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Posterior Fossa Volume and Dimensions: Relation to Pathophysiology and Surgical Outcomes in Classic Trigeminal Neuralgia

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■ OBJECTIVE: **A small posterior fossa (PF) has been hypothesized to explain the increased incidence of trigeminal neuralgia (TN) in females and could make microvascular decompression (MVD) more challenging. The aim of this study was to investigate the association between the PF volume and dimensions in relation to biological sex, type of neurovascular conflict (NVC), and outcome after MVD in classic TN.**

■ METHODS: **In this observational study, 84 patients with TN operated on with MVD with a preoperative head computed tomography(CT) scan were included. Eighty-two adults without TN who had undergone head CT for other reasons were included as controls. PF volume and dimensions (x-axis, y-axis, and z-axis) were evaluated on the CT scans. For the patients with TN, Barrow Neurological Institute (BNI) grade was evaluated 6 months after MVD.**

■ RESULTS: **There was no difference in PF volume or dimensions between the patients with TN and controls. Women showed a smaller volume and narrower (x-axis) PF than men, but these differences did not manifest when comparing patients with TN and controls within each sex. Patients with an NVC involving the superior cerebellar artery had a narrower (x-axis) and shorter (y-axis) PF than did patients with an NVC resulting from other arteries. PF volume or dimensions were not associated with BNI grade after MVD.**

■ CONCLUSIONS: **PF anatomy was related to the NVC type but did not differ between patients with TN and controls and was not related to the surgical outcome after MVD.**

INTRODUCTION

Trigeminal neuralgia (TN) is a rare disorder,[1,2] typically characterized by transient episodes of intense pain in 1 or several branches of cranial nerve V (CN V).[3-5] Classic TN is stipulated to be caused by a neurovascular conflict (NVC) between a cerebral vessel and CN V, which induces dislocation, demyelination, and atrophy of the nerve and elicits the neuralgia.[5,6] TN may also be caused by secondary neurologic diseases (e.g., multiple sclerosis) or be idiopathic.[5,7] TN is initially treated with medications such as carbamazepine and gabapentin.[4] In refractory cases, surgical treatment is indicated, including ablative procedures in all cases of TN and microvascular decompression (MVD) to alleviate the NVC and often cure the disease in cases of classic TN.[8,9]

Based on case reports of patients with TN with Chiari malformation[10] and achondroplasia[11] who showed an anomalous posterior fossa (PF), it has been speculated whether deviations

Key words
- Microvascular decompression
- Neuroanatomy
- Outcome
- Posterior fossa
- Trigeminal neuralgia

Abbreviations and Acronyms
BNI: Barrow neurological institute
CN: Cranial nerve
CT: Computed tomography
ICC: Intraclass correlation coefficient
IQR: Interquartile range
MVD: Microvascular decompression
NVC: Neurovascular conflict
PF: Posterior fossa
SCA: Superior cerebellar artery
TN: Trigeminal neuralgia

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in the PF anatomy may contribute to TN pathophysiology. Consistent with this idea, female patients both show smaller PF volumes[12] and are at higher risk of developing TN.[1] This has been hypothesized to be a causal association, but a few smaller studies have contradicted this idea.[13-15] Another hypothesis is that the axial, coronal, and sagittal PF dimensions influence the risk of developing TN. However, this theory has been investigated in only a few smaller studies.[16] Furthermore, some studies indicate that the PF anatomy may be relevant for surgical outcomes after MVD, most likely related to the difficulty of gaining safe access to the NVC to allow for adequate and sustained NVC relief.[16,17] In particular, a flatter (shorter sagittal dimension) PF has been associated with TN recurrence after MVD.[16] Similar anatomic findings have been found after MVD caused by hemifacial spasm[17] (i.e., another neurologic condition characterized by an NVC in the PF).

Thus, the PF anatomy may be of relevance for the development of TN as well as a prognostic factor after surgery. To better understand these hypotheses, the primary aim of this study was to investigate the association between PF volume and dimensions in relation to controls, biological sex, the type of NVC, and outcome after MVD in patients with classic TN.

METHODS

Patients and Study Design

This was a retrospective observational study. At the Department of Neurosurgery, Uppsala University Hospital, Sweden, MVD was performed between 2012 and 2019 on 184 adult patients diagnosed with TN. Of these patients, 84 gave written consent for their preoperative computed tomography (CT) skull to be analyzed in the present study. Eighty-two other adults without TN who had undergone skull CT for other reasons were included as controls. These patients were randomly selected from the list of examined emergency head CT scans.

Surgery

The MVD was performed via a retrosigmoid burr hole, opening of the dura, aspiration of cisternal cerebrospinal fluid to relax the cerebellum, and dissection toward CN V to approach the NVC, and to keep the nerve and vessel separated using Teflon.

Follow-Up

The level of pain related to TN was evaluated 6 months after MVD according to the Barrow Neurological Institute (BNI) scale, which spans from 1 (free of pain and without medications) to 5 (severe pain).[18] The BNI grade was assessed by a neurosurgeon at a clinical follow-up visit. Outcome was dichotomized as favorable and unfavorable (BNI grade ≤2 and BNI grade >2, respectively).

Evaluation of PF Anatomy

Radiologic assessments were conducted in VuePicture archiving and communication system software (version 11.1.0 [Carestream Health Inc., Rochester, New York, USA]). The volume as well as the x, y, and z dimensions of the PF were assessed on head CT scans in the patients with TN and the controls (Figure 1). The PF volume (mL) was estimated semiautomatically as the sum of multiple slices. The PF borders were defined as the cerebellar tentorium (cranial), ophistion of the foramen magnum (caudal), petroclival bone (anterior), and the infratentorial occipital bone

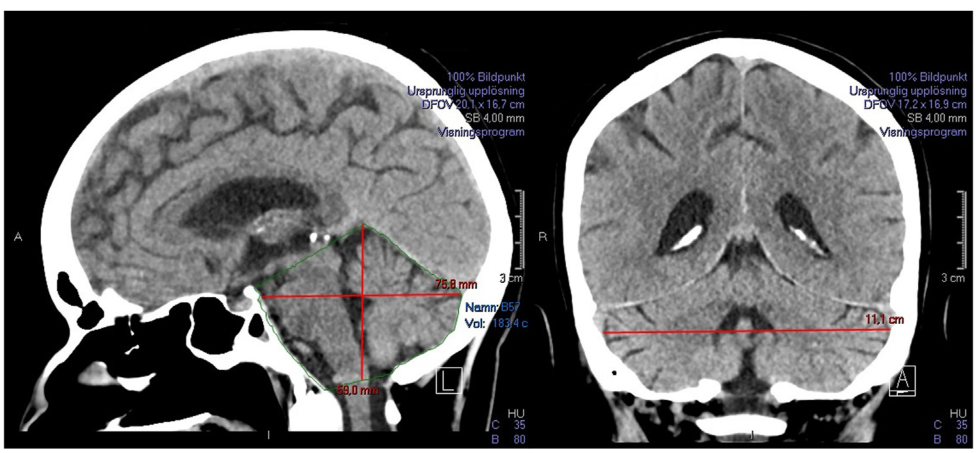

Figure 1. Evaluation of the posterior fossa anatomy and dimensions. The posterior fossa borders were defined as the cerebellar tentorium (cranial), ophistion of the foramen magnum (caudal), petroclival bone (anterior), and the infratentorial occipital bone (posterior). The transverse and sigmoid sinuses were not included in the posterior fossa volume. Length (y) was defined as the distance from the posterior clinoid process to the sinus confluence along the anteroposterior commissure line (y-axis), height (z) was defined as the distance from the most cranial portion of the straight sinus to the foramen magnum along the line perpendicular to the anteroposterior commissure line (z-axis), and width (x) was defined as the distance between the bilateral transverse—sigmoid sinus junctions along the right—left axis (x-axis).

(posterior). The transverse and sigmoid sinuses were not included in the PF volume. The PF borders were drawn manually for each slice and the software then calculated the sum of all of these slices. Length (y) was defined as the distance from the posterior clinoid process to the sinus confluence along the anteroposterior commissure line (y-axis), height (z) was defined as the distance from the most cranial portion of the straight sinus to the foramen magnum along the line perpendicular to the anteroposterior commissure line (z-axis), and width (x) was defined as the distance between the bilateral transverse—sigmoid sinus junctions along the right—left axis (x-axis). In addition to measurements of the x-axis, y-axis, and z-axis, the axial (x divided by y), coronal (x divided by z), and sagittal (y divided by z) dimensions were calculated as ratios between the axes. The radiologic assessments used in the analyses were performed by one of the authors (N.A.T). To evaluate the quality of these assessments, another author (T.S.W) conducted the same analyses (blinded) of these measures in 20 random patients. For all variables, the intraclass correlation coefficient (ICC) indicated excellent reliability (ICC x-axis = 0.93; ICC y-axis = 0.93; ICC PF-z-axis = 0.94; and ICC PF volume = 0.96).

Statistical Analysis

The data were presented as numbers (proportions) and medians (interquartile range [IQR]), depending on the type of data. X^2 tests, Mann-Whitney U tests, and Kruskal-Wallis tests were performed to test if there were any differences in the radiologic measurements of the PF for patients with TN versus controls and if it was related to sex, the type of NVC, and surgical outcome. Missing data were rare and excluded from the analyses. A P value <0.05 was considered statistically significant. All statistical analyses were conducted in SPSS version 27 (IBM Corp., Armonk, New York, USA).

Ethics

The study was approved by the Swedish Ethical Review Authority (Dnr 2020—533) and informed consent was obtained from all patients with TN, but it was waived for the controls.

RESULTS

Patients

Eighty-four patients with TN were included (Tables 1—4), of whom 33 (39%) were men and 51 (61%) were women. The median age was 64 years (IQR, 53—72) and the NVC was attributed to the superior cerebellar artery (SCA) in 64 patients (76%), another posterior circulation artery in 7 patients (8%), and a vein in 13 patients (15%). Sixty-nine patients (82%) showed a favorable outcome 6 months after MVD surgery. The median PF volume was 177 mL (IQR, 166—190), the median PF-x-axis was 10.2 cm (IQR, 9.9—10.5), the median PF-y-axis was 7.4 (IQR, 7.0—7.9) cm, and the median PF-z-axis was 6.5 cm (IQR, 6.2—6.9). The median axial ratio (x/y) was 1.4 (IQR, 1.3—1.5), the median coronal ratio (x/z) was 1.6 (IQR, 1.5—1.7), and the median sagittal ratio (y/z) was 1.2 (IQR, 1.1—1.3).

Patients with TN versus Controls—PF Anatomy

There was no difference in demography or PF anatomy between the patients with TN and the controls (Table 1).

Male versus Female Patients with TN—PF Anatomy and Surgical Outcome

Male patients with TN showed a larger PF volume and a wider PF (longer PF-x-axis) than female patients with TN (Table 2 and Figure 2). However, in Kruskal-Wallis tests, the post hoc analyses showed that these differences held true only between sexes and not between the TN cases and the controls within each sex. There was otherwise no difference in PF anatomy between the sexes for patients with TN. However, male patients with TN

Table 1. Posterior Fossa Dimensions in Patients with Trigeminal Neuralgia versus Controls

Variables	Patients with Trigeminal Neuralgia	Controls	*P*
Patients, n (%)	84 (100)	82 (100)	Not applicable
Age (years), median (IQR)	64 (53—72)	69 (53—80)	0.10
Gender (male/female), n (%)	33/51 (39/61)	39/43 (48/52)	0.35
PF volume (mL), median (IQR)	177 (166—190)	177 (168—189)	0.92
PF-x (cm), median (IQR)	10.2 (9.9—10.5)	10.2 (9.9—10.6)	0.62
PF-y (cm), median (IQR)	7.4 (7.0—7.9)	7.4 (7.2—7.9)	0.66
PF-z (cm), median (IQR)	6.5 (6.2—6.9)	6.5 (6.1—6.8)	0.38
Axial (x/y), median (IQR)	1.4 (1.3—1.5)	1.4 (1.3—1.5)	0.63
Coronal (x/z), median (IQR)	1.6 (1.5—1.7)	1.6 (1.5—1.7)	0.57
Sagittal (y/z), median (IQR)	1.2 (1.1—1.3)	1.2 (1.1—1.2)	0.96

IQR, interquartile range; PF, posterior fossa.

Table 2. Posterior Fossa Dimensions in Relation to Gender in Patients with Trigeminal Neuralgia

Variables	Males	Females	*P*
Patients, n (%)	33 (39)	51 (61)	Not applicable
Age (years), median (IQR)	66 (59—72)	62 (52—72)	0.39
Neurovascular conflict (superior cerebellar artery/other artery/vein), n (%)	26/4/3 (79/12/9)	38/3/10 (75/6/20)	0.31
Barrow Neurological Institute grade at 6 months, median (IQR)	1 (1—1)	1 (1—2)	**0.04**
PF volume (mL), median (IQR)	192 (183—211)	170 (161—178)	**<0.001**
PF-x (cm), median (IQR)	10.4 (10.1—10.9)	10.1 (9.8—10.4)	**0.002**
PF-y (cm), median (IQR)	7.4 (7.2—8.1)	7.4 (7.1—7.9)	0.21
PF-z (cm), median (IQR)	6.6 (6.2—7.0)	6.4 (6.1—6.8)	0.24
Axial (x/y), median (IQR)	1.4 (1.3—1.7)	1.4 (1.3—1.5)	0.78
Coronal (x/z), median (IQR)	1.6 (1.5—1.7)	1.6 (1.4—1.7)	0.51
Sagittal (y/z), median (IQR)	1.2 (1.1—1.3)	1.2 (1.1—1.3)	0.97

Bold values indicate statistical significance.
IQR, interquartile range; PF, posterior fossa.

showed a lower BNI grade 6 months after MVD compared with female patients (median, 1 [IQR, 1—1] vs. 1 [IQR, 1—2]; P = 0.04).

NVC Characteristics in Patients with TN—PF Anatomy and Surgical Outcome

Patients with an NVC resulting from another posterior circulation artery than the SCA showed a longer PF-x-axis and PF-y-axis than did patients with an NVC with SCA (Table 3). There was otherwise no difference in the PF anatomy and BNI grade depending on the NVC characteristics.

Favorable and Unfavorable Surgical Outcome in Patients with TN—PF Anatomy

There was no difference in PF anatomy related to a favorable/unfavorable postoperative outcome after 6 months (Table 4).

Table 3. Posterior Fossa Dimensions in Relation to the Type of Neurovascular Conflict

Variables	Superior Cerebellar Artery	Other Artery	Vein	*P*
Patients, n (%)	64 (76)	7 (8)	13 (15)	Not applicable
Age (years), median (IQR)	63 (53—72)	70 (64—72)	62 (50—73)	0.21
Gender (male/female), n (%)	26/38 (41/59)	4/3 (57/43)	3/10 (23/77)	0.31
Barrow Neurological Institute grade at 6 months, median (IQR)	1 (1—1)	1 (1—1)	1 (1—4)	0.26
PF volume (mL), median (IQR)	174 (165—189)	208 (178—212)	182 (173—185)	0.08
PF-x (cm), median (IQR)	10.2 (9.8—10.5)*	10.6 (10.4—10.9)†	10.2 (10.0—10.6)*,†	**0.02**
PF-y (cm), median (IQR)	7.4 (7.0—7.8)*	8.1 (7.4—8.5)†	7.9 (7.4—8.1)†	**0.01**
PF-z (cm), median (IQR)	6.5 (6.1—6.9)	6.4 (6.2—6.6)	6.7 (6.2—7.0)	0.72
Axial (x/y), median (IQR)	1.4 (1.3—1.5)	1.3 (1.3—1.4)	1.3 (1.3—1.4)	0.16
Coronal (x/z), median (IQR)	1.6 (1.4—1.7)	1.7 (1.6—1.8)	1.6 (1.4—1.7)	0.28
Sagittal (y/z), median (IQR)	1.2 (1.1—1.3)	1.2 (1.2—1.3)	1.2 (1.1—1.3)	0.20

IQR, interquartile range; PF, posterior fossa.
Bold values indicate statistical significance.
*Indicate if there was a statistically significant ($P < 0.05$) difference between the groups after post hoc analysis.
†Indicate if there was a statistically significant ($P < 0.05$) difference between the groups after post hoc analysis.

Table 4. Posterior Fossa Dimensions in Relation to Barrow Neurological Institute Grade at 6 Months

Variables	Favorable	Unfavorable	*P*
Patients, n (%)	69 (82)	15 (18)	Not applicable
Age (years), median (IQR)	64 (52—72)	63 (55—67)	0.49
Neurovascular conflict (superior cerebellar artery/other artery/vein), n (%)	53/7/9 (77/10/13)	11/0/4 (73/0/27)	0.28
PF volume (mL), median (IQR)	178 (166—192)	173 (163—185)	0.39
PF-x (cm), median (IQR)	10.2 (9.9—10.6)	10.1 (9.8—10.2)	0.06
PF-y (cm), median (IQR)	7.4 (7.1—8.0)	7.7 (7.2—7.9)	0.46
PF-z (cm), median (IQR)	6.5 (6.2—6.9)	6.4 (5.9—6.9)	0.66
Axial (x/y), median (IQR)	1.4 (1.3—1.5)	1.3 (1.3—1.4)	0.10
Coronal (x/z), median (IQR)	1.6 (1.5—1.7)	1.6 (1.4—1.7)	0.65
Sagittal (y/z), median (IQR)	1.2 (1.1—1.3)	1.2 (1.1—1.3)	0.32

Barrow Neurological Institute grade ≤2 was defined as favorable and Barrow Neurological Institute grade >2 as unfavorable.
IQR, interquartile range; PF, posterior fossa.

DISCUSSION

In this study, based on 84 patients with classic TN who were operated on with MVD, we found that the PF anatomy was related to the responsible vessel of the NVC, because the PF was narrower and shorter in patients with an SCA-NVC. The PF was narrower and smaller in women, but it did not differ between patients with TN and controls within each sex. There was no difference in surgical outcome after MVD related to the PF volume or dimensions. Altogether, the PF anatomy could influence the probability for the type of NVC but otherwise did not seem to be relevant in pathophysiology or as a prognostic factor after MVD in classic TN.

First, we did not find any differences in PF volume or dimensions in patients with TN with an NVC compared with controls. This finding was consistent with previous studies.[13-15] Second, women showed a smaller volume and narrower (x-axis) PF compared with men, but these differences were sex related in general and not pertinent to TN. Similarly, Hardaway et al.[12] found that females in general showed a smaller PF volume than did males, but there was no difference in PF volume between females with TN versus controls. However, the same investigators did find that the PF volume was smaller in males with idiopathic TN without NVC compared with controls.[12] Our subset of patients reflected those with an NVC who were operated on with MVD and the patients with TN without NVC were not included, which could explain the discrepancy with the latter study.[12] Third, the type of NVC differed depending on the PF anatomy. In particular, SCA as the responsible vessel for the NVC was associated with a narrower (x-axis) and shorter (y-axis) PF compared with when another posterior circulation artery was responsible for the NVC. It is possible that a narrow and short PF primarily allows SCA to come into close contact with the CN V, whereas larger dimensions allow more caudal arteries to loop toward and come into conflict with CN V. Fourth, the PF volume and dimensions were not related to BNI grade at 6 months. This finding was consistent with some previous studies that have found PF volume to be unrelated to MVD outcome.[16] However, it was in contrast to the results of Fukuoka et al.,[16] who found that a flatter (sagittal and coronal ratios) were associated with a higher rate of MVD failure. It was also in contrast with a study by Zhao et al.,[17] who found a flat PF to be prognostic of poor outcome after MVD for hemifacial spasm caused by NVC between CN VII and a cerebral vessel. We cannot fully explain the discrepancies between our findings and those from the previous studies.[16,17] However, it is possible that slight differences in surgical technique (e.g., related to surgical exposure) may be one important factor.

Strengths and Limitations

The role of PF anatomy for TN pathophysiology and its implications for MVD surgical outcomes have been investigated in only a few smaller studies.[12-16] The current study provides further insights into this matter, using a detailed radiologic analysis of the PF anatomy in relation to healthy controls, biological sex, the type of NVC, and long-term outcome after MVD in a relatively large sample of patients with classic TN. There were also some limitations. First, only patients with classic TN were included and it is possible that the PF anatomy may differ in idiopathic TN without an NVC.[12] Furthermore, further studies should be devoted to delineating the role of the anatomy of certain substructures in the PF, such as the volume of the cerebellopontine angle on magnetic resonance imaging.[14]

CONCLUSIONS

The PF anatomy was related to the responsible vessel of the NVC because the PF was narrower and shorter in patients with an SCA-NVC. Women showed narrower and smaller PF volumes than men, but it did not differ between patients with TN and controls within each sex. There was no difference in surgical outcome after MVD related to the PF volume or dimensions. Altogether, the PF anatomy could influence the probability for the type of NVC but

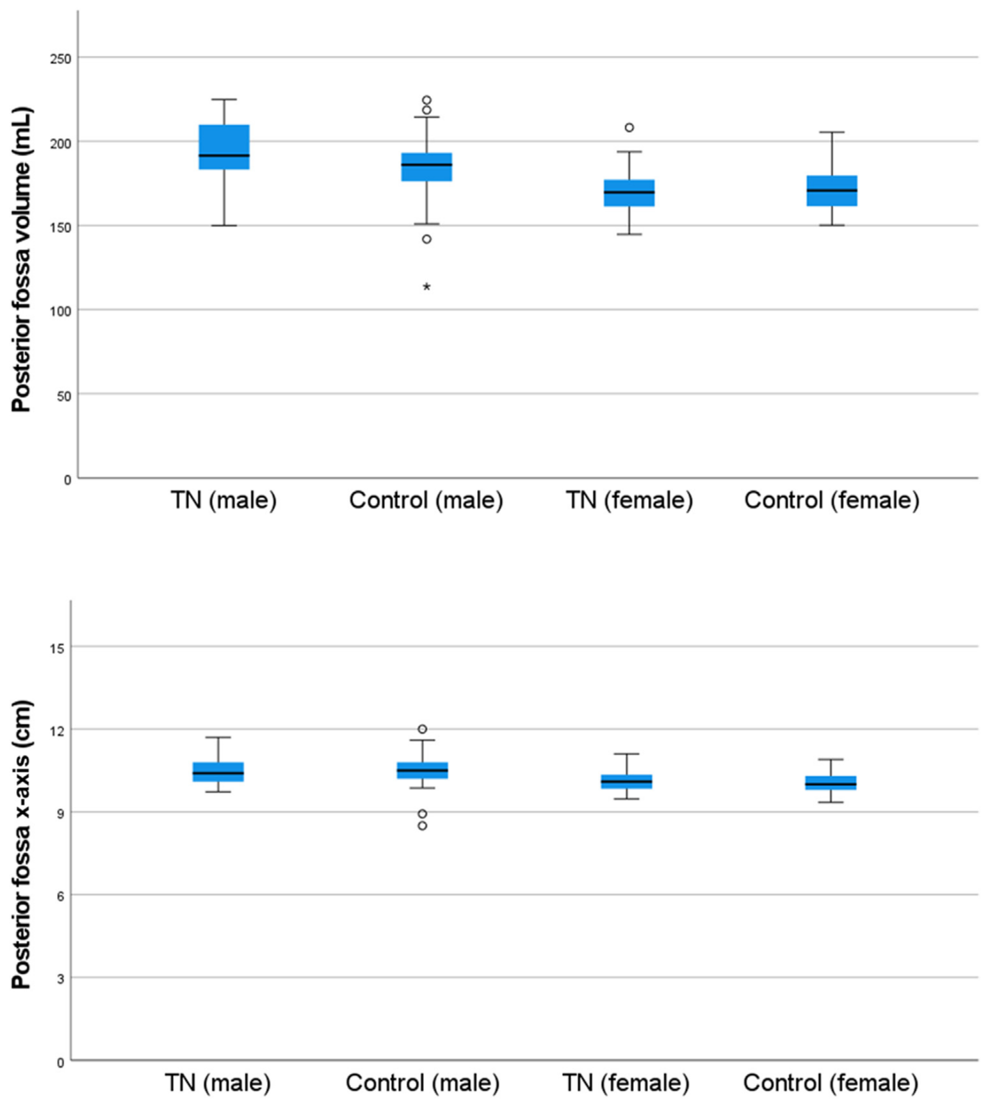

Figure 2. Differences in posterior fossa volume and width among patients with trigeminal neuralgia (TN) and controls for men and women. In Kruskal-Wallis tests (both $P < 0.05$), post hoc analyses showed that men with trigeminal neuralgia and controls had a larger posterior fossa volume and longer x-axis than did women (both $P < 0.05$), but there were no differences in these variables within each sex between patients with trigeminal neuralgia and controls ($P > 0.05$).

otherwise does not seem to be relevant in pathophysiology or prognosis after MVD in classic TN.

CRediT AUTHORSHIP CONTRIBUTION STATEMENT

Nicolas Almqvist Téran: Conceptualization, Methodology, Formal analysis, Data curation, Writing — original draft, Writing — review & editing. **Richard Loayza:** Methodology, Data curation, Writing — review & editing. **Johan Wikström:** Conceptualization, Methodology, Resources, Data curation, Writing — review & editing. **Hans Ericson:** Conceptualization, Methodology, Resources, Data curation, Writing — review & editing. **Sami Abu Hamdeh:** Conceptualization, Methodology, Data curation, Writing — review & editing. **Teodor Svedung Wettervik:** Conceptualization, Methodology, Formal analysis, Data curation, Writing — original draft, Writing — review & editing.

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