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Internal carotid and vertebral arteries diameters and their interrelationships to sex and left/right side

Running head: Left-right and sex differences in calibers of internal carotid and vertebral arteries

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Abstract

The available anatomical data about diameters of inflow vessels to the circle of Willis (COW) reflect various diagnostic and imaging methods used, sample sizes, levels of measurements, and lack of possible specific ethnic, regional or genetic data. Additionally, the data are often without
distinctions about left- right or sex. Therefore, using CT angiography (CTA) we investigated diameters of internal carotid (ICA) and vertebral (VA) arteries in 70 adult persons (28 - 75 years) of both sexes (34 males and 36 females), at predefined cervical parts of ICA (2 cm above carotid bifurcation) and of VA (5 mm before VA penetrated the dura). Sex differences were expressed as highly significant larger diameters of left VA (LVA) in males (3.49 mm) than in females (3.00 mm), and as significantly larger diameters of right VA (RVA) in males (3.20 mm) than in females (2.82 mm), as well as of right ICA (RICA) diameters in males (5.04 mm) than in females (4.56 mm), but without such difference for left ICA (LICA) between males (4.82 mm) and females (4.60 mm). Intrasex (in males or in females) left- right differences of ICA and VA diameters were not significant. Significant positive correlations were found in females between RICA and RVA, and in males between RICA and LICA. Calculated mean sum of ipsilateral diameters of right arteries (RAA= RICA + RVA) was in males 8.25 mm, in females 7.38 mm, and of left arteries (LAA= LICA + LVA) was in males 8.31, and in females 7.60 mm, without statistically significant difference between right (RAA) and left arteries (LAA), neither in males, nor in females. Statistically highly significant larger sums of diameters were in males than in females for both, right (RAA) and left (LAA) arteries. Our findings, as the first data about diameters of ICA and VA systematically obtained by CTA in the population of western Balkans, suggest that in the studies of these diameters is absolutely necessary to analyze separately the data for sex, and to use defined standard levels.

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

INTRODUCTION

In normal circumstances both, internal carotid arteries- ICAs (“anterior circulation”) and vertebral arteries -VAs (“posterior circulation”), completely deliver the blood to the circle of Willis (COW) providing the inflow to the brain. The data about arterial luminal diameters are one of important underlying factors for understanding the hemodynamics of other factors (such as anatomical data, pulses, end-diastolic and peak velocities, total blood flow, etc.). In spite of existence of these multiple factors, in large studies allways is discussed only the degree of stenosis – „only size (diameter) does matter“ [20]. However, stenosis of any of the brain-
supplying arteries (including VA), triggers an increase in blood flow in all available vessels that can supply the brain. The importance of compensatory mechanisms is strongly supported by the increased intracerebral blood flow in patients with ICA obstruction [9]. In patients with impaired collateral system the prognosis of ischemic stroke is worse [41], and in patients with unilateral ICA occlusion, the presence of collateral flow in COW is associated with a low prevalence of border zone infarcts [11]. Hence, the data about arterial diameters can help in understanding of interrelationships between the contralateral or ipsilateral ICA and VA, in the normal and impaired blood supply of the brain. This can be important in considering endarterectomy in cases of asymptomatic 60–79% ICA stenosis which cannot be justified for these patients, for which predominate indications for conservative therapy and presence of collateral circulation is an argument for the initiation of conservative treatment [9], [21], [25]. The potential of the tributaries of COW as collateral pathways [24] could be related to their diameters. Knowledge of the expected normal vessel flows incorporating patient-specific age and accounting for anatomy, is critical to interpreting the hemodynamic effects of cerebrovascular disease [1]. The data about variability of COW are available worldwide (see for example [8], [11], [16], [38], [40]), including regions of Balkans [4], [32], [36], but the data about the diameters of proximal vessels of COW, potentially associated with different specific patterns of normal inflow are not yet known.

The aim of this study is to investigate the luminal diameters of ICA and VA as feeding vessels to COW, and to analyse the relationships and potential side (right-left) and sex differences between their diameters in the population of Republika Srpska (western part of Bosnia and Herzegovina). Also we calculated sums of diameters of ipsilateral ICA and VA, as ipsilateral vessels delivering the blood to the COW and further to the brain.

MATERIAL AND METHODS

We investigated luminal diameters of ICA and VA in 70 subjects (140 ICAs and 140 VAs) of both sexes (34 males and 36 females) and between 28 and 75 years of age (Table I). From the study were excluded the patients with previous or current cerebrovascular accidents or impairment, with the history of cervical injuries, vertebrobasilar insufficiency, abnormal morphology of ICA i VA (variations of origin, kinking and coiling), atherosclerotic changes (affecting more than of 50% of arterial luminal diameter), developmental abnormalities of
cervical spine and with severe spondylarthrosis, as well as patients who did not provided consent to be included into this study. Data were collected and stored in accord to Helsinki Declaration [39] with additional verbal informed consent obtained from the all subjects. Places for computed angiography (CTA) measurements of ICA diameters were about 2 cm distally from the common carotid artery bifurcation, in order to exclude influence of carotid sinus size in region of common carotid artery (CCA) bifurcation. Diameters of VA were measured at atlantic (V3) segment of VA (5 mm before entrance into dural porion of VA), in order to exclude the potential influence of variable collateral branches anatomy from V2 segment [30].

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 maximum intensity projection (MIP) and evaluation and measurements of CTA dataset were performed on 3 mm thick coronal sections.

Statistics

After demographic statistics (Table I) results for each single vessel were analyzed (including the sums of values of ipsilateral diameters - separately for right and for left arteries). In testing of normal distribution of continuous investigated variables we used Kolmogorov-Smirnov test. If the sample had normal distribution we applied parametric T tests (Independent samples test for differences between the sexes and Paired samples test for intrasex differences). If the sample deviated from the normal distribution we used nonparametric tests (Mann-Whitney
U- test for differences between the sexes and Wilcoxon signed ranks test for intrasex differences).

Additionally, we calculated the Spearman's rank correlation coefficients between the RICA and RVA, between the LICA and LVA, as well as between RICA and LICA, and between RVA and LVA, in total sample, and separately in males, and in females. Results were analyzed using statistical software package SPSS (Statistical Product and Service Solutions), version 20.

RESULTS

Demographic statistics of the sample is presented in Table I.

There was not statistically significant difference (Mann-Whitney U test; \( U = 511.500, z = -1.183, p = .237 \)) in age between males and females.

Results of measurements of diameters of right and left vertebral (VA) and internal carotid (ACI) arteries in males and females are presented in Table II.

Internal carotid artery

On the total sample mean luminal diameters of RICA (4.796 mm) and of LICA (4.707 mm) (Table II) were without statistically significant difference (Wilcoxon signed ranks; \( z = -0.404, p = .686 \)). The statistically significant difference (Mann-Whitney U test; \( U = 404.000, z = -2.450, p = .014 \)) was in mean diameters of RICA between males and females, but not (\( U = 479.500, z = -1.560, p = .119 \)) for diameter of LICA between males and females.

Vertebral artery

In the total sample there was not statistically significant difference (Wilcoxon signed ranks test; \( z = -1.946, p = .052 \)) of mean arterial diameters between RVA (3.10 mm) and LVA (3.246 mm) (Table II). However, LVA in males had highly significantly (Mann-Whitney U test; \( U = 335.000, z = -3.263, p = .001 \)) larger diameters than in females, and RVA in males had significantly larger (\( U = 403.000, z = -2.460, p = .014 \)) diameters than in females.

Correlations

In total sample highly significant positive correlations were between diameters of RVA and RICA (\( r= 0.371, n=70, p<0.01 \)), and between RICA and LICA (\( r= 0.327, n=70, p<0.01 \)).
Significant positive correlations were found between right ipsilateral vessels (RICA and RVA) in females ($r=0.375, n =36 , p<0.05$), and between contralateral anterior vessels (RICA and LICA) in males ($r = 0.346, n= 34, p<0.05$). Other investigated relationships did not show significant correlations.

**Sum of ipsilateral diameters (total diameters on one side)**

Calculated sums of diameters of right (RAA= RICA + RVA) and left arteries (LAA= LICA + LVA) are presented in Table III.

In a total sample the sums of diameters on left (LAA) and right (RAA) side were without statistically significant difference (Paired samples test; $t = -.919, df = 69, p = .361$), as well as the sums of diameters between right (RAA) and left arteries (LAA), neither in males ($t=- .281, df = 33, p = .780$), nor in females ($t = -1.033, df = 35, p = .309$). However, Independent samples t- test revealed highly statistically significant larger diameters in males than in females for both, the sum of diameters of right arteries (RAA- males 8.25 mm; females 7.38 mm) ($t = -3.109, df = 68, p = .003$), and of left arteries (LAA- males 8.31 mm; females 7.60 mm) ($t = -3.159, df = 68, p = .002$).

**DISCUSSION**

Using CTA we found significantly larger mean diameter of RICA in males (5.05 mm) than in females (4.56 mm), but without such difference for LICA (males 4.82 mm; females 4.60 mm), and without significant intrasex (in males or in females) left- right differences of ICA or VA diameters (Table II). In males the calculated sums of diameters of right (RAA) and of left arteries (LAA) were highly significantly larger than in females. This could explain the greater stroke-protective effect of carotid endarterectomy, and lower rates of complications after surgery, in men. These gender differences may be caused by biological, anatomical (smaller vessel diameter in women) or hormonal differences [31].

Other authors reported mean diameters of cervical ICA close to our results, as 4.6 mm [5], and with statistically significant larger mean diameters of cervical ICA in men (men 0.5 cm; women 0.49 cm) [37], even after adjusting for body and neck size, age, and blood pressure (men 5.11 mm; women 4.66 mm) [18]. In adults was found the correlation among ICA luminal diameter, flow velocities and overweight between the groups with normal (RICA 5.25 mm,
LICA 5.55 mm) and with high body mass index (RICA 5.15 mm, LICA 5.10 mm), but without significant right- left or sex differences for the paired ICAs between the groups [26]. On carotid arteriograms of 25% of patients right- left differences in cervical carotid calibre were of at least 5 %, and normally diameter of ICA on the two sides can vary up to about 40 % [21], with generally wide range of dimensions [37].

The mean diameters of intracavernous portion of ICA before the origin of significant branches (ophthalmic artery) could be used for analysis (RICA 4.1 mm; LICA 4.0 mm [15], or RICA 4.24 mm; LICA 4.32 mm [40]). Intracavernous ICA diameter of 5.0 mm (men 5.1; women 4.9 mm) was without change based on gender or side, but with significantly larger cavernous ICA diameters and tortuosity in patients aged >60 years [27]. Increased tortuosity in nondiseased ICA with increasing age may be related to degradation and fragmentation of intramural elastin [14], and vessel diameters generally increase with age [19]. The CCA diameters can be also indicative, because the close relationship between the diameters of CCA and ICA enables predicting of ICA size [37]. Additionally, increased ICA diameter can be result of malfunction of factors involved in vasoregulation (cerebral autoregulation), leading to disturbed blood flow regulation [26], [12]. Diameters of the cervical ICA can undergo to dynamic transient changes in form of vasospasm [35], and dysregulation in extradural ICA showed laterality and sex dependence, but no significant age dependence [29].

For investigated atlantic (V3) part of VA, the mean diameters found in our previous study [30] for RVA (males 3.27 mm; females 2.88 mm) and for LVA (males 3.39 mm; females 3.01 mm), were practically identical as in current study, because the sample population was same, with the exclusion of few patients having ICA abnormalities. In previous studies [30], [33], also were found in males larger diameters highly significantly of LVA and significantly of RVA, but not significant intrasex left- right differences. Because of the high interindividual variability, the normal range for diameter, peak systolic velocity and VA blood flow is wide in both VAs [24]. Age range of subjects in our study could not influence the results, because diameters, as well as flow volumes of VA, did not change with age [10], [22].

We found significant positive correlations in females between RICA and RVA (ipsilateral right anterior -posterior circulation), and in males between RICA and LICA (anterior bilateral or left- right circulation). The correlation of the diameters of only the right arteries (RICA and RVA) could not be related to their common origin from brachiocephalic trunk (via
right subclavian and from right CCA), because it is found only in females. Highly significant positive correlations found in the total sample between RICA and LICA, and between RICA and RVA, probably reflected specific different values found in males and in females.

Hypothetically, the data about investigated normal diameters could be important in cases of reduced blood flow in one of vessels proximal to COW (smaller diameter of one ICA or VA). Beside the diameters of ICA and VA as potential compensatory pathways, the data about hemodynamics can help in estimation of risk of cerebrovascular ischemia in considering conservative treatment in asymptomatic stenosis of ICA. Possible cerebral cross-perfusion, as essential for ipsilateral brain viability during unilateral insult, is complicated by the wide variability of COW anatomy [23]. The recognition of the impact of the anatomical variants in the COW is critical to the interpretation of flow measured in the proximal intracranial vessels [1]. The circle of Willis (COW) is known from very old times [6], [3], and descriptions of its variations originate even more than 100 years ago [38], but the relationships of ICAs and VAs diameters to its variations are not clear. There are reports about the absence (Iranian male sample) [8], or the presence of significant differences in the variations of COW between the studies and different populations [16], [40]. In Balkans population (Serbia) [36], among 13 morphological types of COW, most frequent prenatally was normal type, and postnatally COW with unilateral hypoplasia of posterior communicating artery (PoCom) with calibers of right parts of the posterior cerebral artery (PCA) and ICA significantly higher in male than in female adults [36]. In corresponding population (Serbia) origins of PoCom were basilar (82,5%), carotid (10,5 %) and mixed (7 %) [4], but the relationships of these variations of COW and of ICA and VA diameters, and their adequacy to flows in different types of COW, are not yet known. Our findings in males of highly significant larger diameters of LVA, significantly larger of RVA, as well as of RICA, but without such difference between males and females for LICA suggest certain impact of different variants of COW on these results.

Underestimating or denying the collateral flows are reports that the anatomical status and variations of COW (eg. incomplete hemicircles) are without apparent disadvantages [23], do not itself determine adequacy [11], and do not correlate with functional and intraoperative tests of cerebral cross-perfusion [34]. Also, asymptomatic patients with an ICA occlusion do not have an increased collateral function of the COW [11], and the presence of asymmetric COW in more
than one fourth of subjects [1], [32] indicates that these configurations represent rather one aspect of its adaptation [32].

However, prevailing evidence supports the existence of collateral or anastomotic flows via COW. Namely, the patients with ICA stenosis and with collateral flow via COW have less impaired hemodynamic parameters than those without such flow [17], and may have a compensatory increase in the peak systolic velocity and the blood flow volume in both VAs [24]. Also, in patients with cervical ICA occlusion, blood flow velocity and volume were increased in contralateral ICA, and in ipsilateral (27.5%), and in contralateral cervical VA (15%), than in controls [24]. On average 92% of the patients without border zone infarcts had willisian collateral flow, as compared with 60% of patients with border zone infarcts [11]. Anatomic variations of PCoA and PCA affected ICA flows, without a significant difference between males and females and continued to impact indexed flows in the basilar artery and ICA [1]. The anterior circle is the preferential mode of collateral supply in patients with unilateral ICA occlusion, [2], [17] and, an even normally larger carotid on one side related constantly with angiographic preponderance of the anterior cerebral artery on that side due to variation of COW [21]. All above findings support an old statement that COW under normal circumstances is not an equalizer and distributor of blood from different sources, but offers a potential shunt under abnormal conditions [28]. In this context our results contribute in estimation what means “abnormal diameters” in COW feeding vessels. In spite of all this complexities, the entire diagnosis of brain-supplying arterial stenosis is currently focused on blood flow assessment, ignoring the fact that vessels forming COW are supplied by either physiological, (ICAs and VAs), or collateral vessels [9].

Our findings of sex differences in diameters of ICA and VA strongly support the suggestion that further research of these differences and their causes is mandatory and promising in order to reduce the risk of stroke and to improve treatment outcome especially for women [9].

CONCLUSIONS

Our findings suggest that the establishment of an simple relationship between the diameters (flows through) of ICA or VA is impossible, and is related to individual patient-specific characteristics. However, there is the possibility to investigate and define potential genetic profiles of patterns of diameters of COW inflow vessels, related to different COW
configurations. The perspective methods for predicting anatomy, including of COW, require complex analysis but are available [7]. Our study provides basic anatomical data which can contribute to diagnostics and treatment of impaired blood supply of the brain via COW, and to the studies of genetic associations or diversities of ICA and VA diameters, and of their relationships in health and disease.

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**Table I.** Demographic data of investigated sample

<table>
<thead>
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<th>Sex</th>
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<th>Max.</th>
<th>Range</th>
<th>Median (Md)</th>
<th>Mean</th>
<th>Std. Dev.</th>
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</thead>
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Table II. Diameters of right and left ICA and VA in males and females (in mm)

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<th>Min.</th>
<th>Max.</th>
<th>Range</th>
<th>Median (Md)</th>
<th>Mean</th>
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<td>3.400</td>
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</table>

RICA – right internal carotid artery; LICA- left internal carotid artery; RVA - right vertebral artery; LVA- left vertebral artery.

Table III. Sums of diameters of ipsilateral ICA and VA

<table>
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<th></th>
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Right arteries: RAA = RICA + RVA; Left arteries: LAA = LICA + LVA

**Figure 1.** Dotted lines indicate the levels of measurements of diameters of ICA (left) and of VA (right); female (33 years).