroradiol 2007;28:976–80.
[4] Jost GF, Bisson EF, Schmidt MH. Computed tomography-based determination of a safe trajectory for placement of transarticular facet screws in the subaxial cervical spine. J Neurosurg Spine 2012;16:334–9.
[5] Madawi A, Solanki G, Casey AT, Crockard HA. Variation of the groove in the axis vertebra for the vertebral artery. Implications for instrumentation. J Bone Joint Surg Br 1997;79:820–3.
[6] Hong JT, Park DK, Lee MJ, Kim SW, An HS. Anatomical variations of the vertebral artery segment in the lower cervical spine: analysis by three-dimensional computed tomography angiography. Spine 2008;33:2422–6.
[7] Kiresi D, Gumus S, Cengiz SL, Cicekcibasi A. The morphometric analysis of the V2 and V3 segments of the vertebral artery: normal values on MDCT. Comput Med Imaging Graph 2009;33:399–407.
[8] Curylo LJ, Mason HC, Bohlman HH, Yoo JU. Tortuous course of the vertebral artery and anterior cervical decompression: a cadaveric and clinical case study. Spine 2000;25:2860–4.

[9] Ratcliffe JF. Arterial changes in the human vertebral body associated with aging. Spine 1986;11:235–40.
[10] Park SB, Yang HJ, Lee SH. Medial loop of V2 segment of vertebral artery causing compression of proximal cervical root. J Korean Neurosurg Soc 2012;52:513–6.
[11] Bruneau M, Cornelius JF, George B. Anterolateral approach to the V2 segment of the vertebral artery. Neurosurgery 2005;57: 262–7.
[12] Kim C, Lee SH, Park SS, et al. A quantitative comparison of the vertebral artery and transverse foramen using CT angiography. J Clin Neurol 2012;8:259–64.
[13] Sanelli PC, Tong S, Gonzalez RG, Eskey CJ. Normal variation of vertebral artery on CT angiography and its implications for diagnosis of acquired pathology. J Comput Assist Tomogr 2002;26: 462–70.
[14] Tomasino A, Parikh K, Koller H, Zink W, Tsiouris AJ, Steinberger J, et al. The vertebral artery and the cervical pedicle: morphometric analysis of a critical neighborhood. J Neurosurg Spine 2010;13: 52–60.
[15] Xu R, Zhao L, Chai B, Ma W, Xia H, Wang G, et al. Lateral radiological evaluation of transarticular screw placement in the lower cervical spine. Eur Spine J 2009;18:392–7.