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Sex and level differences in the diameters of extradural segment of vertebral artery: computed tomography angiographic study

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Background: *We investigated diameters of prevertebral — V1, and atlantic — V3 parts of extradural segment of vertebral artery (VA). Variable results from the literature about VA diameters reflect variety of diagnostic and imaging methods, various sample sizes, different levels of measurements, and lack of possible specific ethnic, regional or genetic data. Additionally, the data are often without distinctions of left-right or of sex.*

Materials and methods: *For this computed tomography (CT) angiographic study 91 adult people (182 VAs) of both sexes (47 males and 44 females) and of age between 33 and 75 years were selected. Diameters were measured at fixed predefined points of VA, marked as inferior (A) point (at V1 part in region of VA origin), as middle (B) point (the end of V1 part), and superior (C) point, at V3 part — 5 mm before VA penetrated the dura. Inferior (A) and middle (B) points actually represent locations at beginning (A) and at terminal (B) regions of V1 part of VA, and superior point C represents terminal part of V3.*

Results: *In total sample ipsilateral (both left [L] and right [R] sided) diameters on investigated levels of VA showed progressive and highly significant decreases. The mean values were on the right side at point A — 3.63 mm, at B point — 3.31 mm, and at C point — 3.08 mm. On the left side, mean values were at point A — 3.76 mm, at B point — 3.50 mm, and at point C — 3.21 mm. Pattern of increasing sex differences in diameters of VA, was ranging from no differences (point A), trough significant (point B), to highly significant differences (point C). For inferior point (A) we did not find significant differences in VA diameters between males (R 3.78 mm; L 3.89 mm) and females (R 3.50 mm; L 3.62 mm), in middle (B) point sex differences were significant (males: R 3.44 mm, L 3.66 mm; females: R 3.18 mm, L 3.33 mm) and in most superior point (C) differences were highly significant (males: R 3.278 mm, L 3.39 mm; females: R 2.88 mm, L 3.01 mm). However, we did not find significant intrasex (in males or in females) left-right differences in mean values of VA diameters for all three investigated levels.*

Conclusions: *Our findings, as the first data about diameters of VA systematically obtained by CT angiography in the population of western Balkans and wider, suggest that in design of future studies of VA diameters is necessary to analyse separately the data for sex, as well as to use defined standard levels.* (Folia Morphol 2019; 78, 3: 494–500)

Key words: vertebral artery, diameters, left-right differences, sex differences

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INTRODUCTION

Vertebral artery (VA) is a substantial element of the craniocervical transition region and the basic contribute to the posterior brain circulation. Based on anatomical, topographical, medical and specific diagnostic reasons VA is divided into four parts and two segments, extradural segment (including prevertebral — V1, cervical — V2, and atlantic — V3 parts), and intradural segment, as its fourth, or intracranial part (V4) [2].

Regarding VA diameters, special matter of consideration is that published data obtained by variety of diagnostic and imaging methods (mainly ultrasonography, computed tomography [CT] and magnetic resonance imaging [MRI] angiography, contrast angiography, and even virtual reality technology, or dissections, vary in a very wide range [1, 4, 5, 7, 8, 11, 13, 15, 18, 20–24, 27]. Additionally this reflects very different sample sizes, different locations (levels) of measurements, and lack of specified ethnic, regional or genetic data. Also the data about VA diameters are often without distinction about left-right or about sex. The comparisons between the results of different authors require corresponding specific levels of measurements for specific human populations. All this was extremely rarely done and currently makes comparisons almost impossible and the vast majority of these data are not appropriate for meta-analysis [3].

Unfortunately, the specific anatomical data about VA diameters for populations in different regions of the world are also insufficient, disabling more sophisticated analysis of such data. With the exception of few data by Mehinović et al. [11], or by ultrasonography [9, 12], there is a lack of original data about VA diameters available for regions of Balkans.

Therefore we, by the use of consistently fixed measurement locations (levels), investigated left-right and sex differences of the diameters of extradural segment of VA in the population of Republika Srpska (North-Western regions of Bosnia and Herzegovina).

MATERIALS AND METHODS

In period May 2016 – January 2018, total of 793 patients were examined by CT angiography at Clinical Radiology Department, University Clinical Centre of Republika Srpska (Banjaluka). Of these we selected 91 adult persons (182 VAs) of both sexes (47 males and 44 females) and of age between 33 and 75 years (Table 1) for the study of VA diameters. From the study were excluded the patients with abnormal morphology of VA, with unusual anatomical features (variations of origin described previously [26], kinking and coiling) or with previous or current cerebrovascular accidents, with injuries of cervical region, vertebrobasilar insufficiency, atherosclerotic changes of vessels (affecting more than 50% of VA diameter), with developmental abnormalities of cervical spine and with severe spondyloarthrosis. The patients were selected according to the described criteria, and only those of so selected patients who also gave informed consent (91 patients) were finally included in this study.

Data were collected and stored in accord to Helsinki Declaration [28] with additional verbal informed consent obtained from the all subjects.

Imaging generation and visualisation

All measurements were performed in Clinical Radiology Department, University Clinical Centre of Republika Srpska (Banjaluka). Patients were placed in a supine position with their arms alongside the body, head and neck kept at a neutral position. The imaging examination was performed on a 64-detector row CT scanner (GE Lightspeed CT, GE Healthcare, Milwaukee, WI, USA) with the scanning protocol as follows: 120 kVp, 697 mAs, beam collimation 64 × × 0.625 mm, gantry rotation time 0.4 s, section thickness of 0.625 mm, pitch 0.969:1 and reconstruction interval of 0.625 mm. During the procedure, 80 mL of nonionic iodinated contrast medium was infused followed by 40 mL saline and injected via a double power injector into the patient's antecubital vein at a rate of 4 mL/s. Post-processing of source images was performed using maximum intensity projection and evaluation and measurements of CT angiography dataset were performed on 3 mm thick coronal sections.

Measurements

Diameters of different parts of extradural segment of VA were always measured at fixed predefined locations, (marked as inferior A, middle B and superior C points) (Figs. 1, 2). Inferior point I was at V1 part, in region of VA origin, ~3 mm above of subsclavian artery (SCA); the middle point M was close to the end of V1 part, immediately below the entrance into C6 transverse foramen (adjacent to beginning of V2 part); and superior point S was at V3 part — 5 mm before VA penetrated the dura. Inferior and middle locations, A and B, represent locations at beginning (A) and terminal (B) parts of VA1 segment, and superior point C represents terminal part of V3.

Table 1. Structure of the investigated sample by sex and age

Sex	N	Age					
		Minimum	Maximum	Range	Median	Mean	Standard deviation
Males	47	35	75	40	66.00	63.47	9.320
Females	44	33	75	42	64.00	59.14	11.993
Total	91	33	75	42	65.00	61.37	10.856

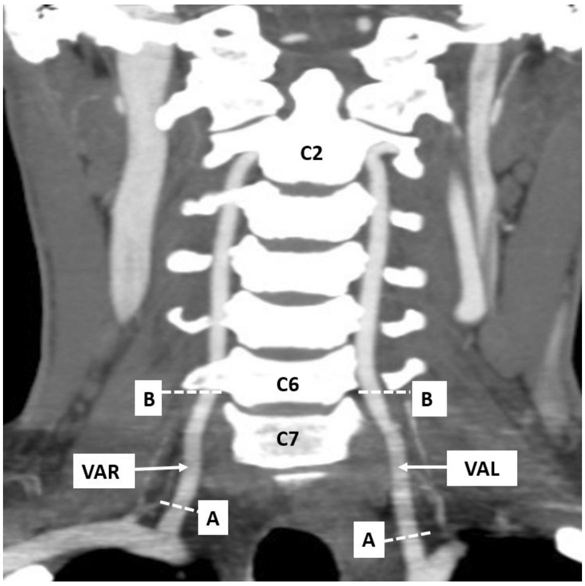

Figure 1. Locations of diameters measurements at inferior (A) and middle points (B); VAL — left vertebral artery; VAR — right vertebral artery; male, 38 years; computed tomography angiography; maximum intensity projection.

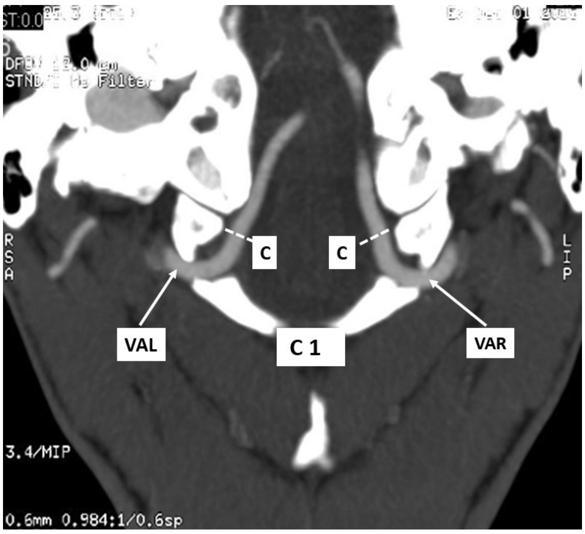

Figure 2. Location of diameter measurements at superior (C) point; VAL — left vertebral artery; VAR — right vertebral artery; male, 38 years; computed tomography angiography; maximum intensity projection.

Statistical analysis

In addition to standard demographic statistics (mean, median, range, standard deviation), obtained diameters and observed differences of mean values were tested with Wilcoxon test for the differences between different ipsilateral levels and with Mann-Whitney U test for the differences between corresponding levels of both sides (left-right) and between the sexes for each of measured locations (Tables 1–5).

RESULTS

Initial step was the evaluation of diameters of VA obtained for the total sample. In the inferior point A, 51 subjects had larger diameter of left VA (mean 3.7659 mm), 38 had larger diameter of right VA (mean 3.6341 mm), and 2 subjects had equal diameters on both sides. With the Wilcoxon test was not found statistically significant difference ($z = -1.263$, $p = 0.207$, $r = 0.132$) between diameters of left and right VA measured in inferior point A. At middle point B, 50 subjects had larger diameter of left VA (mean 3.5066), 37 had larger diameter of right VA (3.3187 mm), and in 4 subjects diameters of left and right VA were equal. The Wilcoxon test did not show a statistically significant difference ($z = -1.523$, $p = 0.128$, $r = 0.16$) in diameters of left and right VA measured in point B. At superior point C, 49 subjects had larger diameter of left VA (mean 3.2121 mm), 38 subjects had larger diameter of right VA (mean 3.089 mm), and in 4 subjects diameters of left and right VA were equal. The Wilcoxon test did not show a statistically significant difference ($z = -1.207$, $p = 0.227$, $r = 0.127$) in diameters of left and right VA measured in the superior point C. So, in general, more subjects in total sample had larger diameters of left VA, albeit without statistical significance, and we can conclude that the diameters of VA pooled for both sexes showed no left-right differences in any of three measured points.

In order to enable the comparisons with the results from the literature, the mean diameters of the total sample are presented in Tables 2 and 3, following by tables showing more detailed presentations of our results.

Table 2. Right vertebral artery (VA) diameters (total sample)

Right VA	Inferior point (A)	Middle point (B)	Superior point (C)
Number	91	91	91
Minimum	1.90	1.40	1.40
Maximum	5.20	4.50	4.90
Range	3.30	3.10	3.50
Median	3.7000	3.3000	3.1000
Mean	**3.6341**	**3.3187**	**3.0890**
Standard deviation	0.77046	0.66448	0.66857

Table 3. Left vertebral artery (VA) diameters (total sample)

Left VA	Inferior point (A)	Middle point (B)	Superior point (C)
Number	91	91	91
Minimum	2.10	1.90	1.70
Maximum	5.90	5.70	5.00
Range	3.80	3.80	3.30
Median	3.9000	3.5000	3.2000
Mean	**3.7659**	**3.5066**	**3.2121**
Standard deviation	0.73910	0.68424	0.64702

Table 4. Sex differences in right vertebral artery (VA) diameters

Right VA	Gender		
	Male	**Female**	**Total**
Point A			
Number	47	44	91
Minimum	2.10	1.90	1.90
Maximum	5.20	4.90	5.20
Range	3.10	3.00	3.30
Median	3.8000	3.4500	3.7000
Mean	**3.7574**	**3.5023**	**3.6341**
SD	0.81234	0.70858	0.77046
Point B			
Number	47	44	91
Minimum	1.90	1.40	1.40
Maximum	4.50	4.40	4.50
Range	2.60	3.00	3.10
Median	3.5000	3.2000	3.3000
Mean*	**3.4468**	**3.1818**	**3.3187**
SD	0.67786	0.62887	0.66448
Point C			
Number	47	44	91
Minimum	1.80	1.40	1.40
Maximum	4.90	4.20	4.90
Range	3.10	2.80	3.50
Median	3.3000	3.0000	3.1000
Mean**	**3.2787**	**2.8864**	**3.0890**
SD	0.68745	0.59046	0.66857

SD — standard deviation; *statistically significant difference; **statistically highly significant differences

Table 5. Sex differences in left vertebral artery (VA) diameters

Left VA	Gender		
	Male	**Female**	**Total**
Point A			
Number	47	44	91
Minimum	2.10	2.20	2.10
Maximum	5.90	5.00	5.90
Range	3.80	2.80	3.80
Median	4.0000	3.7500	3.9000
Mean	**3.8957**	**3.6273**	**3.7659**
SD	0.79152	0.65959	0.73910
Point B			
Number	47	44	91
Minimum	1.90	2.40	1.90
Maximum	5.70	4.50	5.70
Range	3.80	2.10	3.80
Median	3.8000	3.3500	3.5000
Mean*	**3.6660**	**3.3364**	**3.5066**
SD	0.75305	0.56201	0.68424
Point C			
Number	47	44	91
Minimum	1.70	1.70	1.70
Maximum	5.00	4.10	5.00
Range	3.30	2.40	3.30
Median	3.6000	2.9000	3.2000
Mean**	**3.3957**	**3.0159**	**3.2121**
SD	0.69281	0.53524	0.64702

SD — standard deviation; *statistically significant difference; **statistically highly significant differences

The Wilcoxon test showed statistically highly significant differences in diameters of right VA between points A and B ($z = -7.141$, $p = 0.000$, $r = 0.749$), between A and C ($z = -7.836$, $p = 0.000$, $r = 0.821$), and between B and C ($z = -6.361$, $p = 0.000$, $r = 0.667$).

The Wilcoxon test showed statistically highly significant differences in diameters of left VA between points A and B ($z = -6.436$, $p = 0.000$, $r = 0.675$), between A and C ($z = -8.022$, $p = 0.000$, $r = 0.841$), and between A and C ($z = -6.702$, $p = 0.000$, $r = 0.703$).

Results of VA diameter measurements and their comparisons between males and females are presented in Table 4 for right VA, and in Table 5 for left VA.

The Mann-Whitney U test showed statistically non-significant differences in diameters of right VA measured in point A (U = 820.500, z = –1.698, p = 0.089, r = 0.178) between males (N = 47, Md = 3.80) and females (N = 44, Md = 3.45). However, statistically significant difference (*) was found in diameters of right VA measured in point B (U = 765.000, z = –2.140, p = 0.032, r = 0.224) between males (N = 47, Md = 3.50) and females (N = 44, Md = 3.20), and statistically highly significant (**) differences in point C (U = 668.500, z = –2.909, p = 0.004, r = 0.305) between males (N = 47, Md = 3.30) and females (N = 44, Md = 3.00).

The Mann-Whitney U test showed statistically non-significant differences in diameters of left VA measured in point A (U = 812.000, z = –1.765, p = 0.078, r = 0.185) between males (N = 47, Md = 4.00) and females (N = 44, Md = 3.75). However, statistically significant (*) difference was found in diameters of left VA measured in point B (U = 729.000, z = –2.426, p = 0.015, r = 0.254) between males (N = 47, Md = 3.80) and females (N = 44, Md = 3.35), and statistically highly significant (**) differences measured in point C (U = 648.000, z = –3.072, p = 0.002, r = 0.322) between males (N = 47, Md = 3.60) and females (N = 44, Md = 2.90).

We did not find significant intrasex (both in males and in females) left-right differences in mean values of VA diameters for all three investigated levels.

DISCUSSION

First, it should be noted that considering the results for VA diameters, it is more appropriate to use the term "diameter" rather than the sometimes used term "dominance", later being directly related more to flow and other dynamic parameters. The importance of VA diameters illustrate the statements that only the diameter of the VA remained as an independent predictor of moderate to severe basilar artery curvature in the full multivariate model [4], and that the studies which do not account for increases in arterial diameter may severely underestimate cerebral blood flow responses, and therefore limit insight into the contribution of conduit arteries to cerebral blood flow regulation [7]. In some endovascular interventions on VA is also necessary to know if dissected VA is dominant side [14]. Also, the end-diastolic velocity revealed the greatest dependence on diameter asymmetry and was the most vulnerable flow parameter to side-to-side diameter asymmetry [21]. Important is to note that the diameter of the VA is moderately genetically determined, but the role of unique environment remains also important [23].

Relatively small magnitude of VA diameter in humans (in comparison to internal carotid) necessitates greater precision of method used and the results on living subjects usually were obtained by ultrasonography, CT and MRI angiography, as well as digital subtraction angiography. Hence, meta-analysis of these measurements requires comparisons of the different methods [3], which are generally lacking, except of finding that colour duplex ultrasonography and phasic contrast MRI in measurement of cerebral blood flow are nearly equal [8].

In the total sample we found a progressive decrease in VA diameters in ascending direction, what is generally expected for the arteries having collateral branches in related segments. Smaller diameters on higher levels could be related to more or less abundant branches from different parts of VA. So, region of the root of neck supplied by V1 is also supplied by the numerous branches of SCA, while V3 related structures have more extensive supply mainly from VA collaterals [19].

Generally variable in number on different levels [16], VA branches from V2 and V3 parts are supplying posterior neck muscles, vertebrae, spinal cord and roots, and can be abundant and numerous [16, 19, 25]. The V3 part located in the suboccipital triangle has main muscular branch, the suboccipital artery of Salmon, which supplies the suboccipital muscles, but this artery was present in 48% of subjects, bilaterally in 37.1% [10]. It is obvious that the presence or absence of this artery of relative considerably luminal diameter (mean 1.71 mm) and the presence or absence of its anastomoses can be related to measured diameters of its parent VA. Anterior branches of VA were observed at C-3 in all V2 specimens, as well as anterior (central) spinal artery, while the posterior spinal artery was most frequently detected at C-3 (60%) as well as the lateral branches [16]. The VA branches encountered at the C1–2 level were most likely to be muscular, branches at C2–3 osseous, and those at C3–6 radicular (hence of smaller calibre). The greatest concentration of branches per level was found arising from the V2 segment at C2–3 [25]. Hence, the largest branches of the VA originated from upper parts of its V2 segment (C2–3) or from its V3 segment [25] contributing to obtained differences in diameters at upper levels of VA.

Generally, the absolute reported values of left V2 diameters (ultrasonography and MRI) were in the range from 2.39 to 3.72 mm, and of right V2 from 3.23 to 3.42 mm [5, 13, 15]. Our results of mean values in the total sample measured by CT angiography are within these ranges for V1 part (point A — mean left 3.7 mm; right 3.6 mm; point B — mean left 3.5 mm; right 3.3 mm), and for point C or V3 part (mean — left 3.2; right 3.08 mm), with larger, but not significantly, diameters on the left side. Detailed analysis of the reported diameters of VA shows that the available data are not consistent and can be partially related to method used. For example, on CT angiography diameter of left V4 part of VA was significantly larger [4], or left V2 part was usually dominant [22]. On digital subtraction angiography left-right difference in diameters of V3 part was not significant [24], as well as of V2 part on ultrasonography [13]. On ultrasonography left VA was dominant in 57% of subjects, or diameter of right V2 tended to be lower [21], and there was not significant relation between left and right VA on contrast angiography [1]. Only one comparative study showed that cerebral blood flow velocity measured (V3 part — between C2 and C4) with PC-MRI was lower than with colour Doppler ultrasonography (CDUS). However, significant differences were observed only in results for the left between diameters obtained by MRI (3.3 mm) and by CDUS (3.2 mm), and between the right V3 diameters by MRI (2.8 mm) and by CDUS (2.9 mm) [8]. Generally, in almost all of available studies [4, 5, 13, 21, 22], there were significantly or slightly larger (as in our study) left sided diameters of VA, and in few reports left-right difference was not significant [13, 24]. The finding that, because of high interindividual variability, side-to-side flow differences were not statistically significant [21] was confirmed in our total sample where large inter-individual variability did not allowed presence of significant right-left differences in diameters.

In addition, inconsistent histological measurements on different ethnic populations, at different levels and influenced by processing methods (fixation, staining) causing shrinkage of specimens, resulted in lower values than ours (left 2.74 mm; right 2.64 mm) [18, 20], with the tendency to be comparable to ours, with left sided "dominance" [18, 20]. However, in the available literature there was no study systematically comparing diameters at different and corresponding levels of VA, as we did here.

There were even less available data about sex differences in VA diameters. Even if present, these data are usually not systematically obtained including often not precisely defined levels. In inferior point A, we did not find significant differences between males and females in VA diameters, probably because this point is before origin of larger branches of VA. In middle point B, sex differences were significant and in third, most superior point C sex differences were highly significant. Significantly smaller V2 diameters in females were found on ultrasonography [5, 21] and on CT angiography [22], and V3 part was found smaller in females by digital subtraction angiography [24], or by ultrasonography [5]. Others, using digital subtraction angiography found in males larger, but not significantly, V2 part [24] or did not find sex differences by angiography [1]. Significant sex differences we found for terminal part of V1, and highly significant sex differences for terminal part of V3 segment of VA. In one study involving western Balkans population (by MRI angiography), it was found that in most superior parts diameters of right VA were 2.43 mm, of left 2.83 mm, but in 46% of investigated subjects left and right VA were approximately the same [11]. Ultrasonographic study (V2 part — between C6 and C5) from Croatia reported wider left VA in both sexes, and statistically significantly smaller mean diameters of both VA in females (left 3.55 mm, right 3.30 mm) than in males (left 3.63 mm, right 3.48 mm). However 64% of subjects had dominant left VA [9]. In other ultrasonographic study of V2 also from Croatia (between C5 and C6), left VA was significantly wider in both sexes, and was dominant in 64% subjects [12]. The sub-occipital artery of Salmon supplied the obliquus capitis inferior, semispinalis capitis, and splenius capitis muscles, and in its absence they were vascularised by occipital artery [10]. This fact can be related to findings of significant gender differences in posterior neck muscles on C3 vertebral level (but not when muscle size was normalised for body weight), and to highly significant gender differences in all linear dimensions of these muscles [17].

The patterns of progressively increasing differences, ranging from no differences (inferior point A), trough significant (middle point B), to highly significant differences (superior point C), for ipsilateral diameters (both on the left and right sides), as well as for sex differences could be mutually corresponding. We cannot completely explain this, especially highly significant differences for the highest point C. These findings of consistent pattern of diameter decrease support the suggestion that although seemingly diverse in their distribution, the branches of the V2 and V3 parts of the VA may follow a certain consistent arrangement [25]. However, such regular and linear decreases cannot be completely explained by correspondingly "regular" anatomy of cervical collaterals.

Age range in our study could not be the factor influencing the results, because diameters of VA, as well as flow volumes, did not change with age [1, 5, 9, 15, 21], possibly, at least in part, relating to the absence of age changes in size of posterior neck muscles [17]. Also, the thickness of VA intima-media complex was not significantly different on the left and right side of V1 [6], and hence could not, even indirectly, influence our results, even if VA tunica intima was more thickened on the right side [20].

CONCLUSIONS

Generally, the craniocervical transition region has variable vascular anatomy what can be, at least in part, related to highly significant differences of diameters we found for upper regions of VA. According to our findings we strongly suggest to include in designs of morphometric studies of VA diameters only analysis separate data for sex and the use of defined standard levels.

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