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Magnetic resonance imaging evaluation of masticatory muscle changes in patients with primary trigeminal neuralgia before microvascular decompression

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Abstract

Primary trigeminal neuralgia (PTN) is characterized by chronic neuropathic pain. There are few studies exploring masticatory muscle changes in patients with PTN. This study evaluated the changes in the masticatory muscles using magnetic resonance imaging (MRI) and the predictive factors of masticatory muscle changes in patients with PTN. The radiologic outcomes of 52 patients with PTN and 58 healthy adults were evaluated. The temporalis, lateral pterygoid, medial pterygoid, and masseter muscles were assessed using MRI. Atrophy and edema of the masticatory muscles were noted. Multivariate analyses were conducted to identify factors associated with masticatory muscle atrophy. Among the PTN group, the right side (61.5%) and mandibular branch (53.9%) were the most affected. Muscle atrophy of the temporalis ($P < .001$), medial pterygoid ($P = .016$), lateral pterygoid ($P = .031$), and masseter ($P = .001$) were significantly higher in the PTN group than in the control group. Lateral pterygoid edema was significantly higher in the PTN group ($P < .001$). However, no significant difference was found in the temporalis and masseter edema between the two groups. Logistic regression analysis demonstrated that neurovascular conflict (NVC) significantly predicted mastication muscle atrophy ($P = .037$). Patients with PTN had higher rates of masticatory muscle atrophy and edema. The assessment of NVC may be a preoperative imaging biomarker to predict atrophy in PTN.

Abbreviations: DWI = diffusion weighted imaging, MRI = magnetic resonance imaging, NVC = neurovascular conflict, PLA = People's Liberation Army, PTN = primary trigeminal neuralgia, REZ = root entry zone, VAS = visual analog scale.

Keywords: atrophy, edema, magnetic resonance imaging, masticatory muscle, neurovascular, trigeminal nerve disease

1. Introduction

Primary trigeminal neuralgia (PTN) is a chronic neuropathic pain disorder associated with spontaneous and elicited paroxysms of lightning-like or acupuncture-like pain.[1,2] Three types of trigeminal neuralgia have been delineated: classical, secondary, and idiopathic. The classical type, which is the most common, is caused by neurovascular conflict (NVC) in the trigeminal nerve root entry zone (REZ).[1,3] Unilateral masticatory muscle atrophy and edema tend to occur, but these should be considered in the clinical assessment of the motor root of the trigeminal nerve.[4] However, subclinical changes may not be detected during common clinical examinations.

According to the scientific literature,[2,5] follow-up interventions can alter masticatory function, hence accelerating atrophy of the masticatory muscles. It is imperative to explore the indicators of their atrophy, providing guidance for subsequent treatment. Magnetic resonance imaging (MRI) is recognized as the most effective method to assess the extent of NVC and masticatory muscle changes.[6] Previous studies have classified NVC into three types, through MRI evaluation: contact between the nerve and vessel, displacement and/or distortion of the nerve root, and thinning of the nerve root.[6] In addition, NVC frequently exhibits clinical symptoms, such as trigeminal neuralgia, masticatory muscle atrophy, and edema, particularly in grade III.[6] However, masticatory muscle changes have yet to be fully evaluated. There is a gap in knowledge on the association between NVC and masticatory muscle atrophy.

The purpose of the present study is to investigate the changes in masticatory muscles in patients with PTN using MRI and determine whether NVC could effectively predict the atrophy of the masticatory muscles.

XZ and CW contributed equally to this work.

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The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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2. Methods

2.1. Patients

This was a retrospective review of all patients with PTN treated using microvascular decompression at the 900th Hospital of the Joint Logistics Team of the Chinese People's Liberation Army (PLA), Fuzhou, China, between January 2018 and January 2020. Patients enrolled in the study were diagnosed with PTN according to the International Classification of Headache Disorders-3, based on five typical and recognizable diagnostic criteria.[7] Other eligibility criteria included: confirmation of NVC by MRI and microvascular decompression, MRI scans including four mastication muscles, presence of unilateral trigeminal neuralgia, and no prior surgery or any other invasive operation. Patients with secondary trigeminal neuralgia or other diseases leading to trigeminal neuralgia and incomplete MRI data were excluded. Finally, 52 patients were enrolled in the study. In addition, 58 healthy adults were included in the control group. This study was reviewed and approved by the Institutional Review Board of the 900th Hospital of the Joint Logistics Team of the Chinese PLA. The data were anonymous, and the requirement for informed consent from the patients was waived. All study procedures were performed in accordance with the Helsinki Declaration of 1964 and later versions.

2.2. MRI procedure

All patients were examined by thin-layer MRI of the trigeminal nerve before microvascular decompression, and MRI was performed using 3.0T GE superconducting magnetic resonance scanner (Signa HDxt 3.0T, America). During the examination, all patients were instructed to lie in the supine position and scanned using T1WI, T2WI sequence, coronal T2WI, and sagittal T1WI sequence to rule out craniocerebral organic lesions. The patients were then scanned using diffusion weighted imaging (DWI), using a single-shot-spin echo sequence in a transverse plane. The scanning parameters were as follows: TR/TE 8100 ms/73 ms, visual field, 200 mm × 200 mm; matrix, 128 × 160; slice thickness, 4 mm; no layer interval; two b-values, 0 and 800 s/mm^2. Lastly, three-dimensional time-hopping angiography (3D time of Flight MRA, 3D-TOF MRA) was performed parallel to the cistern segment of the trigeminal nerve. Thus, the prepontine cistern segment of the trigeminal nerve was scanned with the pons as the center. 3D-TOF MRA scanning parameters were as follows: TR, 20 ms; TE, 2.5 ms; flip angle, 20°; matrix, 320 × 192; visual field, 162 mm × 200 mm, and layer thickness of 1.2 mm. After the scan was completed, the left and right oblique sagittal and coronal images were reconstructed according to the location and walking direction of the trigeminal nerve shown in the cross-sectional magnetic resonance images, and the blood vessels were reconstructed using maximum intensity projection.

2.3. Data collection

Data pertaining to demographic characteristics, pain duration, location of pain, visual analog scale (VAS) score, use of antiepileptic drugs, and atrophy and edema of the masticatory muscles of the patients were collected retrospectively. VAS scores ranged from 0 to 10 points (0 for no pain, 1–3 for mild pain, 4–6 for moderate pain, and 7–10 for severe pain).[8] Two radiologists with 9 and 10 years of experience in craniocerebral MR diagnosis, respectively, analyzed the scans on the Picture Archiving and Communication System workstation without knowing the surgical results of the patient and reached an agreement. NVC was classified into grade I, grade II, and grade III depending on the relationship between the nerve and vessel.[6] The edema pattern was defined as the presence of intramuscular DWI signal hyperintensity relative to the normal muscle signal intensity, as previously described.[9]

T1W1 MRI was applied to analyze the bulk of the temporalis, medial pterygoid, lateral pterygoid, and masseter muscles in the axial planes, respectively. For temporalis muscle thickness, the anterior commissure-posterior commissure (AC-PC) line was regarded as the reference plane. The thickness of the temporalis muscle was measured 15 mm above the AC-PC line using multiplanar cross-referencing. For the medial pterygoid and masseter muscle thickness, the maximum thickness was measured at the level of the hard palate. For the lateral pterygoid muscle thickness, the maximum thickness was measured in a plane above that of the masseter muscle (Fig. 1). Atrophy in PTN group was defined as follows: [(normal muscle thickness—atrophic muscle thickness)/normal muscle thickness] × 100% ≥ 20%.[4] Atrophy in the control group was defined as follows: [(thicker muscle thickness—thinner muscle thickness)/thicker muscle thickness] × 100% ≥ 20%.

2.4. Statistical analysis

Continuous data were analyzed using the Wilcoxon rank-sum test. Categorical variables were analyzed using the chi-square test or Fisher exact test, as appropriate. Logistic regression analysis was used in the univariate and multivariate settings. The differences were considered significant when the *P*-values were < .05. All statistical analyses were performed using the SPSS software (IBM SPSS Statistics for Windows, version 22.0, Armonk, NY).

3. Results

3.1. Patient characteristics

In total, 75 patients with PTN were treated using microvascular decompression at our hospital during the study period. A total of 23 patients were excluded because of previous surgical treatments (n = 16), missing data (n = 5), and bilateral trigeminal neuralgia (n = 2), leaving 52 patients for analysis. In addition, 58 healthy adults were enrolled in the control group.

The characteristics of patients with PTN are shown in Table 1. The median age was 63.5 years (range: 30–85 years), and 22 were male. The median pain duration before enrollment was 36 months (range: 2–240 months). The right side (61.5%) and the mandibular branch (53.9%) were the most affected, with a mean pain intensity of 6, according to VAS. The pain was partly relieved; 39 (75.0%) patients achieved pain control with carbamazepine while the other 13 (25%) patients required carbamazepine and gabapentin for pain control. Thinning of the nerve root (grade III NVC) was observed in 13 (25%) patients.

3.2. Comparison between PTN group and control group

No significant differences were found in age or sex between the two groups. Temporalis, masseter, and medial pterygoid muscle atrophy on the side with pain were observed in 14 (26.9%), 11 (21.2%), and 5 (9.6%) patients, respectively (Fig. 2). Only 4 (7.7%) patients with PTN exhibited lateral pterygoid atrophy. Notably, the rates of atrophy in all four mastication muscles were significantly higher in the PTN group than in the control group ($P < .05$). Furthermore, lateral pterygoid edema was also significantly higher in the PTN group ($P < .001$) (Fig. 3). However, no significant difference was found in the temporalis and masseter edema between the two groups (Table 2).

3.3. Factors predictive of masticatory muscle atrophy

Logistic regression analysis was performed to identify factors predictive of mastication muscle atrophy. Age, sex, pain duration, pain location, VAS score, nerve branch affected, types of drugs, and NVC were analyzed. Univariate and multivariate

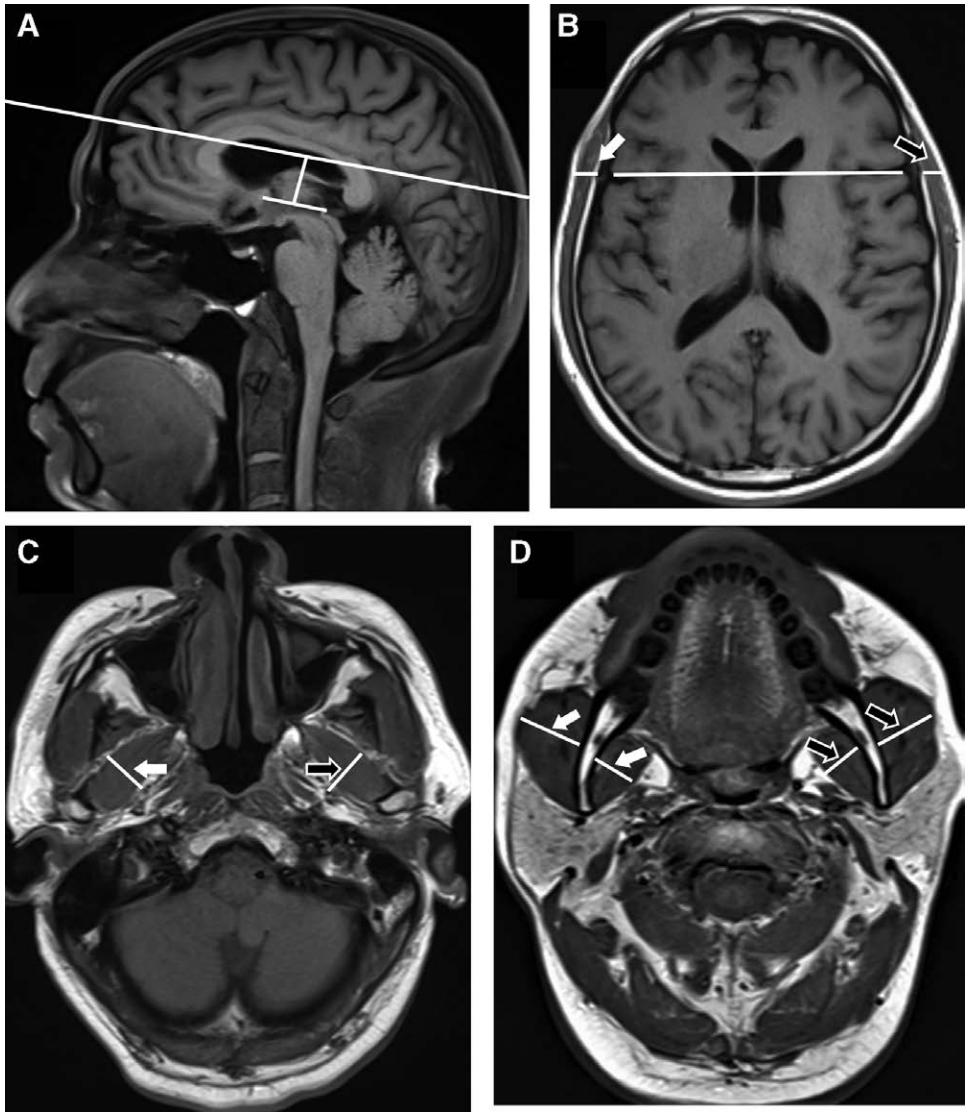

Figure 1. Measurement of muscle thickness and normal muscle anatomy. The temporalis muscle thickness is measured in the axial plane (A), it is parallel and 15 mm superior to the AC-PC line. Normal temporalis muscles (white and black arrows, B), were measured at the point of intersection of a line passing through the anterior limit of the septum pellucidum in the axial section. Normal lateral pterygoid muscles (white and black arrows, C). The maximum muscle thickness was measured perpendicular to the longitudinal axis of the muscle. Normal masseter muscles (white and black arrowheads, D) and medial pterygoid muscles (white and black arrows). The maximum muscle thickness of masseter and medial pterygoid muscles was measured perpendicular to the longitudinal axis of the muscle at the level of the hard palate.

analyses identified NVC as a significant predictor of masticatory muscle atrophy ($P < .05$) (Table 3).

4. Discussion

Radiographically relevant changes in the masticatory muscles in patients with PTN have not been well elucidated. To the best of our knowledge, this study is at the forefront to investigate these muscle changes and explore the predictive factors of masticatory muscle atrophy. The results demonstrated a marked increase in masticatory muscle atrophy in patients with PTN. Previous studies have reported that some patients with TN having significant pain on chewing have disuse atrophy of the muscles of mastication, which is consistent with the findings of this study.[3] Furthermore, the number of patients with muscle edema in the PTN group was higher than that in the control group in this study, especially for the lateral pterygoid muscle. Multivariate analysis identified thinning of the nerve root as an independent predictive factor for muscle atrophy. These findings suggest that the NVC grade, determined using MRI, is potentially predictive of masticatory muscle atrophy in patients with PTN, which will be helpful in evaluating the prognosis of the patients.

In this study, patients in the PTN group had a significantly higher rate of atrophy in the four masticatory muscles, especially in the temporalis, medial pterygoid, and masseter muscles. Fatty replacement and resultant signal changes can occur in atrophied masticatory muscles. This could be caused by muscle disuse and degeneration. Biopsy of denervated muscles, performed by Carrao et al,[10] showed that the atrophic muscle fibers were separated by a large number of adipocytes and connective tissue, which could potentially explain our findings. A previous study[4] demonstrated that patients with PTN preferred to chew food using the side without pain instead of the side with pain. As a result, some patients consumed only liquids or soft food to avoid chewing. Emily et al[11] suggested that the loss of muscle mass was associated with alterations in muscle protein turnover during disuse. At the same time, five patients exhibited hypertrophy of the contralateral masticatory muscles, which may be compensatory hypertrophy.[12] The masticatory muscles play the role of moving the mandible, while the lateral

Table 1

Demographics and clinical characteristics of patients.

Characteristics	n = 52
Age (years)*	63.5 (30–85)
Sex (male/female)	22/30
Pain duration*	36 (2–240)
Pain side	
Right	32 (61.5)
Left	20 (38.5)
VAS*	6 (2-9)
Branches affected	
V1	1 (1.9)
V2	14 (26.9)
V3	21 (40.4)
V1, V2	9 (17.3)
V2, V3	7 (13.5)
Types of drugs	
Carbamazepine	39 (75.0)
Carbamazepine, gabapentin	13 (25.0)
NVC	
Grade I	23 (44.2)
Grade II	16 (30.8)
Grade III	13 (25.0)

NVC = neurovascular conflict, VAS = visual analog scale.
*Median (range).

pterygoid muscles are the only muscles that depress the mandible, and cannot trigger an attack of pain.[4,13] Therefore, disuse atrophy of the lateral pterygoid muscles was less significant than the other masticatory muscles.

Demyelination caused by NVC in the trigeminal nerve allows the transmembrane passage of ions in the underlying axon, causing trigeminal neuralgia.[1] While not all NVC grades exhibit clinical symptoms, 30% and 2% of healthy individuals could be classified as grade I and II, respectively.[6] Only cases of grade III NVC have a definite diagnosis of vascular compression. Therefore, we performed multivariate analysis and identified grade III NVC as a relevant factor of muscle atrophy, referring to grade I or II NVC in the present study. This finding shows that there is a significant correlation between grade III NVC and changes in masticatory function, which plays a positive role in objectively evaluating patients with PTN. It is worth noting that the association between muscle atrophy and pain duration, pain degree, and pain control should not be ignored. The characteristics and methods to relieve pain of trigeminal neuralgia may significantly contribute to masticatory muscle changes.

The present study revealed that masticatory muscle edema was greater in the PTN group, and a significant difference was found in the lateral pterygoid muscles ($P < .001$). Furthermore, patients with lateral pterygoid edema had a shorter median course of disease than those without edema (4.5 months vs 45 months, $P < .05$). Pulsatile compression of the trigeminal nerve is the cause of denervation in patients with PTN, which may be due to long-term compression of blood vessels, leading to nerve inflammation and demyelination, and finally, trigeminal nerve atrophy and denervation of masticatory muscles.[6,14] Several studies have reported that the typical MRI manifestations of muscle denervation are increased signal intensity on T2WI or other sequences that are sensitive to water, especially in the acute or subacute stage.[15,16] We speculate that muscle denervation leads to the edema of the fibrous stroma of the target muscle, with the dilation of blood vessels in the target muscle, hyperemia, congestion, exudation, focal atrophy of muscle fibers, and widening of the muscle space. At this time, the transverse and axial dispersion of water molecules is limited, which will cause an increase in DWI signal.[17] Therefore, DWI can be used to evaluate the pathological changes in muscle tissues. A study by Ahlawat et al[9] found that an intramuscular edema-like signal on both low- and high-b-value sequences was detected with a substantial inter-observer agreement. DWI using a low b-value tends to minimize the perfusion-related contribution and provides a heavier T2WI with anatomic information, while DWI with a high b-value leads to the progressive loss of signals that potentially explains the reduced visibility of intramuscular elevated signals on DWI with low and high b-values.

The degree of masticatory muscle atrophy in patients with PTN, determined using MRI, can be used as an objective index of pain in such patients, which will provide a reference for clinicians to identify patients suitable for surgical intervention, to provide a basis for prognosis evaluation, and in improving the quality of life of patients.

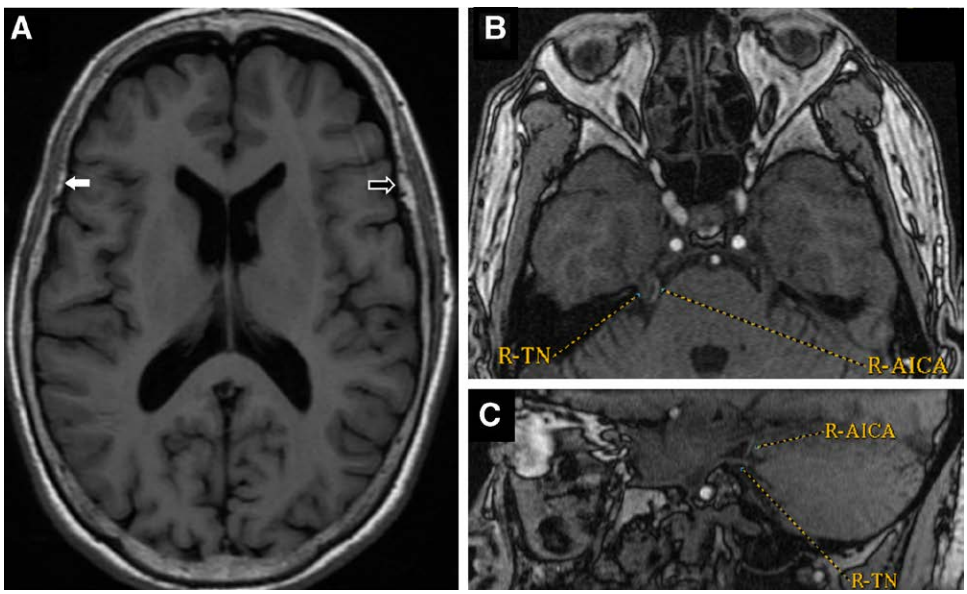

Figure 2. Temporalis muscle atrophy in a patient with right-sided TN. (A) T1-weighted MRI scans showed temporalis muscle atrophy on the right side (white arrow) in comparison to the normal temporalis muscle on the left side (black arrow). (B and C) The axial and sagittal scans of magnetic resonance tomography angiography (MRTA) showed that the right TN was slender. The right anterior inferior cerebellar artery was closely related to the right TN, and the space between blood vessels and nerves was smaller than the diameter of blood vessels.

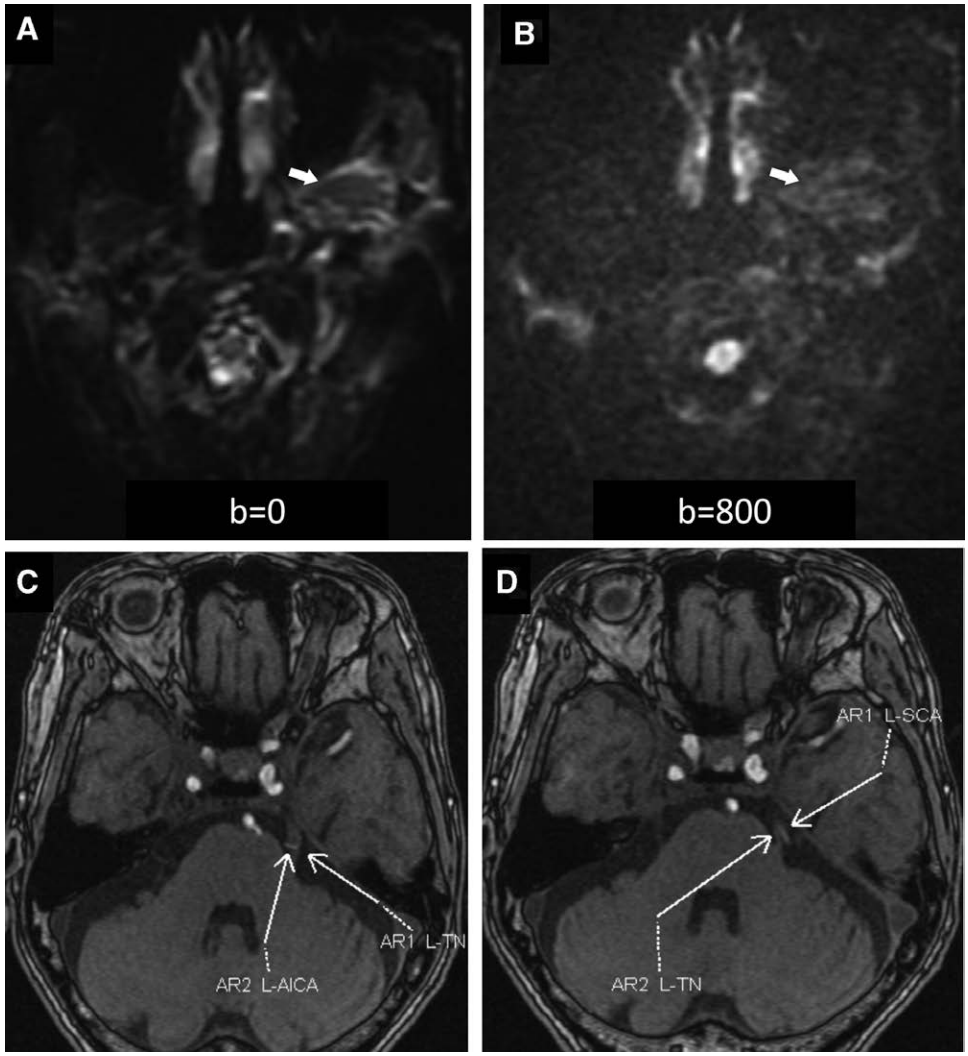

Figure 3. Lateral pterygoid muscle edema in a patient with left-sided TN. (A and B) DWI images obtained in a patient with left-sided TN, showing the signal intensity of left lateral pterygoid muscle was obviously high (white arrow). With the increase of B value, DWI image grain becomes thicker, muscle signal decreases, and image quality decreases. (C and D) MRTA scans showing the left anterior inferior cerebellar artery and superior cerebellar artery was closely related to the left TN, and the space between blood vessels and nerves was smaller than the diameter of blood vessels. DWI = diffusion weighted imaging.

Table 2

Comparison of mastication muscles changes.

Characteristics	PTN group (n = 52)	Control group (n = 58)	*P*-value
Age (years)*	63.5 (30–85)	54 (30–83)	.77
Sex (male/female)	22/30	28/30	.530
Temporalis atrophy	14 (26.9)	1 (1.7)	<.001
Medial pterygoid atrophy	5 (9.6)	0 (0)	.016
Lateral pterygoid atrophy	4 (7.7)	0 (0)	.031
Masseter atrophy	11 (21.2)	1 (1.7)	.001
Temporalis edema	1 (1.9)	0 (0)	.289
Lateral pterygoid edema	16 (30.8)	3 (5.2)	<.001
Masseter edema	3 (5.8)	1 (1.7)	.258

PTN = primary trigeminal neuralgia.
*Median (range).

Table 3

Logistic regression analysis for factors predictive of muscle atrophy.

Variable	Odds ratio	95% confidence interval	*P* value
Univariate analysis			
Age	0.995	0.946–1.046	.841
Sex	2.167	0.706–6.645	.176
Pain duration	0.684	0.987–1.009	.684
Pain location	0.882	0.288–2.699	.826
VAS	1.093	0.756–1.580	.636
Branch affected (single/double)	1.863	0.558–6.217	.312
Types of drugs	2.625	0.690–9.980	.157
NVC (grade I or II/ grade III)	0.232	0.055–0.976	.046
Multivariate analysis			
Pain duration	0.998	0.986–1.010	.703
Branch affected (single/double)	2.994	0.777–11.532	.111
Types of drugs	1.280	0.281–5.830	.750
NVC (grade I or II/ grade III)	0.173	0.033–0.901	.037

NVC = neurovascular conflict, VAS = visual analog scale.

This study had several limitations. This was a retrospective study with a relatively small sample size. In addition, we were unable to assess the medial pterygoid edema because of the defect in our images. Furthermore, patients were unable to follow-up in this study. Thus, further investigation is required in the future.

5. Conclusion

In this study, we assessed the muscles of mastication in patients with PTN through MRI evaluation. We found higher rates of atrophy and edema in the masticatory muscles of these patients. Moreover, multivariate analysis identified grade III NVC as an independent predictor of muscle atrophy. The NVC grade is a feasible and promising factor in patients with PTN to predict subsequent masticatory muscle changes, especially muscle atrophy. Thus, DWI data need to be further collected and analyzed.

Author contributions

Conceptualization: Hui Xiao, Qun Zhong.
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Funding acquisition: Hui Xiao.
Investigation: Xiaojuan Zhang, Dan Zheng.
Methodology: Xiaojuan Zhang, Chuandong Wang.
Project administration: Chuandong Wang.
Software: Xiaojuan Zhang, Chuandong Wang.
Writing – original draft: Xiaojuan Zhang, Chuandong Wang.
Writing – review & editing: Hui Xiao, Qun Zhong.

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