



# ANATOMICAL VARIATIONS OF INTRAOSSEOUS VERTEBRAL ARTERY IN C2 VERTEBRA WITH CT ANGIOGRAPHY PREVALENCE STUDY

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#### ABSTRACT

**Objectives:** Vertebral artery (VA) injury as a complication of C1–C2 transarticular or C2 pedicular screw placement is commonly related to the anatomic positional variations of the VA in C2 intraosseous canal. These variations cause the C2 isthmus or pedicle, which constitute the screw path, to be narrower than normal. Narrowing of the C2 isthmus is well known as a high-riding pattern of VA (HRVA), and narrowing of the C2 pedicle is, recently, named as a medial-shifting pattern of VA (MSVA). Herein, we investigated the prevalence of HRVA and MSVA in general population.

**Methods:** The study population was represented by 216 CT-angiograms consecutively pulled from our radiology database (125 male, 91 female, mean age 62,7 years). VAs were assessed for the anomalous course in the C2 vertebra by measurements of isthmus thickness, internal height, and pedicle width. Particular note was made on VA dominance.

**Results:** In 53 (24 %) of the 216 patients, there was at least one VA variation. HRVA was identified in 40 (18 %) and MSVA in 45 (20,8 %) patients. Ipsilateral co-occurrence of HRVA and MSVA was highly significant ( $P < 0,01$ ). The relationship between VA dominance and variations was statistically significant ( $P < 0,05$ ).

**Conclusions:** Because of the high prevalence of various intraosseous courses of VA and also high possibility of ipsilateral co-occurrence of HRVA, MSVA and as well as dominant VA, preoperative imaging should be performed if C2 instrumentation required.

**Keywords:** CT; CT angiography; Vertebral 24 artery; C2 vertebra; Vascular injuries

**Level of Evidence:** Retrospective clinical study, Level III.

#### INTRODUCTION

Intraosseous vertebral artery (VA) at the level of the C2 vertebra is reported to show asymmetry between two sides, and vary widely between individuals<sup>(9,11,18)</sup>. Preoperative evaluation of VA is deemed essential to decrease the possibility of VA injury during C2 vertebra instrumentation. VA injury is not related solely to the proximity of the artery to the path of the screw, but also to the anatomic variations in the position of the VA in the C2 intraosseous canal. These variations cause the C2 isthmus or pedicle, which constitute the screw path, to be narrower than normal. VA frequently shows a lateral bending in the C2 vertebra just under the superior articular facet of the axis<sup>(9,18)</sup>.

The path of the posterior C1–C2 transarticular screw traverses the isthmus of the C2 pars-interarticularis, passes

the atlantoaxial joint and reaches the C1 lateral mass (Fig. 1a, b).

The C2 pedicle screw, on the other hand, reaches the C2 vertebral body by passing through the C2 vertebra pedicle (Fig. 1c, d).

The technical objective is to place the screw entirely within the bone for both techniques. In both conditions, the screw remains superior and posteromedial to the bending point of the intraosseous segment of VA<sup>(18)</sup>. When the artery shows a prominent superior or posterior course in the intraosseous path, it narrows the bony mass of the C2 vertebral isthmus and restricts the safe passage of the screw. This pattern of the VA is well known and has been named as 'high-riding vertebral artery' (HRVA). When the artery shows a prominent medial course in the intraosseous canal of C2, it may cause a

thinning of the pedicle. This condition - a narrow C2 pedicle has also been of concern to surgeons because the area for the passage of the C2 pedicle screw becomes restricted. More recently, this condition or pattern is referred to as 'medial-shifting vertebral artery' (MSVA) (7,11,27-28). Both anatomic variations are significant in the selection of the technique in C2 instrumentation surgery. Therefore preoperative assessment of the VA at the level of the intraosseous canal of C2 is emphasized (87,12-13,15,19).

Here in, we aimed to determine the prevalence of the HRVA and MSVA and to examine the relationship between these two conditions. We also scrutinized the effect of age, sex, and laterality on both of these conditions. Besides, the rates of coexistence of HRVA and MSVA with dominant VA were analyzed.

## MATERIALS AND METHODS

After approval by our institutional review board, we performed a retrospective review of the image data of consecutive 235 patients who underwent computed tomography (CT) angiography examination in a single institution from January-2013 to May-2016. CT-angiography studies were performed with a 16- or 64-multidetector CT scanner (Siemens Somatom Sensation 16, Siemens Medical Solution, Erlangen, Germany or Siemens Somatom Definition 64, Siemens Medical Solution, Forchheim, Germany). A non-ionic contrast agent (Ultravist 370 (iopromide); Schering, Berlin, Germany), with a total volume of 80 ml, was injected intravenously at a rate of 3 mL/sec. CT acquisition was obtained according to the standard protocol of our institution at arterial phase (usually 20 to 40 seconds after the injection). The parameters used were 90 kVp, 150 mAs, 0.75 mm collimation for 16 slices and 80 kVp, 150 mAs, 0.625 mm collimation for 64 slices. Both scanners used a 512 × 512 matrix and a selected field of view ranging from 180 to 240 mm. The CT-angiography files of 235 patients were collected from the servers of the department of radiology. Demographic data were obtained from each patient's electronic chart.

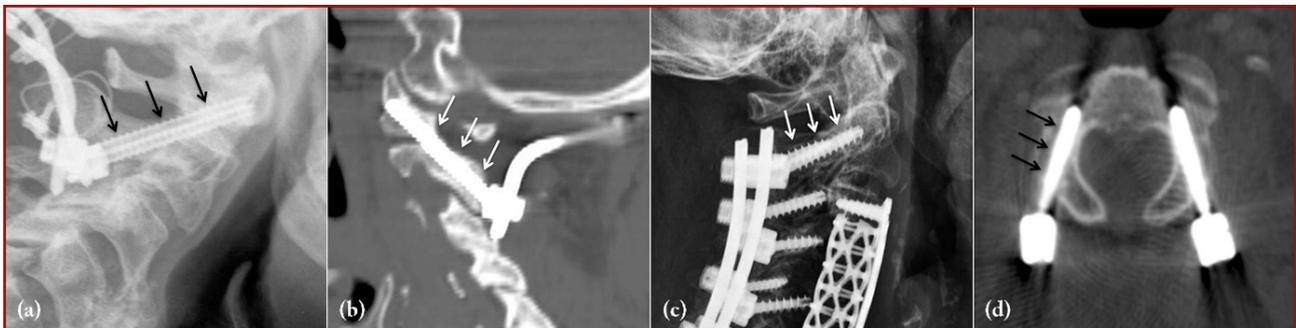
The indications for CT-angiography examination were including medical, vascular, neurological, and/or surgical conditions. Patients with medical conditions distorting the anatomy at the level of the C2 vertebra including a tumor, infection, acquired C1 or C2 deformities, trauma, and postoperative CT-angiography scans, and patients younger than 20 years old were excluded from the study.

Moreover, scans of patients with congenital cervical or craniovertebral junction anomalies were also excluded. In addition, scans with imaging artifacts (i.e., metal or motion artifacts) were excluded. First, DICOM files of CT-angiograms (transverse images with the reconstruction interval of 1.0 mm) were loaded onto the workstation using Siemens Syngo 3-dimensional tools (Leonardo, Siemens Medical System, Erlangen, Germany). Then the sagittal, coronal and axial MPR images that corresponded to the pedicle and isthmus of the C2 vertebra with 1.0 mm slice thickness were obtained using multi-planar reconstruction (MPR), and pedicle and isthmus measurements of the C2 vertebra were evaluated bilaterally.

An HRVA was defined using two parameters. Firstly, the isthmus thickness was measured on the sagittal MPR images by measuring the distance from dorsal to the ventral cortex of the isthmus at the level of the intraosseous canal as shown in Fig. 2a.

Secondly, the internal height was measured on sagittal images by measuring the distance between the roof of the intraosseous canal and superior facet of C2 lateral mass, as also shown in Fig. 2a.

Both of these parameters were measured on a sagittal image passing at the mid-portion of the atlantoaxial joint. An HRVA was considered when the isthmus thickness was less than 5 mm, and/or the internal height was less than 2 mm as previously described (8,14,18-19). MSVA was defined on axial MPR images by using one parameter: the pedicle width measured at the level where the lateral cortical margin of the pedicle was clearly seen at the uppermost level of the intraosseous canal (Fig. 2b).



**Figure-1.** X-ray and CT demonstrations of the paths of the C1-C2 transarticular screw and C2 pedicle screw on two different patients. Postoperative lateral plain radiograph (a) and sagittal CT (b) images of a patient with unstable dens fracture. C1-C2 transarticular screw traverses the isthmus of the C2 pars-interarticularis, passing the atlantoaxial joint and reaching the lateral mass of C1 (black and white arrows). Postoperative lateral plain radiograph (c) and axial CT (d) images of a patient with cervical spinal stenosis. C2 pedicle screw passes the C2 isthmus and pedicle and reaches the C2 vertebral body (white and black arrows)

MSVA was considered to be present when the pedicle is narrower than 4 mm. The diameters of commonly used screws are 3.5 or 4.0 mm; therefore, pedicles with a width of less than 4 mm have been considered to be narrow in the literature<sup>(28)</sup>.

Each scan was also evaluated for the presence or absence of side-to-side asymmetry of the VA (left or right-sided VA dominance or co-dominance). Cases of left or right-sided VA dominance were noted when the lumen diameter of the VA on one side was at least 30 % larger than that of the other side.

The presence or absence of an HRVA and 118 MSVA were determined for each side in all patients. The correlation between the high-riding and medial-shifting occurrences were examined accounting for age, sex, laterality, and existence of ipsilateral dominance of VA.

### Statistical Analysis

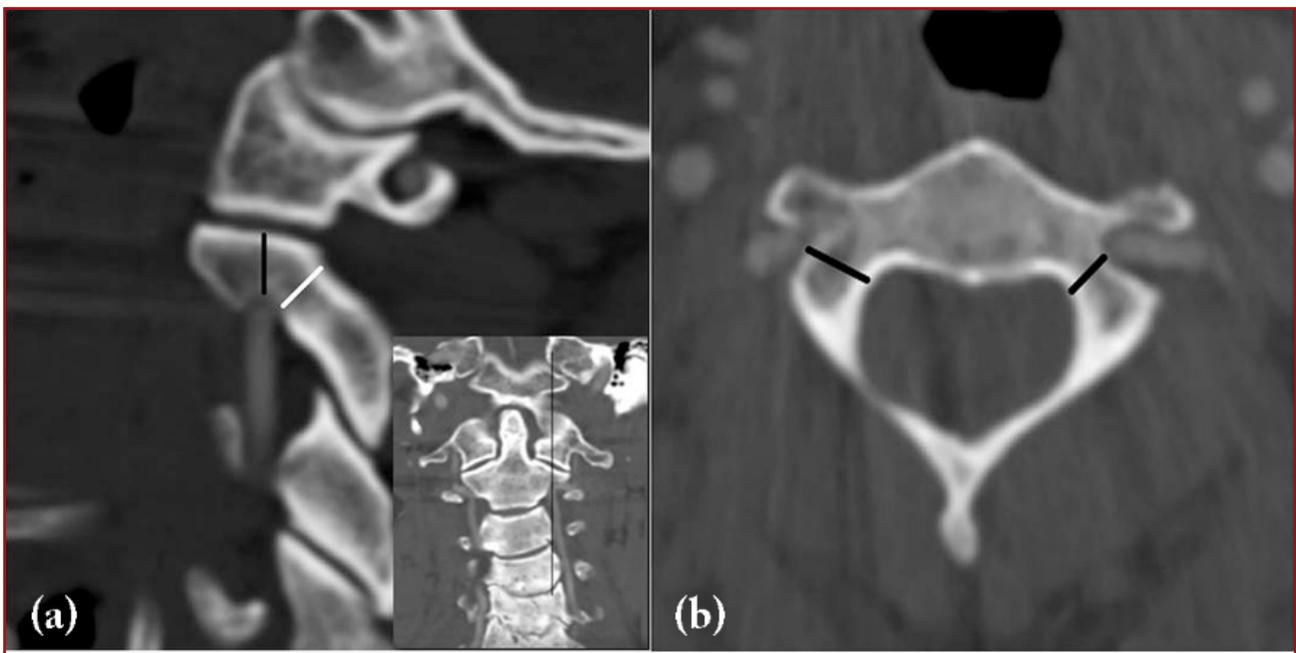
Isthmus thickness, internal height, and pedicle width measurements were made by a single experienced musculoskeletal radiologist analyzing eligible CT-angiograms of 216 patients for a total of 432 VAs. To ensure the reliability of our data, we re-examined the thickness, height and width scores for 45 randomly chosen (using 'sample' function in R-language) CT-angiograms (20% of total) after 8 weeks. For reliability tests, we used a two-tailed paired t-tests within a boot strapping framework. Difference distributions obtained from 10000 random comparisons (of size 25) between the first and second measurements for the same patients show that the two measurements are statistically equivalent in all three sets (0 belongs to 95 % CI).

Differences between isthmus thickness, internal height and pedicle width across different categorizations (male vs. female, right side vs. left side) were examined using a two-tailed Welch's t-test. We also examined the relationship between age and the pedicle and isthmus bone parameters of the C2 vertebra by using Pearson's product moment correlation. Pearson's chi-square test with Yates' continuity correction (to improve the approximation to discrete probabilities) was implemented to spot significant differences between occurrences of HRVA and MSVA across different categorizations (male vs. female, right side vs. left side) and to identify relationships between arterial pathologies and side to side VA asymmetry. Finally, to detect the relationship between age and HRVA and MSVA occurrences, we used comparisons based on Pearson's moment correlation test and a bivariate logistic regression search algorithm.

### RESULTS

We excluded 19 patients based on the exclusion criteria. Finally, a total number of 216 patients, 91 females and 125 males, were enrolled in the study. The mean age of the study population was 62,7 years (range, 20–92 years).

The averaged values and corresponding ranges of the internal height, isthmus thickness, and pedicle width scores are depicted in table 1. Females had significantly lower values compared to males in terms of internal height, isthmus thickness and pedicle width scores ( $P<0,01$ ) (Table-1).



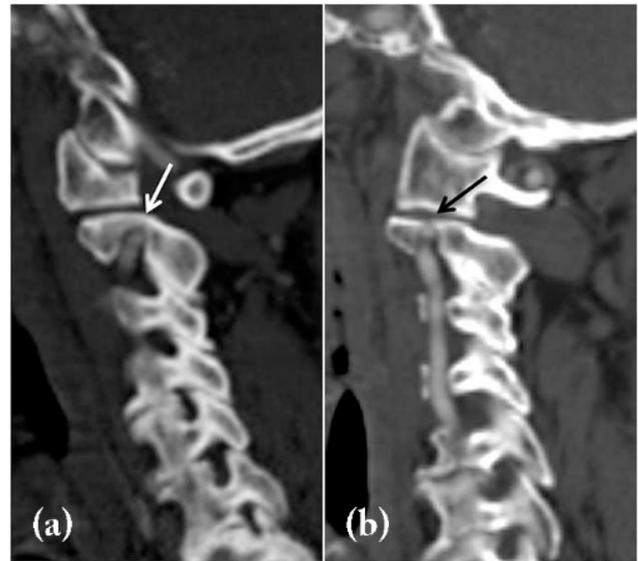
**Figure-2. (a)** Demonstrations of how to measure internal height (black line) and isthmus thickness (white line) on sagittal MPR image for defining high-riding variant. This sagittal image passes at the midpoint of the atlantoaxial joint as shown by the vertical thin black line on coronal image in smaller corner figure. **(b)** Demonstration of how to measure pedicle widths (black lines) on axial MPR image for defining medial-shifting variant

However, there was no significant difference between right and left sides when the male-female difference was ignored ( $P= 0,247$ ). Correlations between bone parameters and age were close to zero and statistically insignificant.

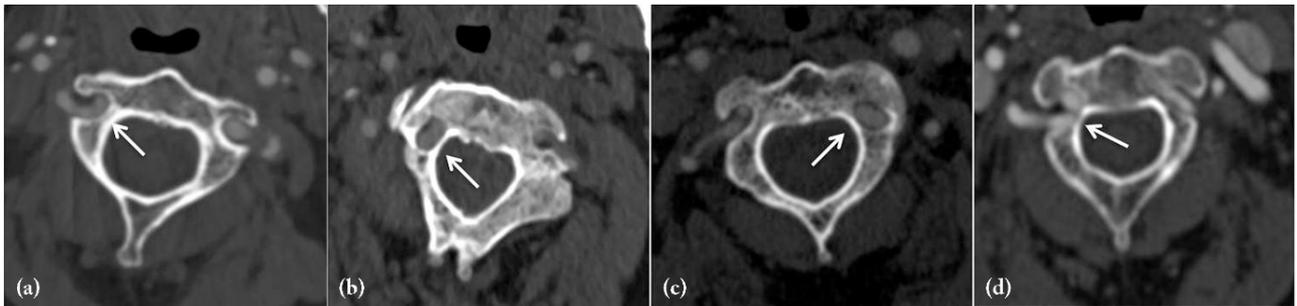
In 53 (24 %) of the 216 patients, there was at least one abnormality in the intraosseous course of VA at the level of C2. In 40 (18 %) of 216 patients, an HRVA (Fig. 3) was detected either unilaterally or bilaterally. Of these 40 patients, 15 were men and 25 were women. MSVA (Fig. 4) was identified in 45 (20,8%) patients (18 men, 27 women). Distributions of VA variations across gender and laterality are shown in Table-2.

Overall there was a statistically significant difference between males and females for HRVA (propensity to have this condition was higher for women) ( $P<0,05$ ) (Table-2). The difference between males and females concerning MSVA occurrence was also statistically significant (women scoring higher) which once again appeared at  $P<0,05$  level (Table-2).

However, in both abnormalities when we ignored male-female distinction and solely focused on the right and left side occurrences we failed to spot any statistical difference ( $P=0,3$ ). When we examined the correlations between increasing age categories (each comprising 10 years) and HRVA and MSVA occurrences, we again failed to detect any significant relationship (Table-3).



**Figure-3.** CT-angiography images of two different patients with high-riding VA. **(a)** Sagittal MPR image shows decrease of isthmus thickness (white arrow) and **(b)** sagittal MPR image shows decrease of internal height (black arrow)



**Figure 4.** CT-angiography axial MPR images through the C2 intraosseous canal of four different patients demonstrate variable degrees of narrowing of pedicles indicating medial-shifting VA for each four cases (arrows)

**Table 1.** Descriptive statistics and male-female differences

	Male (n=125)				Female (n=91)				Differences			
	Mean	Sd	Min	Max	Mean	Sd	Min	Max	Mean	Se	P-value	
<b>Internal height</b>												
Right	4.29	1.00	1.5	7.1	3.46	1.03	1	6	0.83	0.14	0.000	**
Left	4.20	0.97	1.4	7.1	3.31	0.96	0.8	5.5	0.90	0.13	0.000	**
<b>Isthmus thickness</b>												
Right	6.53	1.16	3.5	8.9	5.77	1.17	2.7	8.7	0.76	0.16	0.000	**
Left	6.68	1.12	2.2	9.1	5.82	1.13	2.4	8.3	0.86	0.16	0.000	**
<b>Pedicle width</b>												
Right	5.56	1.339	0.1	9	4.93	1.30	1	7.5	0.63	0.18	0.001	**
Left	5.73	1.336	1.3	8.7	5.06	1.49	1.7	9.1	0.67	0.20	0.001	**

Sd: standard deviation

Se: standard error

\*\* : significant at 0.01

P-values are derived from Welch's t-test.

Of all VAs 14,5 % (63/432) had at least one abnormality - either high-riding or medial-shifting variant, or both. There were 49 high-riding (11,3 %) and 54 medial-shifting VAs (12,5 %) among the 432 VAs. Of the MSVA group, 74,4 % (40/54) had a co-occurrent HRVA variation ipsilaterally. On the other hand, 81,6 % (40/49) of the high-riding VAs had concurrent MSVA variation (Table-4).

We detected unilateral VA dominance in 118 of our subjects 166 (55 % of 216). Left and right sided VA dominance were found in 83 (39 %) and 35 (16 %) subjects respectively. Among the arteries with anatomic variations (63/432), 36,5% (23/63) of these were observed on the artery of the dominant side, 12,6% (8/63) on the non-dominant artery and 50,7 % (32/63) in co-dominant cases.

The laterality of the arterial variation and the VA dominance were more likely to occur on the same side than on opposite sides, and this co-occurrence was more frequent for the left side. When we ignored the co-dominant cases, the laterality of VA dominance and variations were correlated. This relationship between laterality of arterial variation and VA dominance was statistically significant ( $P < 0,05$ ) (Table-5).

**Table 2.** Distribution of variations across gender and laterality

Arterial variations	Male (n=125)	Female (n=91)	P-value	
High-riding	15	25	0.0066	**
Right	7	6	0.7459	
Left	6	12	0.0314	*
Bilateral	2	7	0.0392	*
Medial-shifting	18	27	0.0105	*
Right	9	9	0.5783	
Left	6	12	0.0394	*
Bilateral	3	6	0.1606	

\*\* : significant at 0.01

\* : significant at 0.05

P-values are derived from Pearson's Chi-square test with Yates' continuity correction.

**Table 3.** Relationship between age and VA variations

Age intervals	Observations	Age		High-riding		Medial-shifting		Correlations					
		I	Increasing intervals	II	Counts	III	%	IV	V	Correlating variables	r	P-value	
20-29	11	1		1		9.1		4		36.4			
30-39	17	2		3		17.6		2		11.8	I-II	0.394	0.3812
40-49	17	3		4		23.5		4		23.5	I-III	-0.139	0.7660
50-59	36	4		9		25		9		25	I-IV	0.333	0.4650
60-69	44	5		11		25		12		27.3	I-V	-0.554	0.1963
70-79	63	6		11		17.5		13		20.6	I-III"	0.566	0.2412
80-89^	27	7		1		3.7		1		3.7	I-V"	-0.205	0.6966

r: Pearson's product-moment correlation coefficient.

P-values are derived from correlation test based on t distribution with n-2 df where n is the number of categories.

If p-value > 0.1 then true population correlation equals to zero.

" : seventh age category is ignored in these estimations.

^ : There is only a single person in 90-99 age interval. This patient is not included into the analysis.

**Table 4.** Co-occurrence of high-riding and medial-shifting

High-riding	Medial-shifting		%
	No	Yes	
No	369	14	
Yes	9	40	81.6
	%	74.4	P-value=0.0000 **

\*\* : significant at 0.01

P-value is derived from Pearson's Chi-square test with Yates' continuity correction.

**Table 5.** Relationship between arterial dominance and laterality of VA variations

		Dominancy of VA			
		Codominant	Left	Right	
High-riding or Medial-shifting	None	164	148	57	p-value= 0.01368 *
	Left	19	12	2	
	Right	13	6	11	

\* : significant at 0.05

P-value is derived from Pearson's Chi-square test with Yates' continuity correction.

## DISCUSSION

Up to now, four studies have been evaluated the narrow pedicle concept separately from the HRVA concept. Yeom et al. (28) and Wajanavisit et al. (21) assessed non-enhanced CT of 269 and 200 consecutive patients respectively. However, they did not evaluate the relationships of these variations with age, sex, and laterality with the VA dominance.

On the other hand, Lee et al. (11) and Maki et al. (14) separated the arterial variation into two groups as high-riding and medial-shifting, and each study assessed 100 patients with CT-angiography. Nevertheless, the major limitations of those studies were the small number of patients. To the best of our knowledge, we have conducted the first CT-angiographic study, which separately investigates these two intraosseous VA variations on a sufficiently large number of subjects.

The posterior C1-C2 transarticular screw fixation technique developed by Magerl et al. (13) is used successfully in craniovertebral junction stabilization surgery as an effective method for achieving fusion (2,6,12-13,24-25). However, VA injury is a potential complication, which may lead to morbidity and mortality (2,6,12,24-25). According to previous studies, the rate of vertebral artery injury of C1-C2 transarticular screw placement ranges from 4.1 % to 8.2 % and the reported rate of neurologic events from VA injury is 0.2 % per patient (1.9 % per VA injury) (2,12,18,25). The HRVA is known as one of the significant causes of this complication (15,19).

C2 pedicle screw insertion has become a favorite technique for numerous conditions that require C2 vertebra fixation, and during this procedure, a narrow C2 pedicle would also predispose to VA injury (1,4,11,27,29). Jian et al. (10) reported on a patient in whom one of the C2 pedicle screws was inserted into the C2 intraosseous canal during an occipitocervical posterior fusion operation. The VA injury in this patient resulted in a thrombosis with subsequent brain stem infarction.

Non-enhanced CT is the commonly utilized method for detecting both HRVA and MSVA conditions preoperatively. The assessment is generally carried out by measuring the bone parameters in the C2 intraosseous canal using thin-slice reformatted CT images (2,5,14,22,26).

However, numerous authors have emphasized that the assessment of the VA is as significant as the evaluation of the

osseous canal and advocated the assessment of preoperative risk by CT angiography (5,11,16,22,26-27). Compared to the non-enhanced CT, the additional advantages of CT angiography over non-enhanced CT include ability to determine the presence or absence of dominant VA, the ratio of the VA diameter to the interosseous canal diameter, show relative position of the VA within the C2 canal with respect to the bony edges of the canal, and detect the other vertebral artery anomalies.

Depending on the methods and descriptions, the prevalence of HRVA ranges between 11,7 % and 23 % and the prevalence of narrow pedicle/MSVA reported as between 9,5 % and 32 % (12,14-15,18-19,22-23). In our study, the prevalence of HRVA and MSVA were 18 % and 20,8 %, respectively, and we observed both VA variations were more common in females as similar to those of previous studies.

We did not observe any significant correlation between age and the HRVA-MSVA. However, Lee et al. (11) showed that both high-riding and medial-shifting pattern of VA positively correlated with age and they claimed this might be associated the age-related degenerative process and arterial tortuosity. They also suggested arterial ectasia and/or tortuosity might increase the risk of arterial injury as the arteries occupy a larger area in the intraosseous canal and become more vulnerable.

For patients who have asymmetry of the VA and high-riding and/or medial-shifting variant at the dominant artery side, screw placement procedures should be undertaken carefully or abandoned (5,25). If the dominant VA is injured during surgery, the incidence of neurologic events will be increased. Notably, in our study, slightly more than one-third of all cases with VA variation were observed at the side of the dominant VA contrary to previous studies, in which the relationship between the VA variations and VA dominance was not significant (11,27). We suggested the small sample size in these studies might have led the inconsistencies between the results. We highlight that VA asymmetry should be considered and investigated for patients who had HRVA and/or MSVA detected on non-enhanced CT examination when C2 instrumentation required, particularly for those on the left side.

We had several limitations in our study. First, we used two-dimensional measurements for defining HRVA and MSVA variations. A three-dimensional evaluation would probably

give more precise results for this complex anatomy. In fact, defining easy-to-use three-dimensional measurement parameters for these VA variations would be a fascinating subject for further study.

Second, lacking the assessment of VA anomalies above or below C2 level should be noted as another limitation of our study. It would also be prudent to emphasize that the incidence of anatomical VA variations might be more common in patients with congenital malformations of the cervical spine.

In conclusion, the VAs showed at least one variation in 24 % of our population with high possibility of ipsilateral co-occurrence dominant side; hence, we emphasize VAs should be assessed preoperatively if C2 screw placement required.

### Key Points

- VA injury is a potential complication of C2 instrumentation surgery
- 24 % of population have at least one VA variation at the level of C2 intraosseous canal
- In cases with dominant VA, the laterality of VA dominance and variations were correlated
- Preoperative assessment of the varieties courses of VA at the level of C2 is necessary

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