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Running head: Vertebral artery origin and entrance level

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Abstract
Vertebral artery (VA), the main element of the posterior brain circulation, has many anatomical variations which generally were widely investigated. However, available data vary in wide ranges, reflecting very different sample sizes, lack of data about left-right or sex differences, and about possible ethnic, regionally specific or genetic differences. Certain new findings suggest possible involvement of some environmental factors in VA variations. Accurate anatomical data about VA variations in different regions of the world, including Balkans countries, are still lacking. Therefore we investigated morphological variability of VA origin and its entrance level into cervical transverse foramina in population of Republika Srpska (Bosnia and Herzegovina), including data about the sex and side. Anatomy of VA was investigated in 112 persons (224
arteries) of both sexes (58 males, 54 females; age 19 - 83 years), using 64-slice CT scanner. Origin of VA from subclavian artery (SCA) we found in 95.08% of arteries (52 males, 49 females). Only in one male (0.45 %) left VA and left SCA had an specific origin from aortic arch (AA), which we named as an „common area of origin”. All other observed variations in origin were only of left VA, originating from AA in 4.47 % (5 males, 5 females). Left VA Most often (usual) entrance level into transverse foramen we found at C6 (87.5%), followed by C5 (8.93 %), C4 (3.12 %), and in one case at level C7 (0.45 %). Entry levels at C5 both, on right and on the left side, were 3 times more frequent in males than in females. Wide ranges of differences between the data we obtained on a sample in Republika Srpska (Bosnia and Herzegovina) and the data from many other studies require further and wider investigations.

**Key words:** vertebral artery, anatomy, variations, origin, level, transverse foramina

**INTRODUCTION**

Vertebral artery (VA), an important element of the anatomy of the craniocervical transition region and the basic contribute to the posterior brain circulation, most often originates from the first part of the subclavian artery (SCA). Anatomical variations of VA, both, of its origin and of its level of entrance into transverse foramen, were widely investigated and some general information were published even in the standard atlases, textbooks, and on Internet [3]. Also, there are a variety of published reports about very rare and unusual variations of VA with embryological explanations [9,13], as recent, exhaustive and competent reviews [20,22], as well as about consequences in diagnostic and interventional radiology, neck surgery or orthopedics [5,13,14]. Relatively recent significant findings of differences in incidence of VA variations between the persons born in Southern Australia and in persons who were immigrants in the same region, raised even the question of influence of some environmental factors [2].

However, the published data are actually insufficient because of their extensive variability, probably reflecting very different sample sizes, methods (dissections or imaging), vague reports (percentages of cases or of arteries), ages, lack of possible ethnic or genetic specified data and the lack of data about side (left vs. right) or gender [3, 4]. The heterogeneity in results about VA anatomy is in sharp contrast to the high precision of recent imaging methods.
The use of evidence based anatomy concept increases the potential of study the associations between anatomy and variables such as race and gender, and to form conclusions not possible from single studies with small sample sizes [6].

In addition, specific anatomical data about VA variations for populations in different geographical regions of the world are still insufficient, as well as more sophisticated analysis of such data. With the exception of few papers [21, 22], there is a lack of original data available for regions of Balkans. Therefore in population of Republika Srpska (north-western regions of Bosnia and Herzegovina) we investigated morphological variability of VA origin and its entrance level into cervical transverse foramina.

**METHODS**

We investigated VA anatomy in 112 persons (224 VA) of both sexes (58 males and 54 females) and of age between 19 and 83 years (Table 1). From the study were excluded the patients with previous or current cerebrovascular accidents, with the history of cervical injuries, vertebrobasilar insufficiency, atherosclerotic changes (affecting more than 50% of VA diameter), with developmental abnormalities of cervical spine and with severe spondiloarthrosis. Data were collected and stored in accord to Helsinki Declaration [24] with additional verbal informed consent obtained from the all subjects.

Imaging- generation and visualization

All measurements were performed in Clinical Radiology Department, University Clinical Center 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 x 0.625 mm, gantry rotation time 0.4s, section thickness of 0.625 mm, pitch 0.969:1 and reconstruction interval of 0.625 mm. During the procedure, infused 80 mL of nonionic iodinated contrast was followed by 40 mL saline and injected via a double power injector into the patient’s antecubital vein (4 mL/s).
Postprocessing of source images was performed by using a multi-planar reformation (MPR), maximum intensity projection (MIP), multiplanar reconstruction (MPR) and volume rendering (VR) algorithms.

Investigated were origin of the VA and its level of entrance into vertebral transverse foramen with notification of the sex and side of variation.

In order to enable more simplified comparisons [6] with the results of other authors which used different presentations, our results were presented as numbers of subjects, i.e. „cases“ (Tables 1, 2 and 4), or as percentages of VAs (Tables 3 and 4).

RESULTS

All, but except of only one, of observed variations of origin of VA were variations of left VA, arising from AA (Fig. 1). Generally we did not found the sex differences in the variability of such origin of VA.

However, there was one interesting specific case of male, where left VA and left SCA arise from an specific slightly widened region of AA, for which we propose the term „common area of origin” (Fig 2).

In the total sample the entry site of VA into transverse foramina (beginning of V2 segment) was most often -in 87.5% of VAs- at the level C6 (variable were 28 or 12.5% of total 224 levels), followed by transverse foramina C5 (8.93%), and C4 (3.12 %). Entering at C7 level was only one left VA of male (0.45 %). Level of C5 on both sides in males was most often variation of entry level we found (Table 4.) Also, entry levels C5, both on right and on the left side were 3 times more frequent in males than in females.

In one case there were bilateral aberrant but different levels of entrance, of right VA at C4 and of left VA at C5 level (Fig. 4).

DISCUSSION

Origin of VA often exhibits different variations as result of the disordered embryonal development of the AA branches [13,20,22]. So, our finding of usual VA origin from SCA in 87.5 % is different from 96.2% found on 3D angiographies of 79 vertebral arteries [19]. Generally, variable origins we found only for left VA, with origin from AA found in 4.47 %, what is close to the finding of 3.8% [19]. In an early and exhaustive investigation in Japan (516
cadavers; 404 male and 112 female) origin only of left VA from AA was found in 5.4% of arteries [1], what is not so different from our finding. In relatively recent literature origin of the left VA from AA was reported in a range of 3.1%–8.3% [15, 17, 19]. Using the same method as we did, but on larger sample (2,287 patients), origin of left VA from aorta, between left common carotid artery and left SCA, was found in 4.1% of cases, with the total prevalence of variation in the origin of left VA (6%) [23]. In 40 cadavers left VA originated directly from AA in 7.5% and there was a common stem of left VA and of left SCA from AA in 2.5% [18]. In south Australian sample (81 cadaver of European descent) origin of left VA directly from AA was in subgroup born in South Australia much higher (13.9%) than overall incidence (7.4%) of the whole group (migrated and born) indicating possibility of influence of some environmental factors [2]. The origin of right VA from AA or some of its other variations we did not find in our sample of 112 persons (224 VAs).

In one case (0.45%) we found an slightly widened „common area of origin“ of left VA and of left SCA, without apparent potential pathological features (Fig. 2). This corresponds to the reports of left VA origin as branch from the root of left SCA close to the AA [10] or of left VA „in touch” with left SCA [11]. This form of very close origin of VA and SCA by one specific common widening of AA we consider as not properly described in previous literature as an separate entity. This requires a more careful analysis of the originating region, in terms of one common or two separate openings of related vessels or of blood flow patterns in this region.

Sites of entry of VA into transverse foramina may be variable, usually higher or, rarely, lower (C7) than C6, and very different percentages were reported, based on different methods, different samples (639 cases) without data about side and sex [3], or with data about side (500 VAs–48.6% right sided, 51.4% left sided and 9.2% bilateral abnormalities), but without specification of sex, [4,5]. We found usual C6 entrance level in 87.5% of arteries, what is different from 92%[12], 94.9% (700 VAs on CT) [7] or of left VA at C6 in 93% (2.287 patients) [23]. In our relatively large sample we identified only one VA entering C7 foramen (0.5%), what is similar to 0.8% [4], different from 3% [5], and remarkably different of finding (sample 50 VAs), that VA entered C7 transverse foramina in 8% of cases [12].

In cases when the left VA originates from AA, its entry into transverse foramen is usually more superior (C5 ili C4) than usually, with larger possibility of the compression and decreased flow with the ischemia in posterior cerebral circulation [8,16]. Such cases are also important in
transpedicular fixation or other spinal surgeries with higher risk of iatrogenic vascular injury during anterior cervical surgery and can be detected on preoperative imaging [7,10,12]. In 3 cases (of 79 angiographic images) when VA originated from AA, one of them was entering C7, other entered C6 and third was entering C5 [19]. In cited study [19], from remaining 76 VAs originating from the SCA, 67 (vast majority) were entering C6, as much as 6 VAs enetered C7, 2 VAs entered C5 and one VA C4 transverse foramen [19]. In above cited study from Japan, but on 500 cadavers [1], C7 entrance level of VA was found for 12 arteries, C5 for 45 and C4 entrance level for 7 VAs. Our finding of 87.5% of usual VA entrance through C6, is nearly identical with findings of 88% [3] or 89.8% cases. [7]. However, the differences between our results and of dissection studies from India [18] or of CT angiographic studies from South Korea [7], could be explained by sample sizes and structure, regional, sex or ethnic differences. So, the entrance level of VA through C5 we found in 8.93%, comparing to 5% in Indian [18] or to only 3.3% in South Korean studies [7]), C4 we found in 3.12%, comparing to 5% in India [18] or only 1.6% in South Korea [7]). Large difference was between our finding for C7 level as 0.45%, and of 5% of arteries [18], but with small difference to South Korean 0.3% [8]. Comparison of specific levels between cited studies revealed nearly equal results for some levels [18,7] in spite of different methods (dissection versus CT angiography) or geographical region, and both of them were different from our results. However, results for C7 level, were surprisingly very different between the same two studies, with the results of study from South Korea [7] practically same as ours. Therefore, here can not be concluded about generally present differences, but only for some levels of VA entrance. This illustrates potential very high heterogeneity among the studies, found in anatomical meta-analyses [6]. Additionally, our finding of 3 times more frequent C5 entry level of VA in males than in females strongly suggest impact of sex differences to these results. Our contribution, except providing clinicians with precise anatomical data, should also enable better subsequent analysis by advanced methods (meta-analysis and systematic review) of evidence based anatomy.

CONCLUSIONS

The need for more detailed studies in some specific cases of VA variations is indicated by our finding of AA „common area of origin“ for left VA and left SCA. According to our results is interesting to note the C5 entrance level, both as most often variable entrance level, and
as well as an variation which is three times more often in males than in females. In conclusion, our results and results of numerous other studies is difficult to compare due to very variable sample structures and sizes, different modalities used in studies, different ways of data presentations, potential regional, ethnic, or even environmental differences. Very precise design of these studies is therefore crucial for serious and fruitful analysis of VA variations of origin and of its entrance level into cervical transverse foramina.

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**Figure 1.** Origin of left VA from aortic arch - AA. (LV - left vertebral artery, LSCA - left subclavian artery; CT angiography - MIP; female, 77 years).
**Figure 2.** “Common area of origin” (1) of left subclavian artery (SCA) and of left vertebral artery (2), both arising from specific widened region of aortic arch (AA) (brachiocephalic trunk- BT; CT angiography - MIP; male, 62 years).

**Figure 3.** Left VA (LVA) arises from aortic arch and enters cervical transverse foramen- C7 (CT angiography- MIP; male, 43 years).

**Figure 4.** Bilateral variations of the vertebral artery entry level into cervical transverse foramina: left VA - C5 and right VA - C4 (CT angiography - MIP; male, 64 years).
### Table I. Demographic data of investigated sample (112 subjects - 224 arteries)

<table>
<thead>
<tr>
<th>Gender</th>
<th>N</th>
<th>X mean (years)</th>
<th>Std. Dev.</th>
<th>Max.</th>
<th>Min.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males</td>
<td>58</td>
<td>66.5172</td>
<td>10.56017</td>
<td>83.00</td>
<td>35.00</td>
</tr>
<tr>
<td>Females</td>
<td>54</td>
<td>60.7037</td>
<td>14.84972</td>
<td>81.00</td>
<td>19.00</td>
</tr>
<tr>
<td>Total</td>
<td>112</td>
<td>63.7143</td>
<td>13.07940</td>
<td>83.00</td>
<td>19.00</td>
</tr>
</tbody>
</table>

### Table II. Variability of origin of vertebral artery (VA) (112 subjects; 224 VA)

<table>
<thead>
<tr>
<th>Origin of VA</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCA (usual)</td>
<td>52</td>
<td>49</td>
<td>101</td>
</tr>
<tr>
<td>Left AV from AA</td>
<td>5</td>
<td>5</td>
<td>10</td>
</tr>
<tr>
<td>„Common area of origin“ of left VA and left SCA from AA</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Total</td>
<td>58</td>
<td>54</td>
<td>112</td>
</tr>
</tbody>
</table>

AA — aortic arch; SCA — subclavian artery

### Table III. Variability of origin of vertebral artery (VA) in percentages (112 subjects; 224 VA)

<table>
<thead>
<tr>
<th>Origin of VA</th>
<th>Percentages (of all arteries)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCA (standard )</td>
<td>95.08%</td>
</tr>
<tr>
<td>Left VA from AA</td>
<td>4.47%</td>
</tr>
<tr>
<td>„Common area of origin“ of left VA and left SCA from AA</td>
<td>0.45%</td>
</tr>
<tr>
<td>Total</td>
<td>100%</td>
</tr>
</tbody>
</table>
AA — aortic arch; SCA — subclavian artery

**Table IV.** Variations of the entry level into transverse foramina of cervical vertebra (112 subjects; 224 arteries)

<table>
<thead>
<tr>
<th>Variability of entrance level of VA into transverse foramen</th>
<th>Males</th>
<th>Females</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>VA Right</td>
<td>Left</td>
<td>Right</td>
<td>Left</td>
</tr>
<tr>
<td>Level C4</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Level C5</td>
<td>9</td>
<td>6</td>
<td>3</td>
</tr>
<tr>
<td>Level C7</td>
<td>0</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>Total of variable levels</td>
<td>11</td>
<td>7</td>
<td>5</td>
</tr>
</tbody>
</table>

VA — vertebral artery