### RESEARCH



# The cerebellopontine angle cistern volumetric differences in trigeminal neuralgia patients with and without vertebrobasilar compression: a case-matched study

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Received: 15 March 2023 / Revised: 25 August 2023 / Accepted: 2 September 2023 / Published online: 13 September 2023 © The Author(s), under exclusive licence to Springer-Verlag GmbH Germany, part of Springer Nature 2023

### **Abstract**

Previous studies have indicated that the small cerebellopontine angle (CPA) cistern plays a role in the pathogenesis of trigeminal neuralgia (TN), but they are likely not involved in TN associated with vertebrobasilar artery (VBA) compression because of its rarity. Forty-four patients with VBA-associated TN and 44 age-, sex-, and hypertension-matched TN patients without VBA compression (non-VBA-associated) were included. All patients underwent high-resolution MRI. The CPA cistern volumes were measured bilaterally. The presence of vertebrobasilar dolichoectasia (VBD) and laterality of the vertebrobasilar junction (VBJ) were observed. The CPA cistern volume on the affected side was smaller than the unaffected side (714.4  $\pm$  372.8 vs 890.2  $\pm$  462.2 mm<sup>3</sup>, p < 0.001) in non-VBA-associated TN patients, while VBA-associated TN patients show a larger CPA cistern on the affected side than the unffected side (1107.0  $\pm$  500.5 vs 845.3  $\pm$  314.8 mm<sup>3</sup>, p < 0.001). The prevalence of VBD was higher in patients with VBA-associated TN than in matched non-VBA-associated TN patients (90.9% vs 4.5%, p < 0.001). A positive correlation between the laterality of VBJ and the affected side was found in the VBA-associated TN group (p < 0.0001). Large CPA cistern may be a neuroradiological feature of VBA-associated TN, and most of the VBA-associated TN is accompanied by VBD. The presence of VBD and the lateral shift of VBJ may expand the CPA cistern by squeezing the surrounding tissue on the affected side and also increase the chance of VBA compression on the trigeminal nerve, resulting in the genesis of VBA-associated TN.

 $\textbf{Keywords} \ \ \text{Trigeminal neuralgia} \cdot \text{Vertebrobasilar artery} \cdot \text{Cerebellopontine angle} \cdot \text{Vertebrobasilar dolichoectasia}$ 

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### Introduction

Trigeminal neuralgia (TN) is a neurological disorder characterized by paroxysmal, lancinating, electrical shock-like pain arising in one or more trigeminal nerve branches [1]. Neurovascular conflict (NVC) at the trigeminal root entry zone (REZ) has been considered as the predominant cause of TN [2]. In most cases, NVC is caused by small vertebrobasilar system branches or surrounding veins, such as the superior cerebellar artery, the anterior inferior cerebellar artery, or the petrosal vein [3]. A rare cause of TN is NVC related to the vertebrobasilar artery (VBA), which is reported in only 2 to 7.7% of TN cases in past studies [4].

Advances in magnetic resonance imaging (MRI) technology were not only implemented to rule out secondary causes and identify the responsible offending vessels, but also could investigate the neuroradiological characteristics in TN patients to enhance our understanding of the pathogenesis



of TN [5–9]. Several studies have demonstrated that TN patients possess smaller CPA cisternal sizes on the affected side, which may lead to closer nerve-vessel relations and, therefore, a higher prevalence of symptomatic NVC [6, 10–15]. However, these studies are likely not involved in cases of VBA-associated TN because of their limited sample size and the rarity of this special pathology. Therefore, it is unclear whether patients with VBA-associated TN have a small CPA cistern. When observing MRI scans of patients with VBA-associated TN, it seems that the CPA cistern of the affected side is not smaller. Driven by this impression, a retrospective case—match study with comparison of symptomatic and unaffected sides and age-, sex-, hypertension-, and laterality-matched TN patients with non-VBA-associated TN was performed.

# Materials and methods

# **Patients**

This was a retrospective study conducted to explore the pre-operative neuroimaging features of patients with VBAassociated TN. The study was approved by the institutional review board of Union Hospital, Wuhan, China; the need for written informed consent was waived given the retrospective nature of the study. A retrospective review of medical records was performed for all patients with idiopathic TN who underwent microvascular decompression (MVD) as their first surgical intervention between February 2013 and October 2020 at our department. Patients with tic convulsif, bilateral symptoms, or insufficient pre-operative imaging were excluded from the analysis. Finally, 44 patients were identified as VBA-associated TN according to pre-operative MRI and operative findings; this group was matched 1:1 with a group of patients with non-VBA-associated TN undergoing MVD during the same period. Matching criteria included patient age (±2 years), sex, hypertension, and laterality of pain. VBA-associated TN patients were also matched to health-check examinees with similar age, history of hypertension, identical sex, and same laterality of the vertebrobasilar junction (VBJ) who demonstrate vertebrobasilar dolichoectasia (44 subjects with VBD, control cohort). Hypertension was defined as prior physician diagnosis, current consumption of antihypertensive drugs, or mean systolic and/or diastolic blood pressure  $\geq 140/90$  mm Hg.

# **Imaging protocol**

All subjects were examined by a 3T MRI scanner (Magnetom Trio; Siemens AG, Erlangen, Germany) with a standard head coil prior to MVD. High-resolution MRI was performed with three-dimensional sampling perfection with

application-optimized contrasts using different flip angle evolutions (SPACE) sequence. The parameters used for SPACE imaging were as follows: repetition time, 1000 ms; echo time, 135 ms; flip angle,  $120^{\circ}$ ; number of excitations, 2; matrix,  $384 \times 384$ ; field of vision,  $20.0 \times 20.0$  cm; and slices of 0.5 mm without gap.

### **CPA cistern volume measurement**

Measurements of the CPA cistern volume were performed on on SPACE imaging, according to the method previously described by Hardaway et al. [9]. The upper border of the CPA cistern is the uppermost slice showing the presence of one trigeminal nerve, and the lower border is the lowermost slice showing portion of the same trigeminal nerve. The clivus and the petrous bone are defined as the anterior limit. The anterior surface of the pons and the anterior-most surface of the cerebellar hemispheres are regarded as the posterior limit. The lateral boundary is where the cerebellum meets the temporal bone. The medial border is the midline passing through both the nasal septum and the occipital tuberosity (Fig. 1).

The 3D-Slicer software (3.6.3 version; www.slicer.org.) was used to measure the CPA cistern volumes bilaterally. Figure 1 shows the examples of an axial slice through the measurement area in TN patients with and without vertebrobasilar compression. Measurements were calculated twice with a 4-week interval and then averaged. All works were performed by an experienced radiologist blinded to the clinical information.

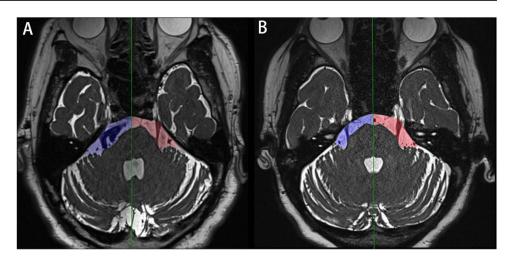
# The brainstem displacement

The brainstem displacement was assessed at the level of pons. We defined the "pons deviation indexa as the numerical value multiplied by 100 to the number obtained by dividing the pons width of the affected side by the total width of the pons on the straight line passing through the trigeminal nerve REZ in TN patients (in controls, dividing the pons width of the side where the vertebral and basilar arteries meet by the total width of the pons). Measurements were also calculated twice with a 4-week interval and then averaged.

The participants were instructed to hold their heads straight during the MRI procedure. Cases of head rotation were corrected by adapting the single MRI series in the midsagittal plane so that a rotation effect was excluded. Therefore, in TN patients without VBA compression, the line passing through bilateral trigeminal nerve REZ is usually horizontal. When the affected trigeminal nerve REZ is severely compressed and even deformed in TN patients with VBA compression or controls so that it often cannot be identified on MRI, the horizontal line passing through the contralateral unaffected trigeminal nerve REZ was adopted to measure the pons displacement.



Fig. 1 These axial SPACE images show measurements of the CPA cistern volume: in a 58-year-old woman with a right-sided non-VBD-associated TN, the CPA cistern volume of the affected side (purple area) is smaller than the unaffected side (red area) (A) (1122.2 vs 937.0 mm³); in a matched non-VBD-associated TN subject, the CPA cistern volume of the affected side (purple area) is large than the unaffected side (red area) (B) (742.3 vs 900.8 mm³)



# **VBD** evaluation

The height and the lateral displacement of the basilar artery (BA) were classified using the scale of Smoker et al. [16]. BA height is graded as 0 (at or below dorsum sellae), 1 (within the suprasellar cistern), 2 (at the level of the third-ventricle floor), or 3 (indenting the third-ventricle floor). BA lateral displacement is also graded as 0 (midline), 1 (medial to the lateral margin of clivus or dorsum sellae), 2 (lateral to those landmarks), or 3 (in the cerebellopontine angle). The diagnostic criteria for VBD include dilated VBA with a maximum size of over 4.5 mm in diameter, BA bifurcation above the suprasellar cistern (BA height  $\geq$  2), or BA located lateral to dorsum sellae or margin of clivus (BA lateral displacement  $\geq$  2).

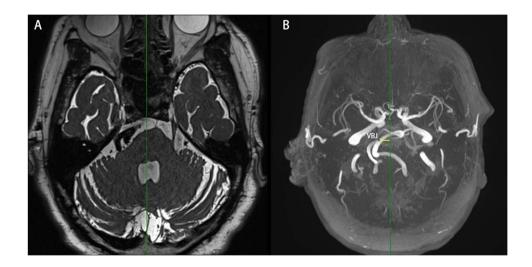
The structure of vessels could be well elucidated in the high-resolution images. The vertebral artery (VA) diameter was measured at 3.0 mm from the vertebrobasilar junction (VBJ). When the diameter difference between both sides is greater than 0.3 mm, the larger VA was considered as the

dominant VA [17]. The VBJ position deviating more than 3.0 mm from the midline is considered as the VBJ shift [18]. The length of the perpendicular line drawn from VBJ to the midline represented the VBJ deviation distance. All images were reviewed and assessed by two independent readers blinded to the clinical information. If the results of both readings were different, the final diagnosis was established by consensus (Fig. 2).

# Statistical analysis

The interobserver agreement in the diagnosis of VBD was determined using Cohen's kappa statistics, and test-retest reliability of the CPA cistern volume measurements was evaluated with intraclass correlation coefficients. Continuous variables were expressed as means  $\pm$  standard deviation, and the differences between the groups were assessed with the paired-samples *t*-test or Wilcoxon signed-rank test, after assessing for normality. Categorical variables were presented as counts and percentages were analyzed by the  $\chi^2$  test with Yate's correction or Fisher's exact

Fig. 2 Preoperative MRI and MRA. A The axial SPACE image showing the right trigeminal nerve compressed by the right VA. B On MRA, the left VA is larger than the right VA and is displaced superolaterally. The VBJ is deviated to the right side of the midline





test as appropriate. All tests were two-sided, with p < 0.05 being considered statistically significant.

### Results

### **Baseline characteristics**

Clinical characteristics of the subjects enrolled in this study are summarized in Table 1. No significant differences were observed between both groups in terms of age, sex, hypertension, and laterality, thus confirming appropriate matching. Among 44 patients with VBA-associated TN, the mean age at the time of surgery was  $61.6 \pm 9.7$  years, and 70.5% of the population were male (31/44); 17 patients were affected on the right side and 27 on the left side; symptom duration ranged from 1 to  $20 \ (3.7 \pm 3.3)$  years.

### Pons deviation index

In the VBA-associated TN group, the pons width was shorter on the affected (12.3  $\pm$ 22.0 mm) than on the unaffected side (16.1  $\pm$  1.6 mm, p < 0.001), while in the non-VBA-associated TN group, no difference was encountered (16.2  $\pm$  1.6 vs 16.4  $\pm$  1.1 mm, p = 0.56). Pons deviation index of the VBA-associated TN patients and the non-VBA-associated TN patients was 42.6  $\pm$  7.3 and 49.7  $\pm$  2.5, respectively (p < 0.001).

## **CPA cistern volume**

The intraclass correlation coefficient was 0.90 for the CPA cistern volume, indicating excellent test-retest reliability.

because we used one only observer. In the VBA-associated TN patients, the mean CPA cistern volume of the affected side was significantly larger than the unaffected side (1107.0  $\pm$  500.5 vs 845.3  $\pm$  314.8 mm<sup>3</sup>, p < 0.001). In the matched non-VBA-associated TN subjects, the mean CPA cistern volume of the affected side was significantly smaller than the unaffected side (714.4  $\pm$  372.8 vs 890.2  $\pm$  462.2 mm<sup>3</sup>, p < 0.001). Although the mean CPA cistern volume on the unaffected side of the VBA-associated TN patients was larger than the mean CPA cistern volume on the unaffected side of the non-VBA-associated TN patients, this difference was not statistically significant (p = 0.58). The mean CPA cistern volume on the affected side of the VBA-associated TN patients was significantly larger than the mean CPA cistern volume on the affected side of the non-VBA-associated TN patients (1107.0  $\pm$  500.5 vs 714.4  $\pm$  372.8 mm<sup>3</sup>, p < 0.001) (Fig. 3).

Measures of interobserver agreement cannot be provided

### Involvement of VBD

The presence of VBD and the offending vessels were revealed by preoperative neuroimaging studies and confirmed during MVD. Although the VBA was always the most prominent offending vessel in the VBA-associated TN patients, most of them had multiple vessel compression. The interobserver agreements in evaluating the presence of VBD, dominant VA, and VBJ shift were 96.6% (kappa = 0.93; p < 0.001), 95.5% (kappa = 0.82; p < 0.001), and 96.6% (kappa = 0.86; p < 0.001), respectively.

Out of the 88 study subjects, 42 were found to have VBD, including 40 VBA-associated TN patients and 2 matched TN subjects (Table 1). The prevalence of VBD was significantly

**Table 1** Demographic and clinical characteristics of the groups

	VBA-associated TN ( <i>n</i> = 44)	Non-VBA-associated TN $(n = 44)$	p value
Mean age (years)	61.6 ± 9.7	61.6 ± 9.6	0.81
Gender (M/%)	31 (70.5%)	31 (70.5%)	1.00
Pain laterality (Lt./%)	27 (61.4%)	27 (61.4%)	1.00
Arterial hypertension	20 (47.7%)	20 (47.7%)	1.00
Pain distribution			
Single branch (V1, V2, or V3)	16 (36.4%)	12 (27.3%)	0.25
V1 + 2	3 (6.8%)	6 (13.6%)	
V2 + 3	18 (40.9%)	13 (29.5%)	
V1 + 2 + 3	7 (15.9%)	13 (29.5%)	
Duration of symptoms, (years)	$3.7 \pm 3.3$	$4.1 \pm 3.6$	0.31
Baseline BNI score, n (%)			
IV	18 (40.9%)	24 (54.5%)	0.29
V	26 (59.1%)	20 (45.5%)	
Offending VA/BA (radiological and/or surgical findings)	35/9	_	

VBA vertebrobasilar artery, M male, Lt left, VBA vertebrobasilar artery, BNI Barrow Neurological Institute, VA vertebral artery, BA basilar artery



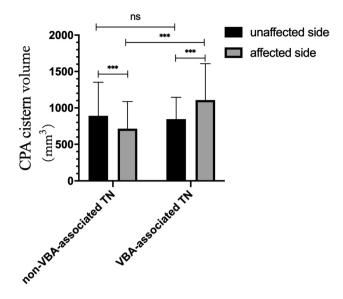


Fig. 3 Comparison of the CPA cistern cross-sectional area measurements in VBA-associated TN patients and non-VBA-associated TN patients. (\*\*\* = p < 0.001; ns, not significant)

higher in the VBA-associated TN group than in the TN without compression group (90.9% vs. 4.5%, p < 0.001) (Table 2). The VBA-associated TN group had significantly higher proportions of the VBJ shift than the non-VBA-associated TN group (97.7% vs. 65.9%, p < 0.001). There was no significant difference in the proportion of dominant VA between the two groups (86.4% vs. 77.3%, p = 0.41). Among these VBA-associated TN patients, a significantly positive correlation was found between the symptom side and the laterality of the VBJ, but this correlation was not observed in non-VBA-associated TN. Additionally, there was no correlation between the affected side and the laterality of dominant VA in both groups (Tables 3 and 4).

### VBA-associated TN vs. controls with VBD

The demographic and clinical data for VBA-associated TN patients and matched healthy controls with VBD are summarized in Table 5. There were no significant differences in baseline characteristics between the two groups.

In the healthy controls with VBD, the mean CPA cistern volume on the ipsilateral side of VBJ was larger than the mean CPA cistern volume on the contralateral side, but this difference was not statistically significant (942.3  $\pm$  482.7 vs 830.4  $\pm$  401.5 mm<sup>3</sup>, p = 0.68). Comparisons of the CPA cistern volume on the VBJ side between the two groups showed a trend toward larger CPA cistern volume with the VBA-associated TN patients, which did not reach statistical significance (p = 0.15). There was no statistically significant difference in the mean CPA cistern volume on the contralateral side of VBJ between these two groups (p = 0.81).

**Table 2** Radiological characteristics of the vertebrobasilar arterial system in VBA-associated TN and non-VBA-associated TN groups

	VBA-associated TN ( <i>n</i> = 44)	Non-VBA- associated TN (n = 44)	p value
VBD ( <i>n</i> , (%))	40 (90.9%)	2 (4.5%)	< 0.001
Diameter of VA (mm)			
Left VA	$4.25 \pm 1.13$	$2.90 \pm 0.61$	< 0.001
Right VA	$3.96 \pm 1.54$	$2.49 \pm 0.57$	< 0.001
Dominant VA			
Presence $(n, (\%))$	38 (86.4%)	34 (77.3%)	0.41
Absence $(n, (\%))$	6 (13.6%)	10 (22.7%)	
Laterality of dominant VA			0.61
Lt. ( <i>n</i> , (%))	28 (63.6%)	23 (52.3%)	
Rt. ( <i>n</i> , (%))	10 (22.7%)	11 (25.0%)	
VBJ shift $(n, (\%))$	43 (97.7%)	29 (65.9%)	< 0.001
Direction of the VBJ			< 0.001
Lt. ( <i>n</i> , (%))	26 (59.1%)	17 (38.6%)	
Rt. ( <i>n</i> , (%))	17 (38.6%)	12 (27.3%)	
Midline $(n, (\%))$	1 (2.3%)	15 (34.1%)	

*VBA* vertebrobasilar artery, *VBD* vertebrobasilar dolichoectasia, *M* male, *Lt.* left, *Rt.* right, *VA* vertebral artery, *VBJ* vertebrobasilar junction

**Table 3** Chi-square test on the directional relationship between the dominant VA and affected side in VBA-associated TN and non-VBA-associated TN groups

	VBA-associated TN (with dominant VA, $n = 38$ )		Non-VBA-associated TN (with dominant VA, <i>n</i> = 34)	
	Lt. $(n = 23)$	Rt. $(n = 15)$	Lt. (n = 19)	Rt. $(n = 15)$
Laterality of de	ominant VA		_	
Lt. $(n, (\%))$	18 (78.3%)	10 (66.7%)	13 (68.4%)	10 (66.7%)
Rt. $(n, (\%))$	5 (21.7%)	5 (33.3%)	6 (31.6%)	5 (33.3%)
p value	0.47		0.99	

VBA vertebrobasilar artery, VA vertebral artery, Lt. left, Rt. right

**Table 4** Chi-square test on the directional relationship between the VBJ and affected side in VBA-associated TN and non-VBA-associated TN groups

	VBA-associated TN ( <i>n</i> = 44)		Non-VBA-associated TN $(n = 44)$	
	Lt. $(n = 27)$	Rt. $(n = 17)$	Lt. $(n = 27)$	Rt. $(n = 17)$
Laterality of V	BJ			
Lt. $(n, (\%))$	26 (96.3%)	0	10 (37.0%)	7 (41.2%)
Rt. $(n, (\%))$	0	17 (100.0%)	7 (25.9%)	5 (29.4%)
Midline ( <i>n</i> , (%))	1 (3.7%)	0	10 (37.0%)	5 (29.4%)
p value	< 0.001		0.79	

VBA vertebrobasilar artery, VA vertebral artery, Lt. left, Rt. right



**Table 5** Radiological characteristics of the vertebrobasilar arterial system in VBA-associated TN and non-VBA-associated TN groups

	VBA-associated TN (n = 44)	Control with VBD ( <i>n</i> = 44)	p value
Mean age (years)	61.6 ± 9.7	61.7 ± 10.1	0.78
Gender (M/%)	31 (70.5%)	31 (70.5%)	1.00
Arterial hypertension	20 (47.7%)	20 (47.7%)	1.00
$\mathrm{VBD}\left(n,\left(\%\right)\right)$	40 (90.9%)	44 (100.0%)	0.12
Dominant VA			
Presence $(n, (\%))$	38 (86.4%)	42 (77.3%)	0.27
Absence $(n, (\%))$	6 (13.6%)	2 (22.7%)	
BA height, mean score (SD)	$1.9 \pm 0.7$	$1.8 \pm 0.5$	0.28
BA lateral displacement, mean score (SD)	$2.5 \pm 0.7$	$2.0 \pm 0.9$	0.02
VBJ shift $(n, (\%))$	43 (97.7%)	42 (95.5%)	1.00
Pons deviation index	$42.6 \pm 7.3$	$48.3 \pm 5.4$	< 0.001
VBJ deviation distance	$15.8 \pm 5.7$	$10.1 \pm 3.9$	< 0.001

VBA vertebrobasilar artery, VBD vertebrobasilar dolichoectasia, M male, VA vertebral artery, BA basilar artery, VBJ vertebrobasilar junction

The pons deviation index was statistically larger in controls with VBD than in VBA-associated TN patients (48.3  $\pm$  5.4 vs 42.6  $\pm$  7.3, p < 0.001). The VBA-associated TN group had significantly longer VBJ deviation distance and larger BA displacement than the control with the VBD group. There were no significant differences in the BA height and the proportion of dominant VA between the two groups.

# Discussion

First-line medical treatment for TN is pharmacological management using sodium channel blockers, e.g., carbamazepine and oxcarbazepine [19]. Thus, it is reasonable to suggest an involvement of sodium channels in the pathophysiology of TN. Some isoforms of sodium channels, such as Nav1.6. Nav1.7, and Nav1.9, have been found to be associated with TN [20]. MVD is generally considered the first-line surgical treatment of TN when NVC can be identified. There is strong evidence that NVC is a major contributor to the pathophysiology of classical TN. As proposed by Jannetta, the constant pressure exerted by vascular pulsation on the nerve results in focal axonal demyelination, and the neuralgia is regarded as the result of ephaptic "short circuits" associated with demyelination [18]. MVD eliminates NVC to obtain successful pain relief that strongly favors the above theory [21, 22]. However, it was puzzling why NVC can also be found in healthy individuals [23, 24], and TN also can occur in patients without NVC [25]. This demonstrated that NVC does not seem to be the independent diagnostic imaging marker and sole pathogenic factor of TN. Furthermore, even for those patients with TN associated with NVC, it is worth exploring what factors contribute to the formation of pathogenic NVC.

With the development of imaging technology, the interest in exploring those morphological factors affecting the occurrence of TN has been revived. It has been suggested that TN patients have a sharper trigeminal-pontine angle [8, 13] and a shorter length or smaller volume of the cistern segment of the trigeminal nerve [6, 8, 11–13, 26] on the affected side. In addition to the above anatomical variations, several studies have been performed to evaluate the CPA cistern crowdedness [6, 10–15], which may represent an optimal factor involved in TN pathogenesis. For example, Park et al. measured the CPA cistern bilaterally on the same section as the REZ. They demonstrated that the cross-sectional area was significantly smaller on the affected side than on the unaffected side. [6]. Parise et al. confirmed the findings of the former and believed that the CPA cistern measurements had potential value for surgical planning and surgical outcome prediction [11]. Both studies support the following hypothesis: a smaller CPA cistern results in a more crowded CPA, thus increasing the incidence of symptomatic NVC. However, such an assumption remains to be confirmed. Horinek et al. reported no correlation between the presence of NVC and any posterior fossa measurements [26]. One reason for these inconsistent results may be that different CPA cistern definitions and measurement protocols were adopted. The medial portion of the CPA cistern was selected to measure in the study of Horinek et al. Considering that the responsible blood vessels do not only appear on the medial side of the trigeminal nerve, this measurement protocol also needs further scrutiny. In addition, none of these studies provided a composition of the size and type of responsible blood vessels in their included patients. Whether or not a particular population, such as VBAassociated TN, has unique CPA cistern characteristics remains an unknown question.

In our study, we measured the CPA cistern volume in a series of 44 consecutive TN patients with VBA compression and 44 age-, sex-, hypertension-, and laterality-matched TN patients without VBA compression. In patients with non-VBA-associated TN, the CPA cistern volume on the affected side was significantly reduced compared to that of the unaffected side. This result lends further credence to the previous hypothesis that states a small CPA cistern size increases the chance of NVC [6, 11]. However, in patients with VBA-associated TN, a significantly larger volume of the CPA cistern was observed on the affected side, suggesting that a smaller CPA cistern seems not to be a neuroimaging feature of VBA-associated TN patients. These findings



drive us to look for other factors facilitating NVC in this particular population.

VBD is an uncommon vasculopathy characterized by enlargement and distortion of the VBA. The histopathological characteristics of VBD include structural arterial wall defect of the internal elastic lamina, reticular fiber deficiency, and smooth muscle atrophy [27, 28]. This disorder is generally related to 3 factors with atherosclerosis: increasing age, male sex, and hypertension [29]. In our study, these three factors were matched in the two groups to exclude their influence on the incidence of VBD. The prevalence of VBD was still higher in VBA-associated TN patients than in non-VBA-associated TN patients, suggesting a link between VBD and VBA-associated TN. Given that the trigeminal nerve lies above and away from the midline, under normal conditions, the VBA is unlikely to be close to the trigeminal nerve. However, in the presence of VBD, the VBA becomes tortuous and elongated, which greatly increases the chance of contacting and compressing the trigeminal nerve, thus leading to the onset of VBA-associated TN. Moreover, our results show that there is a significant correlation between symptom side and VBJ shift in VBA-associated TN patients, and 97.7% (43/44) of them are in the same direction. These findings not only support the above pathogenic speculation for VBA-associated TN patients, but also help to explain why such patients have a larger CPA cistern on the affected side. The dilated and tortuous VBA shifting toward the symptom side occupied a certain space in the CPA cistern on the affected side. In addition to the space-occupying effect of its own volume, the dilated and tortuous VBA also can compress or squeeze the nearby tissue under the influence of abnormal hemodynamics in the vascular lumen. We were trying to validate this through brainstem displacement analysis. The pons deviation index decrease in the VBA-associated TN group is due to the shift of the pons toward the contralateral cistern, which contributes to the larger ipsilateral CPA cistern.

In addition, comparative results of VBA-associated TN patients and controls with VBD indicate that the severe BA lateral displacement may be related to the occurrence of TN. Due to the presence of VBA compression at the trigeminal nerve level, even compared to controls with VBD, VBA-associated TN patients have a larger CPA cistern volume and a more severe pons deviation. MVD for VBA-associated TN is considered to be difficult because of the large diameter and low elasticity of the VBA. Fortunately, a larger ipsilateral CPA cistern provides space for manipulating VBA. We transposed the VBA using the biomedical glue sling technique and achieved satisfactory outcomes [30].

This study has some limitations. First, familiar to any retrospective analysis at a single institution, some unpredictable biases may have altered our results. Second, the sample size was small, which was due to the relative rarity of VBA-associated TN, the referral pattern, and the fact that only the surgical arm was included in this study. Third, magnetic susceptibility

effects and patient's involuntary movement may affect the image quality and measurement. Fourth, the manual delineation of the outline of CPA cistern and ROI placement may be prone to interrater variability. To reduce this potential variability, all the measurement work was performed by one author experienced with the software. An automated measurement in future studies may overcome this shortcoming. Fifth, there are currently no unified diagnostic criteria for VBD, and using a cutoff of 4.5 mm for the BA might result in overestimation of VBD in men and underestimation in women [31]. Additional studies are necessary to determine the best cutoff point.

# **Conclusions**

In cases of non-VBA-associated TN, our results are consistent with those in previous reports and further support the theory that a small CPA cistern may increase the chance of NVC and result in the occurrence of TN. However, this theory is not supported for VBA-associated TN cases where the presence of VBD and VBJ shifting toward the affected side were found to be a common anatomical phenomenon. When the VBD deviates to one side, the ipsilateral trigeminal nerve is susceptible to compression by VBA, thus resulting in the occurrence of VBA-associated TN. Additionally, the space-occupying and squeezing effects of VBD make the CPA cistern on the affected side larger.

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**Funding** Scientific Research Fund of Wuhan Health Commission, Grant ID: WX21D68.

**Data availability** The data used to support the findings of this study are available from the corresponding author upon request.

# **Declarations**

**Ethical approval** The study received full approval from the ethics committee of Tongji Medical College, Huazhong University of Science and Technology, and informed consent was waived due to the retrospective nature of the study.

Competing interests The authors declare no competing interests.

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