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**ORIGINAL ARTICLE** **ÖZGÜN ARAŞTIRMA**

# VERTEBRAL ARTER V1 VE V2 SEGMENTLERİNİN ANTERİOR VE POSTERİOR İSKEMİK İNMELİ HASTALARDA ANATOMİK VE MORFOLOJİK İNCELENMESİ

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**ABSTRACT**

INTRODUCTION: The vertebral artery (VA) rarely exhibits anatomical variations regarding its origin, course, and branching pattern. The aim of our study is to examine the morphological variations of the origin and cervical segment of the VA in patients with ischemic stroke originating from anterior and posterior circulation and to emphasize the anatomical, radiological and clinical importance of the results.
METHODS: In this study, three groups were determined, depending on the arteries where the stroke occurred: anterior ischemic stroke (AIS) patients (n=188), posterior ischemic stroke (PIS) patients (n=88) and control group (n=154). The morphometry of V1 and V2 was retrospectively examined in 430 patients and control groups using multi-detector computed tomography angiography and 3D Slicer software.
RESULTS: 95,8% of the left V1s originated from the subclavian artery, and 143 of these arteries were in patients with AIS, 83 in patients with PIS, and 145 in control group. It was observed that the remaining 4.2% of left VAs originated from the aortic arch, and this observation was consistent with the incidence in previous studies. In our study, the frequency of entry level of right VAs into the transverse foramen (TF) was observed as C6 (93.5%), C5 (5.1%) and C4 (1.4%), respectively. The frequency of entry level of left VAs into the TFs is C6 (93.3%), C5 (4.4%), C7 (1.6%), C4 (0.2%), C5-C6 (0.2%) and C7-T1 (0.2%), respectively. Right and left V2 diameters were found to be 3.68 mm and 3.69 mm, respectively. In the current study, right and left dominances were 22.3% and 24.9%, respectively.
DISCUSSION AND CONCLUSION: The information obtained from this study will assist head and neck surgeons and interventional radiologists in understanding the variable anatomy of the VA and thus preventing iatrogenic injuries, especially in the Turkish population.
**Keywords:** Anterior ischemic stroke, posterior ischemic stroke, vertebral artery, V1 segment, V2 segment.

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# ANATOMICAL AND MORPHOLOGICAL EXAMINATION OF VERTEBRAL ARTERY V1 AND V2 SEGMENTS IN PATIENTS WITH ANTERIOR AND POSTERIOR ISCHEMIC STROKE


## ÖZ

GİRİŞ ve AMAÇ: Vertebral arter (VA)'in çıkış yeri, seyri ve dallanma düzeni ile ilgili anatomik varyasyonları nadirdir. Çalışmamızın amacı anterior ve posterior dolaşım kaynaklı iskemik inmeli hastalarda VA'in çıkış yerinin ve servikal bölümünün morfolojik varyasyonlarını inceleyerek elde edilen sonuçların anatomik, radyolojik ve klinik açıdan önemini vurgulamaktır.

YÖNTEM ve GEREÇLER: Bu çalışmada inmenin meydana geldiği arterlere bağlı olarak, anterior iskemik inme (Aİİ) hastaları (n=188), posterior iskemik inme (Pİİ) hastaları (n=88) ve kontrol grubu (n=154) olmak üzere üç grup belirlendi. Multi-dedektörlü bilgisayarlı tomografi anjiyografisi ve 3D Slicer yazılım programı kullanılarak 430 hasta ve kontrol grubunda yer alan bireyde V1 ve V2'nin morfometrisi retrospektif olarak incelendi.

BULGULAR: Çalışmamızda, sol V1'lerin %95,8'i subklavyen arter'den (SKA) köken alırken bu arterlerin 143'ünün Aİİ'li, 83'ünün Pİİ'li hastalarda ve 145'inin kontrol grubunda yer alan kişilerde olduğu gözlemlendi. Sol VA'lerin kalan %4,2'sinin arkus aorta'dan (AA) ayrıldığı görüldü. Çalışmamızda sağ VA'lerin geçmiş oldukları transvers foramen'lerin (TF) sıklığı sırasıyla C6 (%93,5), C5 (%5,1) ve C4 (%1,4) olarak gözlemlenirken sol VA'lerin geçmiş oldukları TF'lerin sıklığı ise sırasıyla C6 (%93,3), C5 (%4,4), C7 (%1,6), C4 (%0,2), C5-C6 (%0,2) ve C7-T1 (%0,2) olarak tespit edildi. Sağ V2 çapı 3,68 ve sol V2 çapı 3,69 mm olarak bulundu. Mevcut çalışmada sağ dominantlık %22,3 ve sol dominantlık %24,9 idi.

TARTIŞMA ve SONUÇ: Bildiğimiz kadarıyla bu, VA'in morfometrik ve anatomik varyasyonları ile anterior ve posterior dolaşım kaynaklı iskemik inme geçiren hastalar arasında bir ilişki olup olmadığını araştıran ilk rapordur. Bu çalışmadan elde edilen bilgiler baş ve boyun cerrahlarına ve girişimsel radyologlara, özellikle Türk toplumunda, VA'in değişken anatomisini anlamada ve böylece iyatrojenik yaralanmaların önlenmesinde yardımcı olacaktır.


**Anahtar Sözcükler:** Anterior iskemik inme, posterior iskemik inme, vertebral arter, V1 segment, V2 segment

## INTRODUCTION

The vertebral artery (VA) arises from the superior-posterior part of the first segment of the subclavian artery (SCA) and is the thickest branch of this artery. The right and left VAs are anatomically divided into 4 segments on either side of the neck: the first part (V1, prevertebral), which originates from the SCA to C6, the second part of the VA (V2, cervical) through the transverse foramen (TF) of C6 to C1, the third part from the TF of C1 to the level of the dura mater of the foramen magnum (FM) (V3, suboccipital), the fourth part (V4, intracranial), which extends from the FM through the cranium to the pontomedullary border (1,2). The VA and its main branches are also called the vertebrobasilar system (VBS), and the main branches of this system provide the posterior circulation of the brain. The anterior circulation is formed by the main branches of the internal carotid artery (3). VAs provide collateral circulation to other parts of the brain via the circulus arteriosus cerebri (Willis polygon) in occlusive vascular diseases where anterior circulation is insufficient (4).

Anatomical variations related to the origin, course, and branching pattern of the VA are rare (5). Failure to recognize abnormal VA can lead to catastrophic complications such as arteriovenous fistulas, pseudoaneurysm, occlusion, VA dissection, cerebral ischemia, and even mortality (6). For example, the prevertebral portion of the VA originating from the arch aorta (AA) is less protected by bone. Therefore, it may be accidentally ruptured during surgery. The upper part of the prevertebral portion of the left VA of AA origin is hidden under the longus colli, a prevertebral muscle. As the left VA of AA origin lacks the protection of the cervical processus transversus (PT), it is practically unsafe when the longus colli is divided during cervical surgery procedures, including anterior cervical decompression and fusion surgery. Damage to the VA may lead to a lack of blood supplying the VBS. This condition may lead to severe neurological disorders, loss of consciousness, and sometimes respiratory and cardiovascular disorders. Therefore, the incidence of such anatomical variations should be considered preoperatively during cervical surgery, AA surgery, and non-invasive vascular procedures (7).

Determination of V1 and V2 segment variations is vital for investigating the etiology of clinical findings, planning endovascular

intervention procedures, and performing cervical nerve blocks. Changes in diameter, blood flow volume, and arterial dominance in the V2 segment may pose a severe risk during any invasive procedure in the cervical region (8). Therefore, determining the incidence of VA variations is critical for surgeons, especially in endovascular vertebroplasty for the treatment of VA stenosis and aneurysms. Variations of the cervical portion of the VA have been shown to have a significant impact on the pathogenesis of severe diseases such as infarctions, arteriovenous malformations, and transient ischemic attacks (9). Moreover, the VA shows an abnormal flow in the cervical section. The craniocervical junction is a hemodynamically and anatomically complex structure with C1 and C2 vertebrae. A better explanation of the morphology of the cervical part of the VA will also provide various approaches to surgeries and will enable more reliable surgeries in this region (10).

Our study aims to examine the morphological variations in the origin and cervical portion of the vertebral artery (VA) in patients with ischemic stroke related to anterior and posterior circulation, emphasizing the anatomical and radiological significance of the obtained results. Furthermore, the aim is to contribute to the surgical reinterpretation of the relevant arterial feeding area using the data obtained.

## METHODS

**Study population:** In our study, 430 patients and control subjects were retrospectively analyzed using multi-detector computed tomography angiography (MDCTA) and 3D Slicer (version 4.10.2) software. MDCTA images were obtained from the database of the Department of Radiology, Istinye University Gaziosmanpasa Hospital, dated between January 2018 and January 2023. A total of 186 (43.3%) female and 244 (56.7%) male patients were included in the anterior ischemic stroke (AIS) or posterior ischemic stroke (PIS) and control groups. The mean age of the patients in all groups was 65.27±14.6 (age range: 20-96) years.
In this study, depending on the arteries in which the stroke occurred, three groups were identified: AII patients (n=188), PIS patients (n=88), and control group (n=154). MDCTA images with clear visualization of extracranial VA segments and the absence of vasculitis in intracranial arteries were preferred. An expert radiologist reviewed the images and reached a decision based on the inclusion criteria. The control group was selected from those who underwent CTA due to suspected ischemia and did not have any findings.

The images were analyzed using the Picture Archiving Communication Software (PACS) system in the Department of Radiology, Istinye University, Gaziosmanpasa Hospital. A total of 500 three-dimensional (3D) reconstructed images were analyzed, and 70 of these patients were excluded. Patients with VA or basilar artery (BA) dissection, cardioembolism, absence of VA, surgery or occlusion of the carotid artery, and surgery on the VA were excluded. Missing data and images with poor resolution were also excluded.

**Imaging protocol and reconstruction:** Image examination was performed on a multi-detector CT scanner (Somatom Definition AS+ Erlangen, Germany) with 128 sections using a sequential scanning protocol: 120 kVp, 35 mAs, beam collimation 128x0.6 mm, gantry rotation time 0.33 s, slice thickness 0.6 mm and reconstruction interval 0.6 mm. During the procedure, 70 mL of non-ionic iodinated contrast was infused with 40 mL of saline and injected into the patient's antecubital vein (4 mL/sec) using a dual power injector (Medex flowSens, Geubert USA).

To analyze 3D computed tomography angiography images of patients and control subjects, 3D Slicer (version 4.10.2) software (https://www.slicer.org) was employed. All images were uploaded in DICOM format to the software. 3D image reconstruction and volumetric shaping of the image were performed on DICOM images. Measurements were taken from the other three planes in addition to 3D images during the measurement phase..

Measurements were performed using the following parameters:
1) V2 diameter: The diameter of the second part of the right and left VAs was measured. C3 and C4 segments were identified in the coronal plane on multiplanar reconstruction, and the transverse plane passing between them was visualized. The internal lumen diameters of the right and left VAs were then measured in axial sections (Figure 1) (11).
2) V2 dominance: The dominant side was determined in patients with a right-V2 and left-V2 diameter difference of 0.4 mm or more. The V2 with the larger diameter was referred to as the

dominant V2. They were referred to as symmetrical when the diameter of both VAs was similar or when the difference between the VAs was not obvious (Figure 1) (8).

3) Origin of V1s: VAs were tracked on the 3D reconstruction, and their origin locations were determined and recorded (Figure 2) (5).

4) Level of the first entry into the TFs by the VAs: VA was tracked on axia l slices on multiplanar reconstruction and 3D reconstruction from the origin. On the right and left side, the cervical vertebral level of the TF where the VAs first entered was recorded (Figure 3) (12).

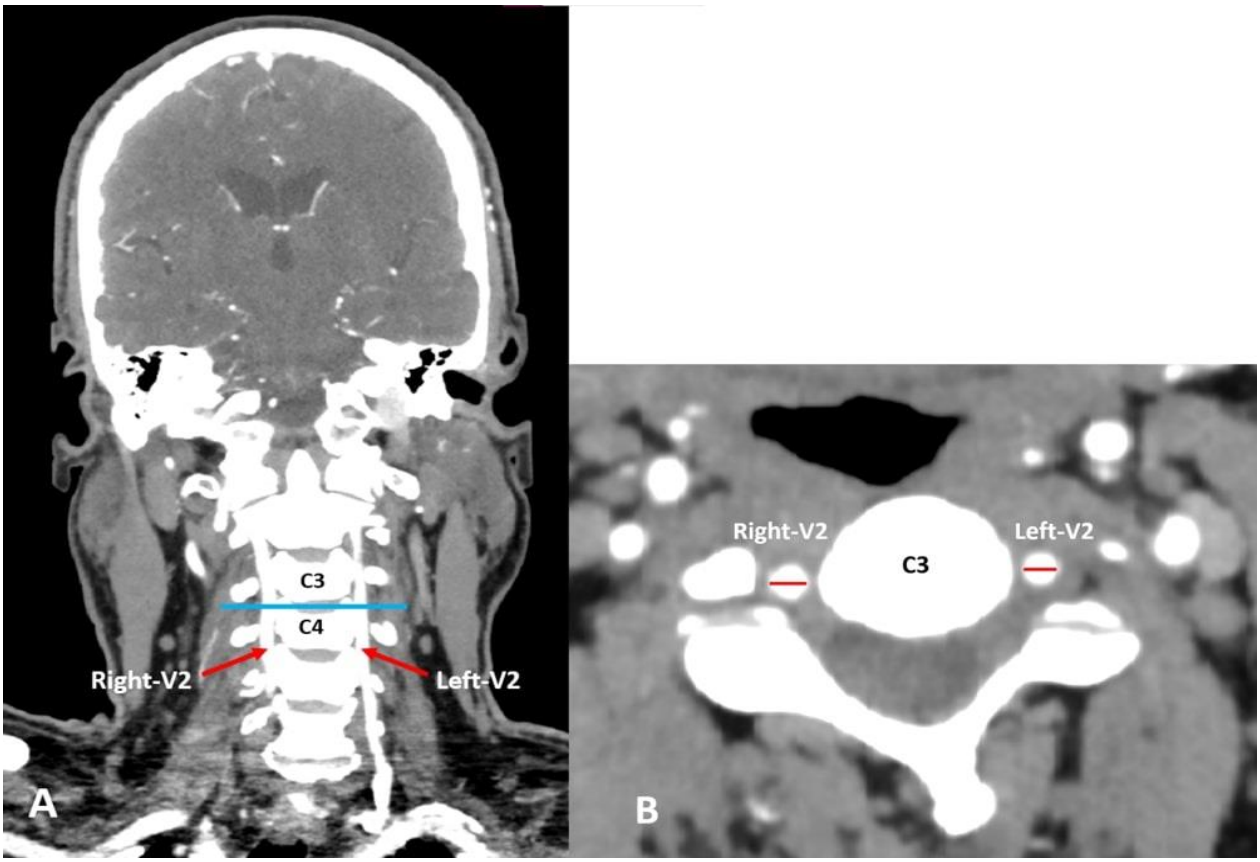


**Figure 1.** Demonstration of VA diameter measurement on multiplanar reconstruction. A. Coronal plane. The blue line represents the axial plane passing between the C3 and C4 vertebrae and the diameter is measured on this plane. B. Axial plane The red lines represent the Right-V2 and Left-V2 diameter measurement. Right-V2: Second section of the right VA. Left-V2: Second section of the left VA.

**Statistical analysis:** Statistical Package for Social Sciences 25 (SPSS, v.25) (IBM Corp., Armonk, New York, USA) was used for data analysis. Mean, median, standard deviation, and minimum and maximum analyses of continuous data were performed in the first phase. For categorical data, numbers and percentages were calculated. In the second phase, normality distributions were examined with Kolmogorov Smirnov. Accordingly, the Kruskall-Wallis test was employed for the comparison of continuous variables, and the Chi-square test was utilized for the comparison of categorical data between AIS, PIS, and control groups. The Mann-Whitney U Test was utilized to compare continuous variables between male and female gender groups, and the Chi-square test was utilized to compare categorical data. The post hoc analysis (Tamhane's T2 test) was used to determine which group was responsible for the significance. The significance was assessed at 95% confidence interval with $p<0.05$.

**Ethical approval:** The protocol of this study was conducted in accordance with the Ethical Standards of the Declaration of Helsinki and approved by the Istinye University Clinical Research Ethics Committee with registration number 3/2022.K-59.

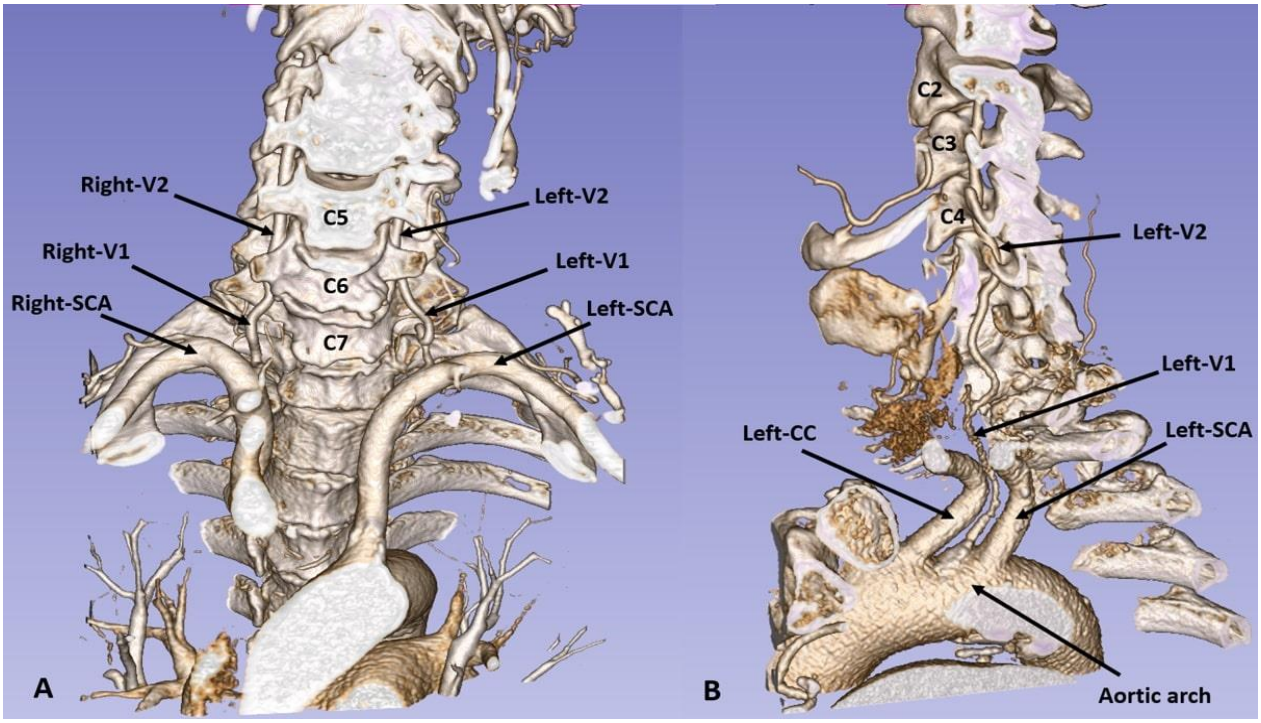


**Figure 2.** Demonstration of VA origin and course on 3D reconstruction. A. It is observed that the right and left VAs originate from the SCA and course through the cervical region after passing through the TFs at the C6 level. B. It is observed that the left VA originates from the AA, passes through the TF at the level of C5, and progresses in the cervical region. Right-V1: the first segment of the right VA, Right-V2: the second segment of the right VA, Left-V1: the first segment of the left VA, Left-V2: the second segment of the left VA, Right-SCA: right subclavian artery, Left-SCA: left subclavian artery, TF: transverse foramen, Left-CC: left arteria carotis communis.

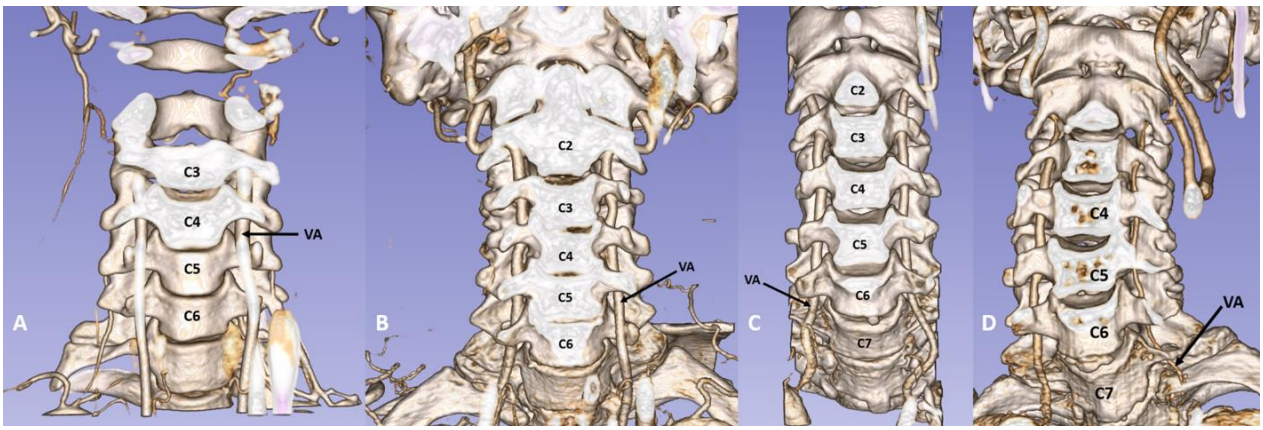


**Figure 3.** Level of the first entry of the VA into the TFs. A. It is observed that the right and left VAs first pass through the TF at the C4 level. B. It is observed that the right VA passes through the TF at the C6 level and the left VA at the C5 level. C. It is observed that the right and left VAs first pass through the TF at the C6 level. D. It is observed that the right VA passes through the TF at C6 and the left VA at C7 level. VA: vertebral artery, TF: transverse foramen..

## RESULTS

Socio-demographic information of the study participants, the distribution of the study groups, and the vascular characteristics of the VA are given in Table 1. It was observed that 43.3% of the respondents were female and 56.7% were male.

The mean age of the participants was 65.27±14.6 (range:20-96) years. According to the group distributions, 43.7% of the participants had AIS, 20.5% had PIS, and 35.8% were in the control group.

**Table 1.** Socio-demographic information of the people included in the study, distribution of the study groups and variational characteristics of VA.

| Characteristics | | Mean value ± SD | Min-max (med) |
|---|---|---|---|
| Age | | 65.27±14.69 | 20-96 (67) |
| Right-V2 diameter | | 3.68±0.65 | 2-6 (3.6) |
| Left-V2 diameter | | 3.69±0.62 | 2-6 (3.6) |
| | | n | % |
| Groups | Patients with anterior ischemic stroke | 188 | 43.7 |
| | Patients with posterior ischemic stroke | 88 | 20.5 |
| | Control group | 154 | 35.8 |
| Gender | Female | 186 | 43.3 |
| | Male | 244 | 56.7 |
| Right-VA origin | Subclavian | 428 | 99.6 |
| | Arcus aorta | 1 | 0.2 |
| | Other | 1 | 0.2 |
| Left-VA origin | Subclavian | 412 | 95.8 |
| | Arcus aorta | 18 | 4.2 |
| Right-VA TF | C4 | 6 | 1.4 |
| | C5 | 22 | 5.1 |
| | C6 | 402 | 93.5 |
| Left-VA TF | C4 | 1 | 0.2 |
| | C5 | 19 | 4.4 |
| | C5-C6 | 1 | 0.2 |
| | C6 | 401 | 93.3 |
| | C7 | 7 | 1.6 |
| | C7-T1 | 1 | 0.2 |
| V2 dominance | Right | 96 | 22.3 |
| | Left | 107 | 24.9 |
| | Symmetrical | 227 | 52.8 |
| | TOTAL | 430 | 100.0 |

The Kolmogorov-Smirnov test was performed, and it was observed that the groups were not normally distributed. There was a statistically significant difference between the groups in terms of age ($p<0.001$). This significance was found to be due to the AIS group (67.9±12.7; 25-93 [70]) and the PIS group (68.1±12.1; 43-91 [69]). A statistically significant difference was found between the groups regarding gender ($p=0.008$). It was determined that this significance was originated from the PIS group (Table 2).

No statistically significant difference was found in total right-V2 diameter and left-V2 diameter values in any group (KW=1.148; $p=0.237$). When V2 dominance was compared with age, groups, and gender variables, no statistically significant difference was determined ($p>0.05$). A statistically significant difference was found between the V2 dominance and the Right-V2 diameter values ($p<0.001$), and this significance was determined to be due to right-sided dominance. A statistically significant difference was found between V2 dominance and Left-V2 diameter values ($p<0.001$), and this significance was determined to be due to left-sided dominance. While no correlation was found between V2 dominance and Left-V2 diameter values, a very weak negative correlation was found between V2 dominance and Right-V2 diameter values (r=-0.167). When V2 dominance was compared with Right-VA origin, Left-VA origin, Left-VA TF, and Right-VA TF, no statistically significant difference was found ($p>0.05$).

No statistically significant difference was found between all groups and Left-VA origin, Right-VA origin, Left-VA TF, Right-VA TF, Left-V2 diameter, Right-V2 diameter, and V2 dominance parameters ($p>0.05$).

The distribution and comparison of the results by gender are presented in Table 3. A statistically significant difference was found between Left-V2 diameter ($p=0.041$) and gender (Table 3).

## DISCUSSION AND CONCLUSION

Ischemic cerebrovascular stroke may originate from the anterior or posterior circulation and usually develops due to embolism, hemodynamic impairment, or small vessel occlusive disease (13). Defining the site based on clinical symptoms and signs alone is often

**Table 2.** Separate evaluation of parameters according to groups.

| Characteristics | | Groups | | | Test value |
|---|---|---|---|---|---|
| | | Patients with AIS | Patients with PIS | Control group | p |
| Age | Mean value ± SD | 67.9±12.7 | 68.1±12.1 | 60.3±16.8 | 21.530 |
| | Min-max (med) | 25-93 (70) | 43-91 (69) | 20-96 (62) | <0.001* |
| Right-V2 diameter | Mean value ± SD | 3.68±0.63 | 3.68±0.59 | 3.69±0.71 | 0.144 |
| | Min-max (med) | 2-6 (3.6) | 2-5(3.6) | 2-6(3.6) | 0.931* |
| Left-V2 diameter | Mean value ± SD | 3.66±0.57 | 3.63±0.55 | 3.7±0.72 | 3.898 |
| | Min-max (med) | 2-6 (3.5) | 2-5(3.5) | 2-6 (3.8) | 0.142* |
| Gender | Female | 80 | 27 | 79 | 9.742 |
| | Male | 108 | 61 | 75 | 0.008** |
| Right-VA origin | Subclavian | 187 | 88 | 153 | 1.792 |
| | Arcus aorta | 1 | 0 | 0 | 0.408** |
| | Other | 0 | 0 | 1 | |
| Left-VA origin | Subclavian | 143 | 83 | 145 | 3.524 |
| | Arcus aorta | 4 | 5 | 9 | 0.172** |
| Right-VA TF | C4 | 4 | 0 | 2 | 0.895 |
| | C5 | 7 | 5 | 10 | 0.639** |
| | C6 | 177 | 83 | 142 | |
| Left-VA TF | C4 | 0 | 0 | 1 | 3.182 |
| | C5 | 7 | 3 | 9 | 0.204** |
| | C5-C6 | 1 | 0 | 0 | |
| | C6 | 177 | 82 | 142 | |
| | C7 | 3 | 3 | 1 | |
| | C7-T1 | 0 | 0 | 1 | |
| V2 dominance | Right | 45 | 19 | 32 | 1.982 |
| | Left | 41 | 20 | 46 | 0.159** |
| | Symmetrical | 102 | 49 | 76 | |

**Kruskal-Wallis test; **Chi-square test; p<0.05

**Table 3.** Distribution and comparison of results by gender.

| Characteristics | | Gender | | Test value |
|---|---|---|---|---|
| | | Female | Male | p |
| Right-VA origin | Subclavian | 185 | 244 | *1.312; 0.252 |
| | Arcus aorta | 1 | 0 | |
| Left-VA origin | Subclavian | 180 | 232 | *0.752; 0.386 |
| | Arcus aorta | 6 | 12 | |
| Right-VA TF | C4 | 4 | 2 | *-0.381; 0.703 |
| | C5 | 9 | 13 | |
| | C6 | 173 | 229 | |
| Left-VA TF | C4 | 1 | 0 | *-1.642; 0.101 |
| | C5 | 10 | 9 | |
| | C5-6 | 1 | 0 | |
| | C6 | 172 | 229 | |
| | C7 | 1 | 6 | |
| | C7-T1 | 1 | 0 | |
| Right-V2 diameter | Mean value±SD | 3.67±0.65 | 3.7±0.65 | **0.209; 0.648 |
| | Min-max (med) | 2-5(3.63) | 2-6(3.71) | |
| Left-V2 diameter | Mean value±SD | 3.76±0.65 | 3.63±0.60 | **4.187; 0.041 |
| | Min-max (med) | 2-6(3,67) | 2-5(3.59) | |
| V2 dominance | Right | 37 | 60 | *5.328; 0.069 |
| | Left | 54 | 48 | |
| | Symmetrical | 95 | 136 | |

SD: standard deviation, med: median, min: minimum, max: maximum, *Chi-Square test; **Mann-Whitney U Test, p<0.05
(V2 dominance: Positive numbers represent right dominance, negative numbers represent left dominance.)

challenging or even impossible, as ischemic events in the anterior and posterior circulation may cause the same symptoms (14). Constituting approximately 20-30% of all ischemic strokes, PIS may have various presentations that differ from AISs in terms of etiology, clinical features, and prognosis (15). It remains unclear whether V1 and V2 morphometry is a risk factor for posterior or anterior ischemic stroke (3). There have been numerous published reports on patients with PIS (3,14-16,17), whereas studies comparing patients with anterior or posterior ischemic stroke are

scarce, and no attempt has been made to characterize them by morphological changes in V1 and V2.

Morphological variations of the VA are known to be an etiological factor for many pathological conditions such as atherosclerosis, infarction, and transient ischemic stroke (10). Determination of VA variations in the proximal sections of the V1 and V2 segments is of vital importance for investigating the etiology of clinical findings, planning endovascular intervention procedures, and investigating cervical nerve blockages (8). The incidence of VA injury during cervical spine surgery varies between 0.3% and 8.2% in normal anatomy (6). However, the abnormal course of VA can cause severe complications during anterior cervical decompression surgery that may result in neurologic damage or mortality (5). Changes in the diameter, blood flow volume, and arterial dominance of the V2 segment of the artery may also pose a severe risk for any invasive procedure in the cervical region (8).

The origin of VA often shows different variations due to the disruption of the embryonal development of AA branches (18). VA originating from AA is less protected by bone. Therefore, it may be accidentally ruptured during surgery. VA originating from AA is most commonly observed on the left side, and its incidence varies between 2.4% and 6.9% (5,7,8,12,18-22). In our study, 95.8% of the left V1s originated from the SCA, whereas 143 of these arteries were observed in patients with AIS, 83 with PIS, and 145 in control subjects. The remaining 4.2% of left VAs were separated from AA, consistent with the incidence in previous studies. According to Yamaki et al., this anomalous origin of the left VA may be explained by the fusion of the left V1, probably the 4th branchial artery, with the upper wall of the AA (22). The direct origin of the left VA from the AA appears to increase blood flow in the left VA (5). Abnormal aortic origin of the right VA is generally rare, ranging from 0.6% to 0.19% (19,22).

In our cases, 99.6% of the right VAs originated from SA, 187 of which were detected in patients with AIS, 88 in patients with PIS, and 153 in control subjects. Consistent with the literature, only 0.2% were found to originate from AA. The possibility that the abnormal V1 segment origin of VA may cause cerebral hemodynamic changes and the risk of shear stress due to high blood pressure in cases of VA branching from AA should be kept in mind during clinical reflections (8). Surgeons should be aware of these variations, as variation in the origin and abnormal proximal course of the VA is potentially hazardous during surgery of the AA or lower cervical region (12).

The standard anatomical location of the V2 segment in the VA is within the TF from C6 to C2 and is protected by the VA PT (11). Differences in the TF entry level of the V2 segment may cause damage to the artery that is not protected by bone (8). Due to VA entry from C5-C3 into TF, they are at risk during anterior cervical surgery as they pass in front of TF. Entry into the third TF may pose a risk for VA dissection or occlusion during cervical rotation (12). VA can enter TF from levels other than C6, and the normal incidence of entry into the V2 segment ranges between 90% and 95% (5,11,12,23,24). In our study, the frequencies of the right VAs passing through the TFs were observed as follows: C6 (93.5%), C5 (5.1%), and C4 (1.4%). Among 188 patients with AISs, 4 passed through C4, 7 through C5, and 177 through C6, whereas among 88 patients with PISs, 5 passed through C5 and 83 through C6. The frequencies of left VAs passing through the TFs were determined as follows: C6 (93.3%), C5 (4.4%), C7 (1.6%), C4 (0.2%), C5-C6 (0.2%), and C7-T1 (0.2%). V2 passing through C4 and C7-T1 TFs could not be detected in patients with ischemic stroke. In AIS patients, the VA passed through C5 in 7, C5-C6 in 1, C6 in 177, and C7 in 3. Among PIS patients, it passed through C5 in 3, C6 in 82, and C7 in 3. The unusual incidence of V2 in the TF ranges from 5.1 to 10%, and the VA entry in the C5 TF is known to be the most common entry site (5,11,12,23-25). In the present study, data were obtained consistent with the literature regarding both the control group and the patients with stroke. Although various aspects of atypical V2 entry have been assessed in some previous reports (5,11,20,22), this condition is documented for the first time in patients with ischemic stroke.

The use of cervical pedicle screws during cervical spine surgery is safe only when performed at C7, where the VA is usually not located in the TF. However, in a small proportion of individuals, VA is located in the TF of C7. In such cases, the risk of VA damage, which can lead to various neurological disorders such as Wallenberg syndrome, may increase (26,27). Therefore, it is crucial to fully understand the patient's anatomy before surgery

to prevent iatrogenic injury and associated complications (20,23). Specifically, the prevalence of VA entry in C7 ranges from 0.8 to 5.4% (23,24). While this rate (C7) was 1% in the study by Uchino et al. (12), it was 6.7% in the study by Kim et al. In the present study, it was found to be 1.6%, mostly in patients with ischemic stroke (6/7).

In cases where the left VA originates from the AA, its entry into the TF is usually higher than usual (at C5 or C4), increasing the likelihood of compression and reduced flow, especially in conjunction with posterior cerebral circulation ischemia (7,8,20). These conditions are also significant in transpedicular fixation or other spine surgeries with a higher risk of iatrogenic vascular injury during anterior cervical surgery and can be identified on preoperative imaging (18). The most common TF entry level of left VA of AA origin is known to be C5, with an incidence of 2.5-4.5% (8,12,22). In our study, 1.06% of the left VAs passed through C5 and 0.53% through C7 TF in patients with AIS, while 1.13% passed through C5-C6 and 2.26% through C7 TF in patients with PIS.

Changes in the diameter, blood flow volume, and arterial dominance of the V2 segment of the artery may pose a severe risk for any invasive procedure in the cervical region (8). In the study by Sureka et al., the diameter of V2 at the C3 level was reported as 3.3±0.6 mm on the right and 3.4±0.6 mm on the left (27). In the investigation by Ozdemir et al., the diameter of V2 was found to be 3.2±0.6 mm on the right and 3.4±0.5 mm on the left (4). Yaprak et al. reported V2 diameter as 3.5 mm for the right side and 3.6 mm for the left side (8). In our study, right V2 diameter was 3.69±0.71 and left V2 diameter was 3.7±0.72 mm. Interestingly, no statistically significant difference was found when right-V2 diameter and left-V2 diameter values were compared in control subjects and patients with ischemic stroke. This finding, except for Kim et al.'s report where the average diameter of the right VA was larger than the left VA (11), is generally inconsistent with other studies that show the average VA diameter is larger on the left side compared to the right side. Further investigation of the link between this condition and ischemic stroke using a broader sample size would be beneficial.

VA dominance is a common congenital variation of the VA and is generally defined as a significant difference between the two sides of the VA diameter. Zhu et al. concluded that there is a direct link between stroke and VA dominance (3). For some endovascular procedures, the dominant VA must be identified (17). In the current study, right dominance was observed in 22.3% (23.9% in AIS patients, 21.6% in PIS patients, and 20.8% in the control group), left dominance in 24.9% (21.8% in AIS patients, 22.7% in PIS patients, and 29.9% in the control group), and symmetry in 52.8% (54.3% in AIS patients, 55.7% in PIS patients, and 49.3% in the control group) of the participants. Although the majority of relevant studies demonstrate left-side dominance, the mechanism behind this trend is not yet known by anyone (4,8,21,25,27). The variation in the reported prevalence of VA dominance in the literature can be attributed to ethnic origin, measurement location, and methodology (17). In our study, the value on the left was slightly higher than on the right, but it did not demonstrate statistical significance. In a study conducted by Zhu et al., it was stated that they believed VA dominance increased the risk of posterior circulation infarction (3). We could not definitively reach such a conclusion. Nevertheless, the role of VA dominance in the risk of cerebral ischemic stroke should be discussed in more comprehensive studies.

Our study has some limitations. Firstly, this study is retrospective and only includes computed tomography angiography. Therefore, a large-scale prospective study may be necessary to confirm the reported pathophysiological relationship between morphological deformations of the VA and stroke. Secondly, the risk factors of the patients were not available to us. Therefore, we could not compare them with our findings. Thirdly, the single-center design of the study may have led to selection bias, influencing the rate of occurrence of VA variations. Finally, the sample size of our study may not have been sufficiently large to analyze the relationships between geometric changes in the VA and ischemic stroke. Future studies should aim to increase the sample size for a more robust analysis. Despite these limitations, our results may have clinical significance.

To the best of our knowledge, this is the first report investigating whether there is a relationship between morphometric and anatomical variations of the VA and patients experiencing ischemic stroke from both anterior and posterior circulation. The insights derived from this study will assist clinicians, particularly

craniocervical surgeons and interventional radiologists, as well as other relevant healthcare professionals in both clinical and pre-clinical settings, especially within the Turkish community, in understanding the variable anatomy of the vertebral artery, thus aiding in the prevention of iatrogenic injuries. A detailed prospective study with larger groups may be useful in determining further pathophysiological and causal relationships between V1 and V2 morphology and anterior or posterior ischemic stroke.

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**Ethics**

**Ethics Committee Approval:** The study was approved by Clinical Research Ethics Committee of İstinye University (Date: 01.07.2022, No: 3/2022.K-59).

**Informed Consent:** The author declared that it was not considered necessary to get consent from the patients because the study was a retrospective data analysis.

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