CLINICAL ARTICLE

Anatomical Variations of the Vertebral Artery: Analysis by Three-Dimensional Computed Tomography Angiography in Chinese Population

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Objective: To analyze the anatomical variations of V3 and V2 segments of the vertebral artery in the Chinese population.

Methods: The current retrospective study was an observational, anatomical, radiological research. Between 1 January 2018 to 31 December 2019, the data of 589 continuous head-and-neck three-dimensional computed tomography angiography were observed and analyzed using the open-source software of Horos. There were 415 males and 174 females with an average age of $44.63 \pm 2.5(18–74)$ years. The variations of the V3 segment were defined as persistent first intersegmental artery (PFIA) and paracondylar processes (PP). The variations of V2 segments were unusual vertebral artery entrance transverse foreman (UE-V2S) and midline migration (MM). The incidences of all variations were summarized and the gender, side characters were compared.

Results: Among the patients, 4.34% (18/415) males and 4.60% (8/174) females were with the variation of PFIA. Meanwhile, 12.29% (51/415) males and 10.92% (19/174) females were with the variation of PP. Then 18.80% (78/415) males and 16.67% (29/174) females were with UE-V2S. All the variations above were not different in genders. As for the variation of MM, 3.86% (16/415) males and 8.62% (15/174) females were identified, and the difference of genders was significant for this type of variation ($P < 0.05$). The differences between each side were also observed and analyzed for all variations and no differences were found.

Conclusion: There are several variations of V3 and V2 segments of the vertebral artery are associated with the cervical surgeries, most were without differences in genders and sides, except the variation of MM.

Key words: Anatomic variations; Anatomy; Cervical spine; CT angiography; Vertebral artery

Introduction

Cervical surgeries could be applied to patients with degenerative diseases, trauma, tumor, infectious diseases of the cervical spine. Anterior and posterior approaches m be used according to the specific requirement and the conditions of the patients. Several complications during or after the operations might occur associated with the approaches. Through the complications of the anterior approach might be different with the posterior approach, there are some complications that might exist in both approaches, such as the injury of the important structures. For both approaches, injury to the vertebral artery (VA) is disastrous and should be avoided by all methods.

Several factors may be associated with the injury of the VA, among which the existence of the variations is an

important element. When there were variations, even standard operations as incising, exposing, appearing tissues might injury the blood vessels. Meanwhile, discectomy and laminectomy could be dangerous and with uncertainty. When implants were input such as anterior plate, posterior screws and artificial disk, the abnormal VA might bring unexpected complications both during and after the operations[1]. When the VA was injured, presentations could be uncontrollable bleeding, delayed hemorrhage of pseudoaneurysm and syndromes associated with neck swelling such as dyspnea. All of these complications are disastrous and life-threatening. So, surgeons should observe the radiological data thoroughly preoperatively to find the variations. Meanwhile, the thorough understanding about the variations of VA was also important. For example, the incidences of the variations and the characters of the variations distribution should be surveyed.

Many authors have tried several methods to research the variations of VA. The methods included cadaver studies, radiographic studies of CT (computed tomography)[2,3] and MRI (magnetic resonance imaging)[4]. There were some limitations of these methods. For example, it is difficult to ensure the numbers of the samples in the cadaver studies. Also, the blood vessels of the cadaver samples were often with certain degree of change in the shape and could not exhibit the exact anatomic relationship of different structures such as the bone and the blood vessels. As for the CT and MRI studies, the numbers of samples were large enough. But both these two technologies could not display the characters of the blood vessels exactly. So, in recent years, the examination of CTA (computed tomography angiography) became the major technology for the research of the variations of VA[5–9] for because of the advantage of making the bone and the blood vessel visible at the same time.

Normally, the running course of VA was divided into three segments between the origin and the occipital bone as V1-3. V2 and V3 segments are associated with cervical operations closely. There are several variations of the VA in both V2 and V3 segments, which could bring more probability of injury. The incidence of every variation is different and with different character, even the incidence of different populations may vary markedly[7,10,11]. Thus, it is important to survey the anatomical variations in a specific population and analyze their influence to the operations in order to ensure the safety of cervical operations[12]. It is likely to suppose that the Chinese population may have specific incidences of the variations of the VA than other populations, and the characters might have some differences also.

In previous researches, some kinds of software were tried and obtained wonderful effects. But most image observation and 3D-reconstruction software are not free. The price of the software is often beyond the paying ability of patients for a personal working station. Meanwhile, surgeons expect the freedom to observe the image data and reconstruct the region of interest using personal computers. In recent years, the emergence of open-source software meets these needs. The advantages of the open-source include the convenience of access and free use. Also, the feature of open-source attracts many researchers to

programs or upload big data for it. These advantages make it possible for this kind of software to develop rapidly with the gradual maturity of big data technology. In the current study, an open-resource software of Horos was applied to finish the research on the digital working station of a personal notebook computer. By this way, the combination of this hardware and software has been confirmed as having the ability of accomplishing the current work satisfactorily.

Therefore, in the current retrospective study we used the software of Horos to analyze the CTA data of 589 Chinese patients. The samples with variations of V2 and V3 segments were identified, then the gender and side of the samples were compared. The aims of the current research were: (i) to investigate the incidences of variations occurring in the V2 and V3 segments of the VA in the Chinese population；(ii) to analyze the characters of the variations such as the distributions of genders and sides; and (iii) attempt to establish the digital working station on the personal computer using the open-source software Horos.

Methods and Materials

Between 1 January 2017 to 31 December 2018, the data of 589 continuous head-and-neck CTAs were collected and analyzed retrospectively using Horos. All relevant patients met the criteria as following: (i) between 18–80 years; (ii) underwent the CTA examination for dizziness, headaches and other neurological diseases; and (iii) the images of the data were intact and clear for analysis in the software. Then the exclusion criteria were: (i) younger than 18 years or older than 80 years; (ii) had the history of operations around the neck; and (iii) examinations confirmed the existence of tumor or severe malformation of the cervical spine.

A personal notebook computer MacBook Air was used as the working platform with the configuration as follows, processor 1.8 GHz Intel Core i5, memory 4GB 1600 MHz DDR3, graphics card Intel HD Graphics 4000. The system of the computer was macOS Mojave 10.14.5. and the open-source software Horos 3.3.5 (Horosproject) was the working software. The CTA data were collected under the conditions of following: scanning condition 120kV, 30mA, FOV 500mm, slice thickness 0.9mm (Philips Briliance 64-layer spiral CT). The DICOM images were imported into the software, then observed and measured in the mode of orthogonal MPR under the 3D viewer option.

Two of the authors (SW and WR) observed and measured the images separately. When there were different results, all authors discussed them and reach a consensus.

The variations of V3 and V2 segments of the VA were observed and analyzed respectively. Recoded data included the number of every kind of variation and the side, gender of the patients.

Variations of V3 Segment

These variations located in the region of upper cervical spine and associated with the V3 segment of the VA. Two kinds of variations were included as follows.
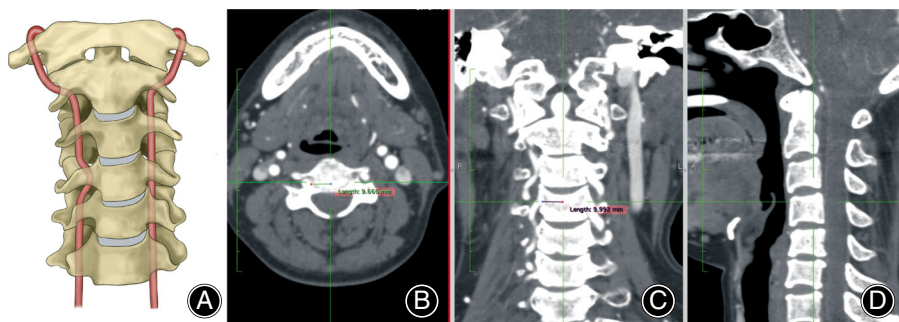
Fig. 1 PIFA variation of the V3 segment. (A) The schematic diagram of PIFA on the left side and the right side was normal. The black arrows on the horizontal plane (B), coronal plane (C) and sagittal plane (D) indicated the location of the VA, which running under the posterior arch of C_1. Also, the black arrow on the 3D reconstruction image (E) point to the blood vessel under the arch of C1.
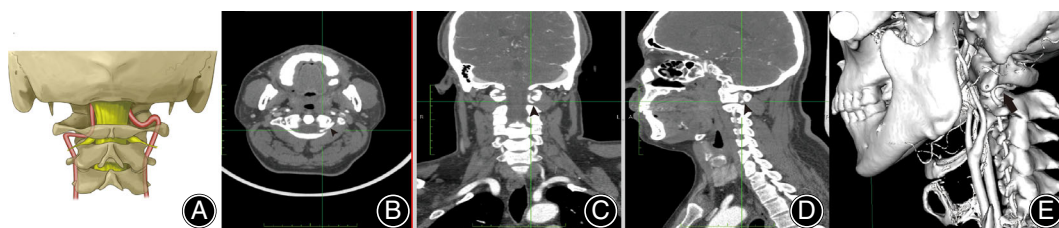

Fig. 2 PP variation of the V3 segment. (A) The schematic diagram of PP on the left side and the right side was normal.The black arrows on the horizontal plane (B), coronal plane (C) and sagittal plane (D) indicated the location of the VA, which surrounded by the bone structure upon the posterior arch of C1. Also, the black arrow on the 3D reconstruction image (E) point to the blood vessel surrounded by the bony bridge upon the posterior arch of C1.
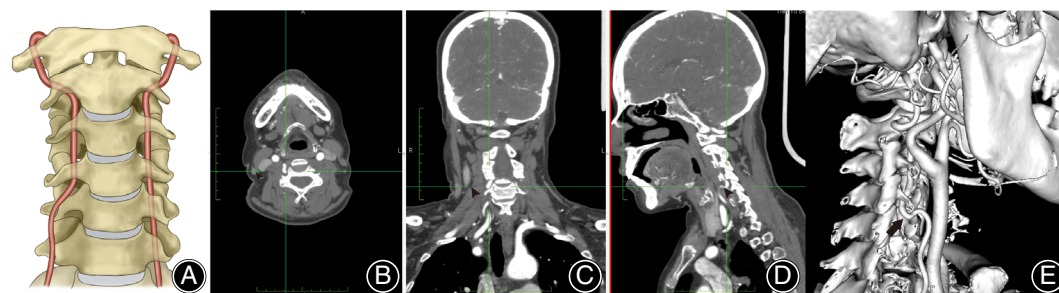

Fig. 3 UE-V2S variation of V2 segment. The schematic diagram of UE-V2S on the right side and the left side was normal.The black arrows on the horizontal plane (B), coronal plane (C) and sagittal plane (D) indicated the location of the VA, which entering the transverse foreman of C4, instead of C6. Also, the black arrow on the 3D reconstruction image (E) point to the blood vessel.

Persistent First Intersegmental Artery (PFIA)
This is a variation of the blood vessel, which refers to the condition that the artery runs under the posterior arch of the atlas, instead of from the upper side of the arch as usual. (Fig. 1).

Paracondylar Processes (PP)
This variation refers to the bony bridge between the posterior arch of atlas and the superior articular process (Fig. 2).

Variations of V2 Segment
V2 segment of vertebral artery runs through the lower cervical spine and two variations are associated with the cervical operations.

Unusual Entrance Transverse Foreman of V2 Segment (UE-V2S)
Generally, the VA enters into the transverse foreman (TF) of C6 first. In the current research, when the first-entering TF was not C6 it was recorded as the variation of unusual entrance transverse foreman of V2 segment of the VA. (Fig. 3).

Midline Migration (MM)
The running course of the VA was observed in this region and the distance between the media wall of VA and the midline of the cervical vertebra was measured. When the distance was less than 1cm, it was defined as the variation of midline migration. (Fig. 4).
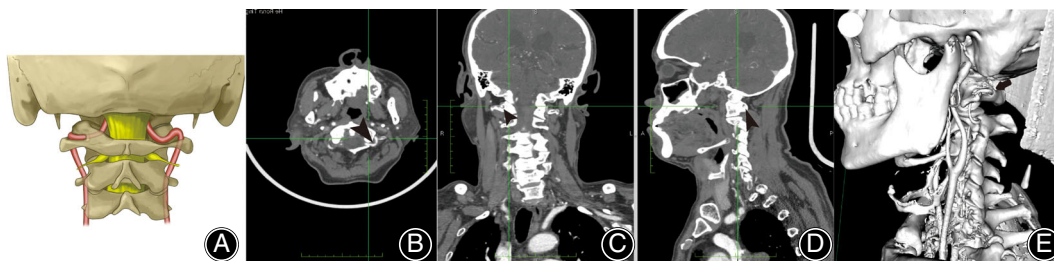
Fig. 4 MM variation of the V2 segment.(A) The schematic diagram of MM on the right side and the left side was normal. The minimum distance between the medial wall of the VA and the midline of the cervical vertebra was measured both on the horizontal plane (B) and the coronal plane (C). Then the average value of these two distances was considered as the distance of the minimum distance of VA to the midline in this region. When the value was less than 10mm, it was recorded as the variation of MM. Also, the level could be observed on the sagittal plane (D).

Statistical Analysis

SPSS version 19.0 (IBM Corporation, Armonk, NY, USA) was used to perform the statistical analyses and $P < 0.05$ was considered significant. The numbers of male or female patients, cases of every variation or each side were compared by chi-square test. The Kappa value was applied in order to examine the consistency of the two observers.

Results

Five hundred eighty-nine patients were included in the current research after screening by the inclusion criteria and exclusion criteria. The average age was 61.87 ± 12.67 (21–79) years and there were 415 males and 174 females. Two authors (SW and WR) completed the observation separately and their classifications of the variations were consistent with the Kappa value of 0.92.

Variations of V3 Segment

Two variations were observed in the region of the upper cervical spine, the PFIA and PP. They were both important variations associated with the operations such as the atlantoaxial internal fixation.

As for the variation of PFIA, 26 cases were observed in the current research. Among them, 18 cases were males and 8 cases were females. So, the incidence of PFIA was 4.34% in males and 4.60% in females respectively. There was no difference between the incidences of genders ($P > 0.05$) (Table 1). Then the incidence in each side was also calculated. There were 11 cases of PFIA in the left side and 15 cases in the right side. So, the incidence was 1.87% in the left side and 2.55% in the right side. The incidences of the sides were without difference. (Table 2).

The other kind of variation in V3 segment is PP, which indeed referring to the variation of the posterior arch of atlas. In this situation, bone bridge could be observed and the VAs were often surrounded by the bone bridge. In the current research, 51 cases of males and 19 cases of females were with the variation of PP. Since then, the incidence of

TABLE 1 Variations of V3 and V2 segments of the VA in different genders			
Genders		Male	Female
Total		415	174
V3	PFIA	18	8
	Percentage	4.34%	4.60%
	χ^2	0.02	
	P	0.89	
	PP	51	19
	Percentage	12.29%	10.92%
	χ^2	0.22	
	P	0.64	
V2	UE-V2S	78	29
	Percentage	18.80%	16.67%
	χ^2	0.37	
	P	0.54	
	MM	16	15
	Percentage	3.86%	8.62%
	χ^2	5.58	
	P	0.01	

MM, Midline migration; PFIA, Persistent first intersegmental artery; PP, Paracondylar processes; UE-V2S, Unusual entrance transverse foreman of V2 segment.

PP was 12.29% in males and 10.92% in females, these incidences revealed that the existence of PP was without difference in each gender ($P > 0.05$). (Table 1) As for the incidence of each side. There were 30 cases of PP in the left side and 39 cases in the right side, so the incidence was 5.09% and 6.62% respectively, which was without difference too (Table 2).

Variations of V2 Segment

In this region, two kinds of variations were considered and they were both associated with the operations of the lower cervical surgery such as the anterior cervical discectomy and fusion.

Totally, 78 males and 29 females were observed with the variation of UE-V2S. So, the incidence was 18.80% in

TABLE 2 Variations of V3 and V2 segments of the VA in different sides

Sides		Left	Right
Total		589	589
V3	PFIA	11	15
	Percentage	1.87%	2.55%
	χ^2	0.63	
	P	0.43	
	PP	30	39
	Percentage	5.09%	6.62%
	χ^2	1.25	
	P	0.26	
V2	UE-V2S	57	51
	Percentage	9.68%	8.66%
	χ^2	0.32	
	P	0.57	
	MM	24	22
	Percentage	4.07%	3.74%
	χ^2	0.09	
	P	0.76	

MM, Midline migration; PFIA, Persistent first intersegmental artery; PP, Paracondylar processes; UE-V2S, Unusual entrance transverse foreman of V2 segment.

male patients and 16.67% in female patients (Table 1). Analyzing the sides of this variations, it was found that 57 cases were in the left side with an incidence of 9.68% and 51 cases in the right side with an incidence of 8.66% (Table 2). There were no differences between the genders ($P > 0.05$) or the sides ($P > 0.05$).

MM was the other variation of V2 segment included in the research, which referred to a VA with a closer distance to the midline of the cervical spine. Since the distance between the vessel and the midline was shorter than the normal case, it might be injured in the operations. After observation, the MM variation was identified in 24 cases in the left side and 22 cases in the right side. So, the incidence was 4.15% in the left side and 3.74% in the right side respectively. The incidences of each sides were without differences ($P > 0.05$) (Table 2). Then there were 16 males and 15 females with the MM variation, the incidence was 3.86% and 8.62% respectively with significant difference in genders ($P < 0.05$) (Table 1).

Discussion

Incidences of V2 and V3 Variations of the VA in the Chinese Population

The vertebral artery originates from the subclavian artery and ascends along the medial side of the anterior scalenus muscle. The vertebral arteries of each side converge at the lower edge of the pons as a basilar artery. There are several kinds of classifications to define the courses of the VA. In this research, the whole course of the extracranial vertebral artery is divided into three segments, V1 segment means the

ascending part before entering the transverse foramen, V2 segment runs between the entrance transverse foramen and C_2 foramen, and V3 segment refers to the artery between the C_2 transverse foramen and occipital foramen magnum[13].

Generally, the V3 and V2 segments are possibly injured during cervical surgery and these injuries can cause catastrophic consequences such as critical bleeding, cerebral ischemia and even death. These injuries occur rarely when the surgeons keep to standard operation procedures. But when variations of the VAs exist, even the standard procedures cannot prevent the injury to the blood vessel completely. So, it is important to reveal the variations preoperatively.

The incidences of the variations were reported by many authors. For example, Jae *et al.*[14] reported the incidence of UE-V2S as 5.1% and Bruneau *et al.*[15] revealed a different incidence of 7.0%. Other authors from Korea reported a higher incidence of 11.4%[8] and Japanese authors concluded the incidence as 8.1%[9]. A retrospective study of American authors presented an incidence of 15.7%, higher than most studies.

It was possible that the incidences were different because they were summarized from different populations. So, it may be necessary to survey the incidence of the variations in special kinds of populations. Hence in the current research, the variations of V3 and V2 segments of the VA were observed and analyzed in order to demonstrate the occurrences of them in the Chinese population.

Characters of the Variations in the Region of V2 and V3 Segments of VA

The V3 segment of vertebral artery is crucial to the safety of the upper cervical spine operations[6,16,17]. The VA is more likely to be injured with the existence of variations [18], so it is important to identify the variations before operations through the examinations include CTA. Two variations are associated with the cervical operations in this region as PIFA and PP. Their influences on the operations are mainly concerning the determination of entry point of the posterior C1 screws[10,14,19].

The PIFA is a variation which refers to the artery running below the posterior arch of C_1[7,20]. Since the lateral mass might be covered by the PIFA, the procedure of inserting screws into the lateral mass was dangerous. So, under this condition, the pedicle screw of C_1 might be an alternative. PP is the osseous variation of vertebral artery V3 segment and it is also a risk factor for inserting a screw into the atlas[7,21–24], especially for the pedicle screws, since the existence of PP does not make it easy to observe the upper wall of posterior arch of C_1. For these reasons, when the variation of PP was observed, the entry point of C_1 fixation screws should be selected more cautiously in order to avoid the injury to the VA[25].

The variations of V2 segment of the VA are associated with the operations of the subaxial cervical spine[26,27]. In the case of the variation of UE-V2S, VAs below the entrances

were not protected by the bone structure and could be injured more easily. Eskander *et al.* also defined this kind of variation as extraforaminal VA anomalies[4]. When the UE-V2S was observed, the procedures below the entrance should be more cautious and closer to the midline in order to avoid the injury of the VAs[8]. Generally, most anterior injuries occurred at the region of C4-C6[3,28,29]. Several factors might be associated with these injuries. For example, this region is often more susceptible to be affected by diseases and traumas. Also, in the current study, the results show that the UE-V2S was more frequent in this region and could be one possible reason for these injuries. Also, the current research summarized similar results with the previous research that the UE-V2S was not relevant with the difference of laterality and gender[26].

The variation of MM is associated with the subaxial cervical spine surgery, too. Since the artery is closer to the midline of the vertebra, it could be injured more possibly[1]. So, it is important to detect this variation preoperatively and perform more cautiously during the operations.

Establishment of the Digital Working Station on the Personal Computer

In the current research, the software of Horos was applied. As a free and open-source medical image viewer for Mac OS X, Horos is based on OsiriX TM. It is a practical software to observe and measure the clinical imaging data according to special needs. A special advantage of Horos is that it is an open-source software (OSS), which is convenient for users. Also, this character attracts thousands of users and make it possible for them to improve the software through programming or uploading data. In this article, the data were collected through the picture archiving and communication system of the hospital (PACS), then the observation and measurement were all proceeded in Horos.

There are some limitations of the current research. Firstly, the samples were relatively small to an anatomic research for variations. Secondly, the data came from only one medical center and presented the character of the population around local region. In the future, more samples from different regions should be included and observed. Since then, more variations may be recovered and their relationship with the cervical operations should be analyzed thoroughly.

Authorship Declaration

The authors of the current article acknowledge: (i) all authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors; and (ii) that all authors are in agreement with the manuscript.

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