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Analysis of the cervical double transverse foramen in present Spanish population

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SUMMARY

The aim of our study was to investigate the prevalence and morphometry of double transverse foramina in cervical vertebrae in a living population and to discuss their clinical importance. This is a retrospective single-center study. 253 (84.3%) computed tomography scan images of the cervical spine were collected from a total sample of 300 Spanish subjects that underwent a computed tomography study, 173 from men (68.3%) and 80 from women (31.6%), aged between 18 and 90 years old. The presence or absence of a double transverse foramen of each cervical vertebra was recorded, and the maximum right-left diameter, maximum antero-posterior diameter and area of each transverse foramen were measured. The applied statistics were multivariate models for repeated measures, Student t test and Pearson's chi -squared test.

Double transverse foramina in C4, C5, C6 and C7 were observed, the most prevalent being in C6 (45.8%), followed by C5 (23.5%), C4 (4.7%) and C7 (4.3%). The unilateral formation was significantly the most frequent. No differences were found based on sex. In the vertebrae with a double transverse foramen, the principal transverse foramen was significantly larger than the accessory transverse foramen. However, in these vertebrae the principal transverse foramen was significantly smaller when compared with the transverse foramen of normal vertebrae.

C6 presents the greatest prevalence of double transverse foramina, although they are also observed in C4, C5 and C7. The double transverse foramen causes the principal transverse foramen to be smaller when compared with normal vertebrae, thus it should be taken into account in clinical practice.

Key words: Anatomy – Skeleton – Spine – Computed tomography – Spain

INTRODUCTION

The cervical spine presents biomechanical and anatomical differences in comparison with dorsal and lumbar vertebrae. One of the differences is the presence of a transverse foramen (TF) in the transverse process of cervical vertebrae, through which the vertebral artery and veins and sympathetic nerves pass, with the exception of the TF in C7 which the vertebral artery does not pass through (Jovanovic, 1990) (Fig. 1A).

The vertebral arteries are composed of four segments (Fig. 1B and Fig. 1C). Segment V1, the extra-osseous segment, goes from the beginning of the vertebral artery until the transverse foramen of the C6. Segment V2 is the foraminal

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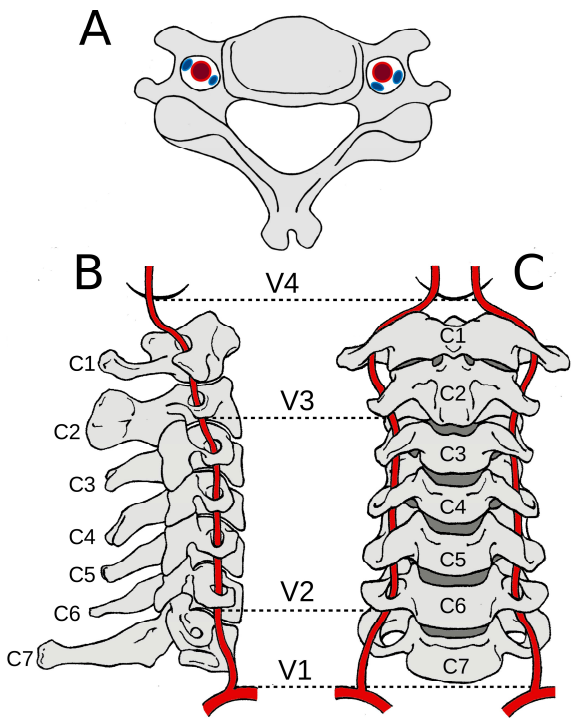

Fig. 1. Scheme of the vertebral arteries in the cervical vertebrae TF. (**A**) Transversal view of a typical cervical vertebra showing the vertebral artery and veins passing through the TF. (**B**) Lateral view of cervical spine and vertebral artery. (**C**) Anterior view of cervical spine and vertebral arteries. The vertebral artery is composed of 4 segments: V1 begins at the origin on the subclavian artery and extends to the C6 TF; V2 runs from the C6 TF to the C2 TF; V3 extends from the C2 TF to the foramen magnum; V4 runs from the foramen magnum to the vertebrobasilar junction.

segment, where the artery passes through the transverse foramina from C6 to C2. The extraspinal segment, V3, begins at the foramen transversarium of C2. At this segment, the vertebral artery passes along the superior aspect of the posterior ring of C1, and then twists antero-superior towards the foramen magnum where it pierces the dura. Lastly, V4, the intradural segment, courses to the pontomedullary junction, where the basilar artery is formed (Desouza et al., 2011).

Moreover, the cervical spine is the segment with the most mobility of the spine. Therefore the relevant clinical implications of the TF are obvious in cases of possible compression or trauma of structures that cross it, especially in relation to the vertebral artery, depending on whether or not it affects normal blood flow (Taitz et al., 1978). In this context, variations in TF number and size are involved in the etiology of some clinical syndromes and symptoms like headache, migraine, fainting, vertebrobasilar insufficiency as a response to certain neck movements, and blackouts due to low blood pressure in the vertebral artery (Bulsara et al., 2006).

The TF can be multiple or absent and may present anatomical variations with respect to its shape and size. When it is multiple, the accessory TF (ATF) usually appears posterior to, and smaller than, the primary foramen (PTF) (Kaya et al., 2011). This anatomical variant, called double transverse foramen (DTF), has been found in the inferior cervical rachis, either unilaterally or bilaterally, and located more often in C6 (Murlimanju et al., 2011; Chandravadiya et al., 2013). In terms of its etiology, DTF may be related to variations of the course and development of the vertebral artery (Das et al., 2005). In addition, it is fundamental to understand the anatomic variations of the TF in order to properly plan surgical procedures of the cervical spine including screw fixation, since the osseous and vascular variations of the cervical spine can place the vertebral artery at risk during surgery (Peng et al., 2009).

We hypothesize that there were morphometric differences between the PTF, the ATF and the normal TF at all the cervical levels presenting DTF. Following on from this, the aim of our study was to investigate the quantitative anatomy and morphometry of TF with emphasis on the prevalence of DTF in order to increase and consolidate the current anatomic knowledge, as the TF is fundamental for surgical treatment of vertebral artery dissection and laceration.

MATERIALS AND METHODS

Patient sample

This was a morphologically based, retrospectively designed and single-center study. It was approved by the Ethics Committee in Human Research of the University of Valencia (ref. H1414410627187). The procedures were performed in accordance with the World Medical Association Declaration of Helsinki (1975 and subsequent additions).

We reviewed computed tomography (CT) cervical scans of 300 consecutive Spaniard subjects aged between 18 and 90 years old. CT studies were carried out at the CT ERESA Unit at the University General Hospital of Valencia, Spain. The CT scans were reviewed by two different radiologists. Only when both radiologists coincided in the diagnosis the CT images were used for the study.

Inclusion criteria were Spanish subjects aged more than 18 years that underwent a CT study. The exclusion criteria were: incomplete studies (when the complete cervical spine was not included), metal artifact imaging, previous cervical spine surgery, trauma or vertebral fractures, tumor history or cervical spine infections, severe rheumatic disease, myelopathies and congenital cervical malformations, as well as those related to Down Syndrome, Turner Syndrome, Arnold-Chiari malformation, Klippel-Feil Syndrome, and other

Table 1. Number of CT scan images analyzed and number of CT scan images discarded by diagnosis disparity between radiologists

Cervical level	CT scan images analyzed	CT scan images discarded
C1	226 (89.3%)	27 (10.6%)
C2	193 (76.2%)	60 (23.7%)
C3	233 (92.0%)	20 (7.9%)
C4	234 (92.4%)	19 (7.5%)
C5	234 (92.4%)	19 (7.5%)
C6	214 (84.5)	39 (15.4%)
C7	207 (81.8%)	46 (18.1%)

CT = computed tomography scan

congenital malformation syndromes.

In accordance with our inclusion and exclusion criteria, 253 (84.3%) CT scan images of the cervical spine were collected from a total sample of 300 Spanish subjects (100%), 173 men (68.3%) and 80 women (31.6%). Table 1 shows the number of images that were analyzed at each cervical level as well as the number of images that were discarded because there was no coincidence between radiologists.

The mean overall age of the study sample was 63.5 ± 13.0 years old. The mean age of the men (64.7 ± 11.2 years old) was slightly higher than that of the women (60.9 ± 16.1 years old) and this difference was statistically significant (Student t test p = 0.033). The main reason for performing the CT scans that were analyzed in this study was internal carotid artery diseases (82.6%), followed by other vascular diseases that did not affect the vertebral artery (10.6%), certain types of neoplasms (4.4%), and cerebrovascular diseases (2.4%).

CT scan protocol

All the image studies were performed with a GE LightSpeed VCT 64 Slice CT system (General Electric, Milwaukee, WI, USA) providing an axial-field of view of 350-400 mm and a trans-axial slice thickness of 0.5 mm. A low-dose CT scan from the aortic arch through the orbitomeatal baseline was obtained with the patient in the supine position (120Kvp, 300mAs, 0.5-s rotation time, 16x0.5mm collimation, pitch of 0.64).

An 18 to 20 gauge angiocath was inserted into the antecubital vein of all the patients. Over 70–120 ml of non-ionic iodinated contrast media (iopamidol 300) followed by 30 ml of saline solution was injected with an automatic injector at a rate of 5 ml/sec. The bolus-tracking method proved very useful for correct filling of the vertebral arteries. The region of interest was positioned at the aortic arch, and the threshold was set at 100-120 HU; when it was surpassed, helical scanning was automatically initiated.

Morphometric parameters

Images were analyzed on a GE Advantage Windows 4.5 workstation. Three measurements for each TF of all cervical vertebrae were obtained using screen images: its width (maximum right-left diameter) its depth (maximum antero-posterior diameter) and its area were recorded. The larger TF was deemed the principal (PTF) in the vertebrae with a DTF, while the smaller and accessory of the two foramina was deemed the ATF. Fig. 2 shows an example of a dry C6 vertebra with bilateral DTF, and Fig. 3 shows CT scan images of C4, C5 and C6 vertebrae with unilateral DTF.

Statistical analyses

The descriptive statistics were calculated to define the sample. Multivariate models for repeated measures were used to adjust for uncertain variables like age and sex. Student t test was used to estimate the differences of the means between two independent groups. Pearson's chi-squared test was used to compare the distributions of the frequencies. A p value of ≤ 0.05 was considered significant. Continuous variables are showed as average and standard deviation of the mean. Category variables are shown as frequencies. The statistical analyses were performed with SPSS ver.13 statistical software package (SPSS Inc., Chicago, IL, USA).

RESULTS

After adjustment for uncertain variables like sex and age, there were no statistically significant differences between men and women regarding the presence of DTF: 7 C4 vertebrae (4.3%) with DTF in men, and 4 (5.6%) in women (p = 0.453); 35 C5 vertebrae (21.7%) with DTF in men, and 20 (27.4%) in women (p = 0.217); 69 C6 vertebrae (46.6%) with DTF in men, and 29 (43.9%) in women (p = 0.415); 4 C7 vertebrae (2.8%) with DTF in men, and 5 (7.6%) in women (p = 0.119).

The general prevalence of DTF in all the vertebrae analyzed was 11.2%. The presence of DTF

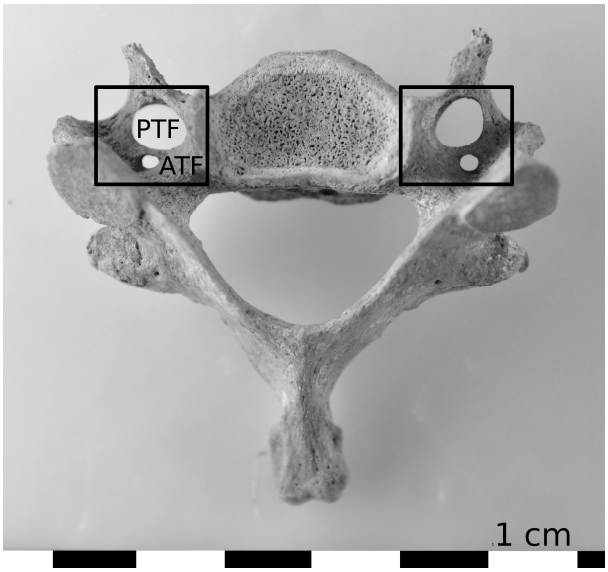

Fig. 2. Image of a dry C6 vertebra with bilateral DTF. PTF: principal transverse foramen. ATF: accessory transverse foramen.

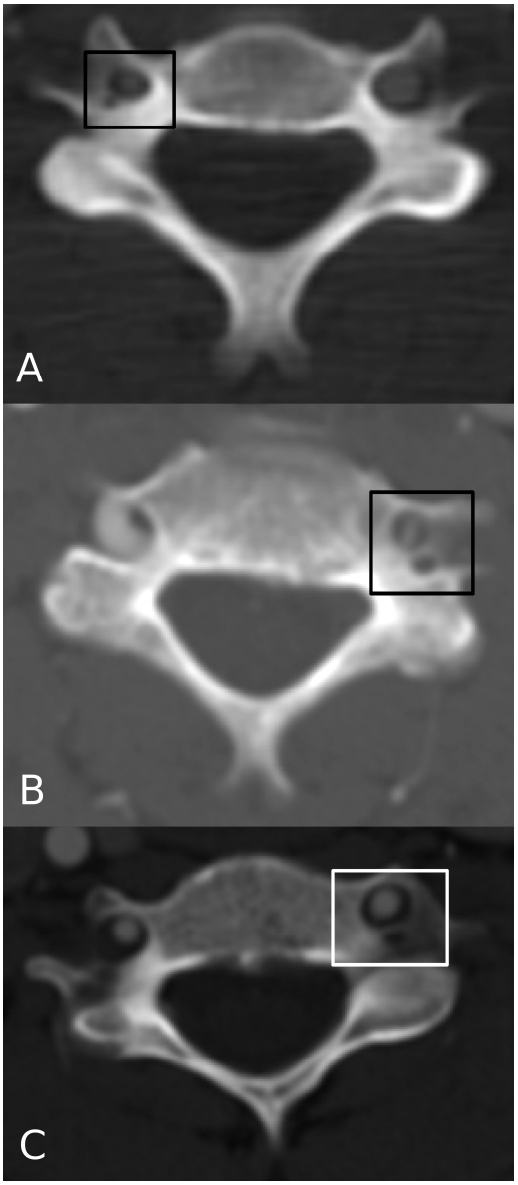

Fig. 3. CT scan images of cervical vertebrae with DTF. (**A**) C4 vertebra with a right DTF. (**B**) C5 vertebra with a left DTF. (**C**) C6 vertebra with a left DTF.

was more frequent in C6 (98 vertebrae, 45.8%), followed by C5 (55 vertebrae, 23.5%), C4 (11 vertebrae, 4.7%) and C7 (9 vertebrae, 4.3%). Depending on which side was the altered one, the frequency of DTF by cervical level was as follows: in C4, 7 (0.2%) on the right side, 3 (1.2%) on the left side and 1 (0.4%) bilateral; in C5, 30 (12.8%) on the right side, 13 (5.5%) on the left side and 12 (5.1%) bilateral; in C6, 35 (16.3%) on the right side, 21 (9.8%) on the left side and 42 (19.6%) bilateral; and in C7, 6 (2.8%) on the right side, 3 (1.4%) on the left side and 0 (0,0%) bilateral. There was a statistically significant greater prevalence of unilateral DTF than bilateral cases in C4 (p=0.004), C5 (p=0.001) and C6 (p=0.001). In addition, there was a greater prevalence of DTF on the right side at all four cervical levels studied, although this difference was not statistically significant (C4 p=0.476, C5 p=0.154, C6 p=0.303, C7 p=0.453).

In the vertebrae presenting DTF (C4-C7) we observed sexual differences in TF measurements. The lateral diameter, antero-posterior diameter and area of TF were bigger in men than in women. This difference was statistically significant for the antero-posterior diameter at C1, the lateral diameter at C1-C6 and the area at C1, C3-C6 (Table 2).

The antero-posterior diameter, lateral diameter and area of the PTF were larger than the ones of the ATF in all the vertebrae with DTF, and these differences were statistically significant at all the cervical levels analyzed, except in the case of the lateral diameter and area of the PTF of C7, in both men and women (Table 3).

As Table 4 shows, when comparing the dimensions of the PTF in vertebrae presenting DTF with the dimensions of the TF in vertebrae without a DTF at the cervical levels C4, C5, C6 and C7, the presence of DTF determined a smaller size of the PTF in comparison with the TF of normal vertebrae. This difference was statistically significant in both men and women (except for the lateral diameter of C6 and C7 in men, and the lateral diameter of C6 in women).

Table 2. Sexual differences in measurements of TF of normal cervical vertebrae

Cervical level		Men		Women		
		Media ± SD	Range	Media ± SD	Range	p[4]
C1 (♂=154, ♀=72)	Ø AP [1]	7.1 ± 1.0	3.2 - 10.0	6.7 ± 1.0	3.8 - 9.6	0.001
	Ø lat [2]	5.9 ± 0.9	3.6 - 9.1	5.5 ± 0.8	3.7 - 7.8	<0.001
	Area [3]	31.7 ± 6.7	12.6 - 48.9	27.3 ± 5.0	15.4 - 37.9	<0.001
C2 (♂=132, ♀=61)	Ø AP [1]	6.3 ± 1.1	3.2 - 10.3	6.3 ± 1.2	3.4 - 9.3	0.878
	Ø lat [2]	6.1 ± 1.3	3.0 - 9.8	5.6 ± 1.0	3.6 - 8.1	0.001
	Area [3]	29.2 ± 6.9	13.1 - 53.7	27.8 ± 6.0	10.3 - 43.2	0.057
C3 (♂=159, ♀=74)	Ø AP [1]	4.8 ± 0.6	3.0 - 7.4	4.7 ± 0.6	3.2 - 6.5	0.051
	Ø lat [2]	6.5 ± 0.7	3.9 - 8.4	6.1 ± 0.8	4.0 - 8.5	<0.001
	Area [3]	24.7 ± 4.8	8.7 - 42.7	22.4 ± 5.0	12.1 - 36.9	<0.001
C4 (♂=152, ♀=71)	Ø AP [1]	4.8 ± 0.6	3.1 - 6.6	4.8 ± 0.7	3.0 - 7.8	0.845
	Ø lat [2]	6.4 ± 0.7	3.6 - 8.4	6.0 ± 0.7	4.2 - 8.2	<0.001
	Area [3]	24.2 ± 4.8	9.2 - 43.9	22.3 ± 5.2	11.9 - 38.7	<0.001
C5 (♂=122, ♀=57)	Ø AP [1]	5.2 ± 0.7	2.9 - 7.8	5.0 ± 0.6	3.2 - 7.1	0.052
	Ø lat [2]	6.4 ± 0.9	3.4 - 9.1	6.0 ± 0.8	4.1 - 7.9	<0.001
	Area [3]	26.3 ± 5.2	9.9 - 44.4	23.5 ± 4.8	8.4 - 33.4	<0.001
C6 (♂=79, ♀=37)	Ø AP [1]	5.5 ± 0.8	3.2 - 7.6	5.3 ± 0.8	1.8 - 7.8	0.085
	Ø lat [2]	6.6 ± 1.0	3,4 - 10.0	6.0 ± 1.0	1.7 - 8.7	<0.001
	Area [3]	28.3 ± 6.0	10.5 - 48.1	24.7 ± 5.3	3.5 - 33.7	<0.001
C7 (♂=135, ♀=63)	Ø AP [1]	5.0 ± 1.4	1.4 - 10.1	4.8 ± 1.3	1.7 - 8.8	0.178
	Ø lat [2]	3.2 ± 0.9	1.0 - 6.2	3.1 ± 1.0	1.2 - 8.5	0.433
	Area [3]	12.7 ± 6.3	2.0 - 41.0	11.6 ± 5.8	1.6 - 38.0	0.112

SD: Standard Deviation; [1] antero-posterior diameter (mm); [2] lateral diameter (mm); [3] area (mm2); [4] P-value in comparison between men and women (Student t test)

DISCUSSION

In this study we analyzed the prevalence of DTF in complete cervical sets taking into account both the overall prevalence of DTF and the prevalence corresponding to each cervical level. The overall frequency of DTF is one of the data that is most usually reported in previous studies, but DTF prevalence presents very variable results, possibly because of the diverse research methodologies that are used. The overall frequency observed in our sample population was 11.2%, which is similar to that reported by previous authors on cervical sets (4.7% - 16.5%) (Taitz et al., 1978; De Boeck et al., 1984; Jovanovic, 1990; Jaffar et al., 2004; Sanchis-Gimeno et al., 2005; Sharma et al., 2010; Chandravadiya et al., 2013; Gupta et al., 2014; Patil et al., 2014). However, among these studies there are authors who did not analyze complete cervical sets, but rather cervical segments only. Jovanovic (1990) only studied C6-C7; Sharma et al. (2010) and Agrawal et al. (2012) analyzed only C3-C6. Therefore the frequencies observed by these three authors do not in fact refer to the seven cervical levels as a whole.

Although other studies provide values that refer to the overall prevalence of DTF in the cervical spine, their results do not refer to cervical sets, whether complete or incomplete, but to the compendium of isolated vertebrae brought together in order to be studied; in addition, the number of subjects such studies were from is not stated (Nagar et al., 1999; Aydinoğlu et al., 2001; Das et al., 2005; Kaya et al., 2011; Murlimanju et al., 2011; Chaudhari et al., 2013; Rathnakar et al., 2013; Katikireddi and Setty, 2014; Mishra et al., 2014; Murugan and Verma, 2014; Ramachandran et al., 2014; Shah et al., 2014; Yadav et al., 2014; Dofe et al., 2015; Kumari et al., 2015; Patra et al., 2015). The random nature of the origin of the vertebrae that were analyzed in these studies makes the overall frequencies of DTF very variable, ranging from 1.4% to 42.6%. Their results are not comparable with ours because of the different methodologies they used in the selection of the

Table 3. Quantitative differences between the PTF and the ATF in vertebrae with DTF

Cervical level			Men			Women		
			Mean ± SD	Range	P-value [4]	Mean ± SD	Range	P-value [4]
C4	ATF	Ø AP [1]	1.4 ± 0.4	1.0 - 2.2	<0.001	1.2 ± 0.2	0.9 - 1.5	<0.001
	PTF		4.2 ± 1.1	3.0 - 6.8		3.9 ± 0.4	3.3 - 4.3	
	ATF	Ø lat [2]	2.0 ± 0.4	1.5 - 2.8	<0.001	1.6 ± 0.4	1.0 - 2.2	0.002
	PTF		5.5 ± 1.1	4.0 - 7.6		5.6 ± 1.4	3.7 - 7.1	
	ATF	Area [3]	2.2 ± 1.2	1.1 - 4.5	<0.001	1.6 ± 0.5	0.8 - 2.2	0.002
	PTF		18.5 ± 7.6	11.4 - 33.6		15.9 ± 5.4	9.7 - 23.0	
C5	ATF	Ø AP [1]	1.4 ± 0.3	0.9 - 2.4	<0.001	1.3 ± 0.2	1.0 - 1.8	<0.001
	PTF		5.0 ± 1.2	1.0 - 7.6		4.5 ± 1.7	1.0 - 6.6	
	ATF	Ø lat [2]	1.9 ± 0.4	1.1 - 3.2	<0.001	1.8 ± 0.5	0.8 - 2.8	<0.001
	PTF		5.9 ± 1.4	1.3 - 9.1		5.4 ± 2.0	1.0 - 7.8	
	ATF	Area [3]	2.2 ± 1.2	1.0 - 5.5	<0.001	1.8 ± 0.8	0.7 - 3.4	<0.001
	PTF		23.3 ± 7.3	1.2 - 36.5		20.5±10.9	1.0 - 36.5	
C6	ATF	Ø AP [1]	1.5 ± 0.4	0.4 - 3.7	<0.001	1.5 ± 0.4	1.0 -3.5	<0.001
	PTF		5.3 ± 0.7	3.1 - 7.5		5.4 ± 0.9	2.4 - 7.2	
	ATF	Ø lat [2]	2.1 ± 0.7	0.3 - 3.7	<0.001	2.1 ± 0.7	1.1 - 5.0	<0.001
	PTF		6.3 ± 1.1	0.3 - 3.7		6.5 ± 0.9	4.2 - 8.7	
	ATF	Area [3]	2.6 ± 1.4	0.4 - 9.0	<0.001	2.6 ± 1.2	1.0 - 6.6	<0.001
	PTF		26.4 ± 5.8	10.5 - 39.8		27.3 ± 6.9	10.3-40.8	
C7	ATF	Ø AP [1]	2.1 ± 0.3	1.8 - 2.6	0.048	1.5 ± 0.6	0.6 - 2.5	0.038
	PTF		3.2 ± 0.9	1.9 - 4.1		3.4 ± 1.4	1.5 - 5.5	
	ATF	Ø lat [2]	2.0 ± 1.1	1.4 - 3.9	0.648	1.7 ± 0.2	1.6 - 2.1	0.068
	PTF		2.3 ± 0.4	1.6 - 2.6		2.6 ± 0.8	1.8 - 3.9	
	ATF	Area [3]	3.1 ± 0.7	2.3 – 4.0	0.223	1.8 ± 0.7	0.9 - 2.7	0.073
	PTF		5.1 ± 2.9	2.1 – 8.7		7.4 ± 5.9	1.7 – 17.5	

SD = Standard Deviation; ATF = accessory transverse foramen PTF = principal transverse foramen; [1] antero-posterior diameter (mm); [2] lateral diameter (mm); [3] area (mm2); [4] P-value in comparison between ATF and PTF (Student t test)

vertebrae that they analyzed. Moreover, it is worth mentioning that the diverse ethnic origin of the samples the preceding authors studied may have affected the different frequencies they observed. Table 5 shows the frequencies of DTF encountered in these studies.

We consider that it is of great clinical relevance to know the prevalence of DTF at each cervical level, for a more precise diagnosis and individualized therapy. In this regard few authors provide data (Taitz et al., 1978; De Boeck et al., 1984; Jovanovic, 1990; Wysocki et al., 2003; Jaffar et al., 2004; Sanchis-Gimeno et al., 2005; Sharma et al., 2010; Agrawal et al., 2012; Chandravadiya et al., 2013; Gupta et al., 2014; Kwiatkowska et al., 2014; Patil et al., 2014; Ramachandran et al., 2014). Unfortunately, once again the methodology applied may have affected the results obtained. There are studies in which, as in our case, the prevalence of DTF is reported at different cervical levels (Taitz et al., 1978; De Boeck et al., 1984; Wysocki et al., 2003; Jaffar et al., 2004; Sanchis-Gimeno et al., 2005; Sharma et al., 2010; Chandravadiya et al., 2013; Gupta et al., 2014; Kwiatkowska et al., 2014; Patil et al., 2014), although in the study by Taitz et al. (1978) C6 and C7 were addressed together. Similarly, other authors like Kwiatkowska et al. (2014) and Wysocki et al. (2003) analyzed the relative prevalence of DTF at the different cervical levels with reference to the total number of TF and not to the number of vertebrae. Table 5 summarizes the frequencies of DTF at each cervical level relative to the total number of vertebrae within each cervical level, from different studies in which cervical sets were complete or incomplete. In line with our results, previous studies also notice the absence of DTF in C2 and occasional presence in C1

Table 4. Comparative dimensions between the PTF of vertebrae with DTF and the TF of vertebrae without DTF

Cervical level		Men			Women		
		PTF Mean ± SD	TF Mean ± SD	P-value [4]	PTF Mean ± SD	TF Mean ± SD	P-value [4]
C4	Ø AP [1]	3.8 ± 0.3	4.8 ± 0.6	<0.001	3.8 ± 0.5	4.8 ± 0.7	0.008
	Ø lat [2]	5.0 ± 1.0	6.4 ± 0.7	<0.001	5.2 ± 0.3	6.0 ± 0.7	0.013
	Area [3]	15.2 ± 4.2	24.2 ± 4.8	<0.001	14.5 ± 1.6	22.3 ± 5.2	0.002
C5	Ø AP [1]	4.6 ± 0.6	5.2 ± 0.7	<0.001	4.4 ± 0.9	5.0 ± 0.6	0.001
	Ø lat [2]	5.7 ± 0.8	6.4 ± 0.9	<0.001	5.5 ± 0.7	6.0 ± 0.8	0.031
	Area [3]	19.4 ± 4.2	26.3 ± 5.2	<0.001	19.2 ± 5.7	23.5 ± 4.8	<0.001
C6	Ø AP [1]	5.2 ± 0.6	5.5 ± 0.8	0.010	4.9 ± 0.5	5.3 ± 0.8	0.039
	Ø lat [2]	6.3 ± 0.8	6.6 ± 1.0	0.063	6.1 ± 0.6	6.0 ± 1.0	0.417
	Area [3]	24.2 ± 5.6	28.3 ± 6.0	<0.001	23.3 ± 5.3	24.7 ± 5.3	0.039
C7	Ø AP [1]	3.3 ± 1.7	5.0 ± 1.4	0.015	3.2 ± 0.8	4.8 ± 1.3	0.006
	Ø lat [2]	2.8 ± 0.8	3.2 ± 0.9	0.358	1.9 ± 0.4	3.1 ± 1.0	0.012
	Area [3]	7.0 ± 7.2	12.7 ± 6.3	0.021	5.0 ± 2.5	11.6 ± 5.8	0.009

PTF = principal transverse foramen DTF = double transverse foramen TF = transverse foramen; SD = Standard Deviation; [1] antero-posterior diameter (mm); [2] lateral diameter (mm); [3] area (mm2); [4] P-value in comparison between PTF and TF (Student t test)

(De Boeck et al., 1984; Wysocki et al., 2003), and the highest frequency in C6, followed by C5, C4 and C7 (Taitz et al., 1978; De Boeck et al., 1984; Sharma et al., 2010; Chandravadiya et al., 2013; Patil et al., 2014). Although we did not find DTF in C3, other studies describe DTF in C3, although at a very low frequency (De Boeck et al., 1984; Wysocki et al., 2003; Sanchis-Gimeno et al., 2005; Sharma et al., 2010; Ramachandran et al., 2014).

Despite the abundance of studies on DTF, there is a lack of data regarding the distribution of DTF by sex, mostly because this information was not recorded or reported. Only four studies show data on DTF distribution based on sex (De Boeck et al., 1984; Wysocki et al., 2003; Kaya et al., 2011; Kwiatkowska et al., 2014), but none of them reported on whether they observed any statistically significant differences depending on sex regarding the presence of DTF. In our study, we reported for the first time the absence of statistically significant differences on DTF prevalence based on sex.

Another interesting point to be analyzed is the possible predominance according to the side of the TF affected by DTF, or the bilaterality of this variant. However, only a few authors have analyzed these aspects (Jovanovic, 1990; Aydinoğlu et al., 2001; Murlimanju et al., 2011; Agrawal et al., 2012; Rathnakar et al., 2013; Gupta et al., 2014; Katikireddi and Setty, 2014; Kwiatkowska et al., 2014; Ramachandran et al., 2014; Shah et al., 2014; Patra et al., 2015). In our case, DTF were encountered more frequently unilaterally than bilaterally with statistical significance, which coincides with findings of other previous studies (Jovanovic, 1990; Aydinoğlu et al., 2001; Murlimanju et al., 2011; Agrawal et al., 2012; Rathnakar et al., 2013; Gupta et al., 2014; Katikireddi and Setty, 2014; Ramachandran et al., 2014; Shah et al., 2014). However, this is contrary to the work by Patra et al. (2015), who observed that the bilateral formation (11.33%) was more prevalent than unilateral formation (10.67%), although these authors did not report whether this difference was statistically significant or not. With regard to the side with a greater prevalence of DTF, as in the study by Murlimanju et al. (2011), in our case the presence of DTF was more frequent at the right side, although this difference was not statistically significant. Nevertheless, Kwiatkowska et al. (2014) found no statistically significant differences between the right and the left.

The results obtained in our study on normal FT measurements are similar to those from other cervical CT studies (Zhao et al., 2008; Malik et al., 2009; Evangelopoulos et al., 2012; Nishinome et al., 2013; Kotil et al., 2014). However, since the presence of DTF may affect the size of the PTF, we excluded the vertebrae with DTF from the measurements of the TF. Unlike in our case, none of the other studies mention whether the vertebrae with DTF were excluded from the study sample. Moreover, only Zhao et al. (2008), Malik et al. (2010) and Evangelopoulos et al. (2012) analyze possible sexual differences in the TF measurements. Like in our case, Malik et al. (2010) and Evangelopoulos et al. (2012) found bigger dimensions of TF in men, while Zhao et al. (2008) did not find sexual differences. This could be explained by

Table 5. Summary of DTF frequencies observed by other authors

Authors and publication year	C1	C2	C3	C4	C5	C6	C7	Total
Taitz et al. (1978)	0.0%	0.0%	0.0%	0.0%	14.7%	43.9%		14.3%
De Boeck et al. (1984)	1.6%	0.0%	5.0%	5.0%	17.0%	23.0%	15.0%	NR
Jovanovic (1990)	NA	NA	NA	NA	NA	NR	14.2%	NR
Nagar et al. (1999)	NR	NR	NR	NR	NR	NR	NR	8.6%
Aydinoğlu et al. (2001)	0.0%	0.0%	18.5%				35.2%	14.4%
Jaffar et al. (2004)	NR	0.0%	NR	NR	NR	70.0%	NR	NR
Das et al. (2005)	0.0%	0.0%	NR	NR	NR	NR	NR	1.5%
Sanchis et al. (2005)	0.0%	0.0%	2.6%	14.2%	30.3%	41.9%	10.7%	10.0%
Sharma et al. (2010)	NA	NA	2.0%	6.0%	8.0%	16.0%	NA	8.0%
Kaya et al. (2011)	NR	NR	NR	NR	NR	NR	NR	22.7%
Murlimanju et al. (2011)	0.0%	0.0%	0.0%	0.0%	0.0%	1.4%		1.4%
Agrawal et al. (2012)	NA	NA	3.7%				NA	3.7%
Chandravadiya et al. (2013)	0.0%	0.0%	0.0%	0.0%	6.6%	20.0%	6.6%	4.7%
Chaudhari et al. (2013)	0.0%	0.0%	16.9%				41.6%	16.5%
Rathnakar et al. (2013)	NR	NR	NR	NR	NR	NR	NR	5.7%
Gupta et al. (2014)	NR	0.0%	NR	NR	NR	60.0%	NR	16.5%
Katikireddi and Setty (2014)	NR	NR	NR	NR	NR	NR	NR	3.0%
Mishra et al. (2014)	NA	NA	14.0%				NA	14.0%
Murugan and Verma (2014)	0.0%	0.0%	NR	NR	NR	NR	NR	12.6%
Patil et al. (2014)	0.0%	0.0%	0.0%	12.0%	12.0%	12.0%	4.0%	5.7%
Ramachandran et al. (2014)	0.0%	0.0%	3.7%	41.9%	12.5%	50.0%	10.2%	15.8%
Shah et al. (2014)	NR	NR	NR	NR	NR	NR	NR	16.1%
Yadav et al. (2014)	NA	NA	6.6%				NA	6.6%
Kumari et al. (2015)	NR	NR	NR	NR	NR	NR	NR	9.8%
Patra et al. (2015)	NA	NA	0.0%	0.0%	NR	NR	36.6%	22.0%
Present Study (2016)	0.0%	0.0%	0.0%	4.7%	23.5%	45.8%	4.3%	11.2%

NR = Non reported; NA = Non analyzed

the diverse ethnic origin of the studied samples.

In relation to the morphometry of the DTF, our study shows that the ATF is smaller in the antero-posterior diameter, the lateral diameter and area than the PTF at all the cervical levels presenting DTF, except for the lateral diameter in C7, and that such difference was statistically significant. These data are in agreement with previous studies (Mishra et al., 2014; Murugan and Verma, 2014; Patra et al., 2015). Considering that a TF with a smaller caliber could affect the vascular flow of the vertebral artery (Taitz et al., 1978), it would be of greater clinical relevance to ascertain whether the presence of this anatomical variant causes a smaller size of PTF in the vertebrae with DTF when compared with normal vertebrae. In this context, we verified that the presence of DTF at C4, C5, C6 and C7 does significantly correlate with a smaller size of the PTF, compared with the TF of normal cervical vertebrae. This finding is relevant in relation to the possible correlation between the compressive pathology of the vertebral artery at the C4-C6 levels and the vertebral artery surgery. In this regard, it would be advantageous to verify whether the caliber of the vertebral artery is also reduced in these vertebrae with DTF. Additionally, it could be interesting to extend our study to a voluntary healthy cohort of samples in order to establish a putative correlation between DTF presence and symptoms of vertebrobasilar insufficiency.

In sum, this study provides new data on the prevalence of DTF at each cervical level from complete cervical sets. Furthermore, we have established that the presence of DTF may determine a smaller size of the PTF in the vertebrae affected when compared with normal vertebrae, which should be considered in clinical practices

such as interpretation of cervical imaging studies and planning of surgical procedures in the cervical region.

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REFERENCES

AGRAWAL D, MOHANTY BB, SETHY S, PARIJA B, HAZARY SK, CHINARA PK (2012) Variations in foramen transversarium: an osteological study in eastern India. *Int J Curr Res,* 4(9): 120-122.

AYDINOĞLU A, KAVAKLI A, YEŞILYURT H, ERDEM S, EROĞLU C (2001) Foramen transversarium bipartite. *Van Tip Dergisi,* 8: 110-112.

BULSARA KR, VELEZ DA, VILLAVICENCIO A (2006) Rotational vertebral artery insufficiency resulting from cervical spondylosis: case report and review of the literature. *Surg Neurol,* 65(6): 625-627.

CHANDRAVADIYA L, PATEL S, GODA J, CHAVDA V, RUPARELIA S, PATEL S (2013) Double foramen transversarium in cervical vertebra: morphology and clinical importance. *Int J Res Med,* 2(1): 103-105.

CHAUDHARI ML, MAHERIA PB, BACHUWAR SP (2013) Double foramen transversarium in cervical vertebra: morphology and clinical importance. *Indian Journal of Basic & Applied Medical Research,* 2(8): 1084-1088.

DAS S, SURI R, KAPUR V (2005) Double foramen transversaria: An osteological study with clinical implications. *Int Med J,* 12(4): 311-313.

DE BOECK M, POTVLIEGE R, ROELS F, DE SMEDT E (1984) The accessory costotransverse foramen: a radioanatomical study. *J Comput Tomogr,* 8: 117-120.

DESOUZA RM, CROCKER MJ, HALIASOS N, RENNIE A, SAXENA A (2011) Blunt traumatic vertebral artery injury: a clinical review. *Eur Spine J,* 20:1405-1416.

DOFE MY, KASOTE AP, MESHRAM MM (2015) The study of cervical vertebrae showing variational presentation of foramen transversarium. *Int J Anat Res,* 3(2): 1128-1132.

EVANGELOPOULOS D, KONTOVAZENITIS P, KOURIS S, ZLATIDOU X, BENNEKER L, VLAMIS J, KORRES D, EFSTATHOPOULOS N (2012) Computerized tomographic morphometric analysis of the cervical spine. Open Orthop J, 6: 250–254.

GUPTA RP, RAI A, GUPTA N (2014) A study of anatomical variations in foramen transversarium and its clinical importance. *International Journal of Contemporary Surgery,* 2(1): 147-150.

JAFFAR AA, MOBARAK HJ, NAIM SA (2004) Morphology of the foramen transversarium a correlation with causative factors. *Al-Kindy Col Med J,* 2(1): 61- 64.

JOVANOVIC MS (1990) A comparative study of the foramen transversarium of the sixth and seventh cervical vertebrae. *Surg Radiol Anat,* 12(3): 167-172.

KATIKIREDDI RS, SETTY SNRS (2014) A study of double foramen transversarium in dried cervical vertebra. *Int J Health Sci Res,* 4(1): 59-61.

KAYA S, YILMAZ NR, PUSAT S, KURAL C, KIRIK A, IZCI Y (2011) Double foramen transversarium variation in ancient byzantine cervical vertebrae: preliminary report of an anthropological study. *Turk Neurosurg,* 21 (4): 534-538.

KOTIL K, KILINCER C (2014) Sizes of the transverse foramina correlate with blood flow and dominance of vertebral arteries. Spine J, 14(6): 933-937.

KUMARI M, OMAR S, DEB S, ALAM K (2015) An osteological study on accessory transverse foramina in cervical vertebrae and their clinical significance. *Int J Recent Sci Res,* 6(6): 4514-4516.

KWIATKOWSKA B, SZCZUROWSKI J, NOWAKOWSKI D (2014) Variation in foramina transversaria of human cervical vertebrae in the medieval population from Sypniewo (Poland). *Anthropological Review,* 77 (2): 175-188.

MALIK SW, STEMPER BD, METKAR U, YOGANANDAN N, SHENDER BS, RAO RD (2010) Location of the transverse foramen in the subaxial cervical spine in a young asymptomatic population. Spine (Phila Pa 1976), 35(12): E514-9.

MISHRA GP, BHATNAGAR S, SINGH B, MISHRA PP, MISHRA A (2014) Anatomical variations in foramen transversarium of typical cervical vertebrae and clinical significance. *IJBR,* 5(6): 405-406.

MURLIMANJU BV, PRABHU LV, SHILPA K, RAI R, DHANANJAYA KV, JIJI PJ (2011) Accessory transverse foramina in the cervical spine: incidence, embryological basis, morphology and surgical importance. *Turk Neurosurg,* 21(3): 384-387.

MURUGAN M, VERMA S (2014) A study on variations of foramen transversarium of cervical vertebrae. *NJCA,* 3(1): 4-7.

NAGAR Y, TAITZ C, REICH R (1999) What can we make of these fragments? Excavation at “Mamilla” cave, byzantine period, Jerusalem. *Int J Osteoarchaeol,* 9: 29-38.

NISHINOME M, IIZUKA H, IIZUKA Y, TAKAGISHI K (2013) An analysis of the anatomic features of the cervical spine using computed tomography to select safer screw insertion techniques. Eur Spine J, 22 (11): 2526–2531.

PATIL NP, DHAPATE SS, PORWAL S, BHAGWAT VB (2014) The study of incidence of accessory foramen transversaria in the cervical vertebrae. *Journal of dental and medical sciences,* 13(7): 85-87.

PATRA A, KAUR H, CHHABRA U, KAUSHAL S, KUMAR U (2015) Double foramen transversarium in dried cervical vertebra: An osteological study with its clinical implications. *Indian J Oral Sci,* 6: 7-9.

PENG CW, CHOU BT, BENDO JA, SPIVAK JM (2009) Vertebral artery injury in cervical spine surgery: anatomical considerations, management, and preventive

RAMACHANDRAN K, RAVIKUMAR PC, MANAVALAN MS (2014) A study on the foramen transversarium in cervical vertebrae. *International Journal of Health Sciences and Research,* 4(12): 178-183.

RATHNAKAR P, REMYA K, SWATHI (2013) Study of accessory foramen transversaria in cervical vertebrae. *NITTE University Journal of Health Science,* 3(4): 97-99.

SANCHIS-GIMENO JA, MARTÍNEZ-SORIANO F, APARICIO-BELLVER L (2005) Degenerative anatomic deformities in the foramen transversarium of cadaveric cervical vertebrae. *Osteoporos Int,* 16: 1171-1172.

SHAH ST, ARORA K, SHAH KP (2014) Study of Accessory Foramen Transversarium in Cervical Vertebrae. *GCSMC J Med Sci,* 3(2): 21-24.

SHARMA A, SINGH K, GUPTA V, SRIVASTAVA S (2010) Double foramen transversarium in cervical vertebra an osteological study. *J Anat Soc India,* 59 (2): 229-231.

TAITZ C, NATHAN H, ARENSBURG B (1978) Anatomical observations of the foramina transversaria. *J Neurol Neurosurg Psychiatry,* 41: 170-176.

WYSOCKI J, BUBROWSKI M, REYMOND J, KWIATKOWSKI J (2003) Anatomical variants of the cervical vertebrae and the first thoracic vertebra in man. *Folia Morphol,* 62(4): 357-363.

YADAV Y, GOSWAMI P, BHARIHOKE V (2014) An osteological study of foramen trasversarium: variations and clinical aspects. *J of Evolution of Med and Dent Sci,* 3(68): 14562-14566.

ZHAO L, XU R, HU T, MA W, XIA H, WANG G (2008) Quantitative evaluation of the location of the vertebral artery in relation to the transverse foramen in the lower cervical spine. Spine (Phila Pa 1976), 33(4): 373-378.