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Diffusion Tensor Imaging of the Lateral Pterygoid Muscle in Patients with Temporomandibular Joint Disorders and Healthy Volunteers

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Objective: This study aimed to explore the feasibility of functional evaluation of the lateral pterygoid muscle (LPM) using diffusion tensor imaging (DTI) in patients with temporomandibular joint disorders (TMDs).

Materials and Methods: A total of 119 patients with TMD (23 male and 96 female; mean age ± standard deviation, 41 ± 15 years; 58 bilateral and 61 unilateral involvements for a total of 177 joints) and 20 healthy volunteers (9 male and 11 female; 40 ± 13 years; 40 joints) were included in this prospective study. Based on DTI of the jaw in the resting state, the diffusion parameters, apparent diffusion coefficient (ADC), fractional anisotropy (FA), $\lambda 1$, $\lambda 2$, and $\lambda 3$ of the superior and inferior heads of the LPM (SHLPM and IHLPM) were measured. Patients with TMD with normal disc position (ND), anterior disc displacement with reduction (ADWR), and anterior disc displacement without reduction (ADWOR) were compared.

Results: Patients with TMD overall, and ADWR and ADWOR subgroups had significantly higher ADC, $\lambda 1$, $\lambda 2$, and $\lambda 3$ in both the SHLPM and IHLPM than those in volunteers ($p < 0.05$ for all), whereas the ND subgroup only had significantly higher ADC and $\lambda 1$ ($p < 0.001$). Meanwhile, significant differences in FA in the SHLPM and IHLPM were found between volunteers and ADWOR ($p = 0.014$ and $p = 0.037$, respectively). Among the three TMD subgroups, except for $\lambda 3$ and FA in the ADWR subgroup, ADWR and ADWOR subgroups had significantly higher ADC, $\lambda 1$, $\lambda 2$, and $\lambda 3$ and lower FA than those in the ND group ($p < 0.050$). There was no significant difference in diffusion variables between ADWR and ADWOR. In ADWOR, the osteoarthritis group had significantly higher $\lambda 3$ and lower FA values in the IHLPM than those in the non-osteoarthritis group.

Conclusion: DTI successfully detected functional changes in the LPM in patients with TMD. The unsynchronized diffusivity changes in the LPM in different subgroups of TMD signified the possibility of using diffusion parameters as indicators to identify the severity of LPM hyperfunction at various stages of TMD.

Keywords: *Diffusion tensor imaging; Lateral pterygoid muscle; Temporomandibular joint disorder*

INTRODUCTION

Temporomandibular joint disorder (TMD) is a complex and multifactorial disorder that affects the normal function of the temporomandibular joint (TMJ) and masticatory muscles, resulting in pain and disability [1]. Although

there are four primary masticatory muscles related to the function of the TMJ, the lateral pterygoid muscle (LPM) plays a more significant role because of its anatomy and physiological function [1-5]. Previous studies have demonstrated the relationship between the LPM and TMD using electromyography [4,5]; however, non-invasive visual

evaluation of LPM function *in vivo* remains challenging. Our previous study [6] confirmed that diffusion tensor imaging (DTI), a functional MRI technique, could enable non-invasive visual evaluation of the function of the LPM during jaw movement in healthy volunteers because it can detect the anisotropy of water molecule diffusion *in vivo*. Therefore, the present study aimed to quantitatively evaluate diffusivity changes in the LPM of patient with TMD and the feasibility of staging TMD by evaluating the severity of LPM dysfunction using DTI.

MATERIALS AND METHODS

This prospective study was approved by the Institutional Review Board of Tongji Medical College, Huazhong University of Science and Technology (IRB No. TJ-IRB20160381). All patients with TMD and volunteers provided informed consent to participate in the study before the examination.

Study Populations

Figure 1 shows a flowchart of the study. A total of 162 patients with TMD (affecting a total of 263 TMJs, including 61 patients with unilateral and 101 with bilateral TMD) were recruited from September 2016 to July 2020. The 'Diagnostic criteria for temporomandibular disorders (DC/TMD) for clinical and research applications' [7], as recommended by the International the Original Research

Diagnostic Criteria for TMD (RDC/TMD) Consortium Network and Orofacial Pain Special Interest Group was applied. The inclusion criteria for patients with TMD were as follows: 1) pain in the temporomandibular region, 2) joint clicking, popping, and/or snapping noise during jaw movements, 3) maximum assisted opening (passive stretch) movement, including vertical incisal overlap, < 40 mm, and 4) no head or neck treatment before MRI examination. Forty-two TMJs with TMD were excluded because of susceptibility artifacts on MRI (29 TMJs in 17 patients, 5 with unilateral and 12 with bilateral TMD) and fully limited jaw opening (13 TMJs). Most disc displacement occurs in the anterior direction [8], and previous studies have shown that anterior disc displacement is closely related to the LPM [9-11]. To study the relationship between LPM dysfunction and TMD, 44 TMJs with side disc displacement were excluded to eliminate the influence of side disc displacement. Twenty volunteers who met the following inclusion criteria were selected: 1) no clinical symptoms of TMD, 2) normal occlusion, and 3) no head or neck treatment before the MRI examination. Table 1 summarizes the demographic information of patients with TMD and volunteers.

MRI Acquisition

All patients and volunteers underwent TMJ imaging on a 3T scanner (Discovery 750; GE Medical Systems) with a 32-channel head coil. First, oblique sagittal and oblique
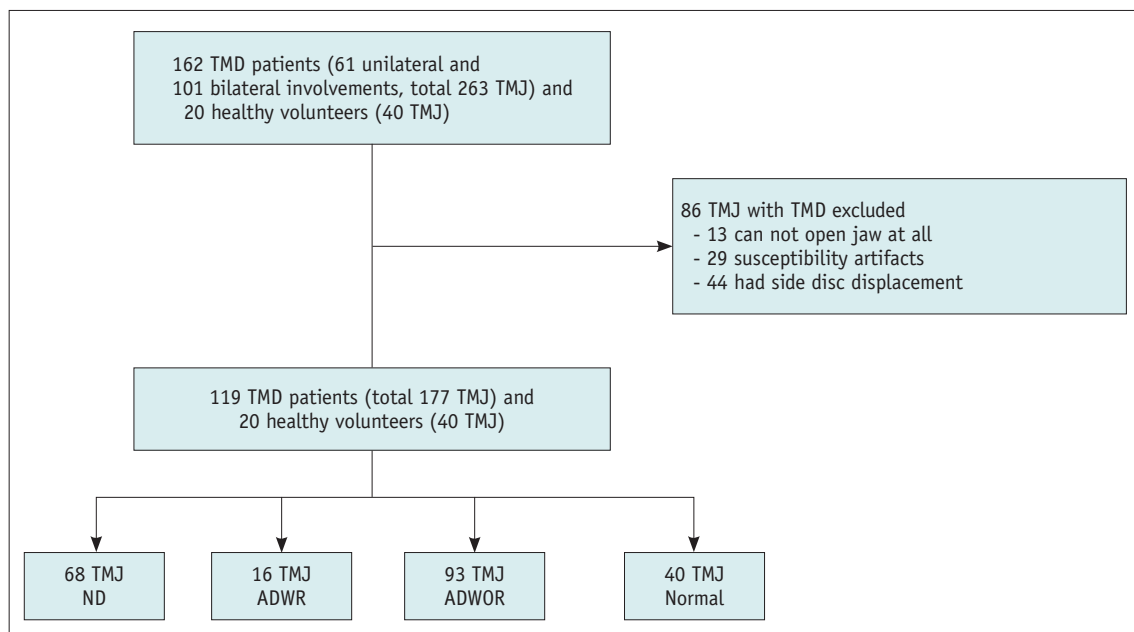

Fig. 1. Study enrollment of TMD patients and volunteers. ADWOR = anterior disc displacement without reduction, ADWR = anterior disc displacement with reduction, ND = normal disc position, TMD = temporomandibular joint disorder, TMJ = temporomandibular joint

Table 1. Characteristics of TMD Patients and Volunteers

	TMD Patients (n = 119)	Volunteers (n = 20)
Demographic data		
TMJ number	177	40
Age in years, mean ± SD	41 ± 15	40 ± 13
Age range in years	18 to 72	16 to 58
Male:female ratio	23:96	9:11
Clinical symptoms*		
Pain in temporomandibular region	113 (63.8)	
Joint clicking	16 (9)	
Limited mouth opening	97 (54.8)	
Disease duration, acute:chronic	38:139	

*Data are number of patients with percentage in parentheses, unless specified otherwise. SD = standard deviation, TMD = temporomandibular joint disorder, TMJ = temporomandibular joint

coronal T2-weighted fast spin echo with fat saturation (FS-FSE-/T_2WI; repetition time/echo time [TR/TE], 2875/84 ms) and proton density-weighted fast spin-echo (FSE-PDWI; TR/TE, 2700/12 ms) were performed in the closed and open mouth positions. A three-dimensional brain volume (3D-BRAVO) sequence was then performed in the closed mouth position with the following parameters: TR/TE, 8.3/3.2 ms; matrix, 256 x 256; thickness/gap, 1.2/0 mm; number of excitations (NEX), 1; field of view (FOV), 24 mm. Finally, spin-echo echo-planar imaging (SE-EPI)-DTI was performed in the closed-mouth position with the following parameters: TR/TE, 6500/81.4 ms; matrix, 128 x 128; thickness/gap, 2.0/0 mm; FOV, 20 cm; NEX, 2; motion-probing gradients were applied in 25 different directions with b-values of 0 and 600 s/mm². According to previous studies [12,13], the musculature has a much shorter T_2/T_1 ratio than the brain, especially for higher strength magnetic fields. Therefore, the signal-to-noise ratio in diffusion-weighted images of the musculature is relatively poor for higher b-values. Thus, DTI applications in the musculature usually use b-values of 400–700 s/mm²; the b-value in this study was set to 600 s/mm². In addition, to ensure that the LPM is in a resting state [14], the patients and volunteers were asked to maintain their postural position on the examination table for more than 15 minutes before DTI imaging.

Image Analysis

MRIs from all patients with TMD and volunteers were reviewed by two radiologists (with 13 and 18 years of experience) to evaluate the MRI characteristics, including disc displacement, presence or absence of limited jaw opening, joint effusion, and osteoarthritis (OA). According to the status of disk displacement [7], TMD patients

were categorized into three subgroups: 1) normal disc position (ND): the posterior band of the disc located at approximately the 12 o'clock position relative to the condyle apex in the maximum intercuspal position, while the middle band is placed between the condylar head and articular eminence at the full opening, 2) anterior disc displacement with reduction (ADWR): the posterior disc band located anterior to the 11:30 position in the maximum intercuspal position and return to normal position on the full opening, and 3) anterior disc displacement without reduction (ADWOR): the posterior disc band is located anterior to the 11:30 position in the maximum intercuspal position, while it remains in an anterior to the condyle at full opening. Furthermore, based on the presence or absence of OA, the ADWOR group was further divided into two subgroups: non-OA (NOA) and OA.

Post-processing of DTI was performed by two radiologists using DTI Studio software (http://www.mristudio.org). First, the axial DTI B0 image and BRAVO image of the superior and inferior heads of the LPM (SHLPM and IHLPM) in the plane of the maximum axial cross-section of the muscle were overlapped. The shape and size of the overlapping region were used to set regions of interest (ROIs), which were then placed on the DTI B0 images (Fig. 2). The fascia, blood vessels, and fat were avoided when creating the ROIs to ensure consistency and accuracy of the measurements. Diffusion-related variables, including ADC, fractional anisotropy (FA), λ1, λ2, and λ3, were calculated and compared between healthy controls and patients with TMD and their subgroups.

Statistical Analyses

Statistical analyses were performed using IBM SPSS Statistics for Windows, Version 20.0 (IBM Corp.). The chi-squared test and Mann-Whitney U test were used to evaluate the sex and age differences between patients with TMD and volunteers. The interclass correlation coefficient (ICC) was used to evaluate the interobserver agreement of the quantitative measurements. The indicator for good agreement was set at an ICC > 0.75. The Mann-Whitney U test was used to assess the difference in diffusion variables between volunteers and all patients with TMD, as well as between volunteers and three TMD subgroups after testing the normality of the data distribution using the Shapiro-Wilk test. The Mann-Whitney U test was also used to evaluate the difference between the two ADWOR subgroups. The Kruskal-Wallis one-way analysis of variance test was

applied to evaluate differences in diffusion variables between TMD subgroups in a post hoc analysis. $p < 0.050$ was considered statistically significant.

RESULTS

A total of 119 patients with TMD (177 TMJs) and 20 healthy volunteers (40 TMJs) were included in the current study after following the inclusion and exclusion criteria. Based on the disc position, TMD patients (177 TMJs) were further divided into three subgroups: ND (68 TMJs), ADWR (16 TMJs), and ADWOR (93 TMJs). The ADWOR group was further divided into two subgroups based on the absence or presence of OA: NOA (58 TMJs) and OA (35 TMJs).

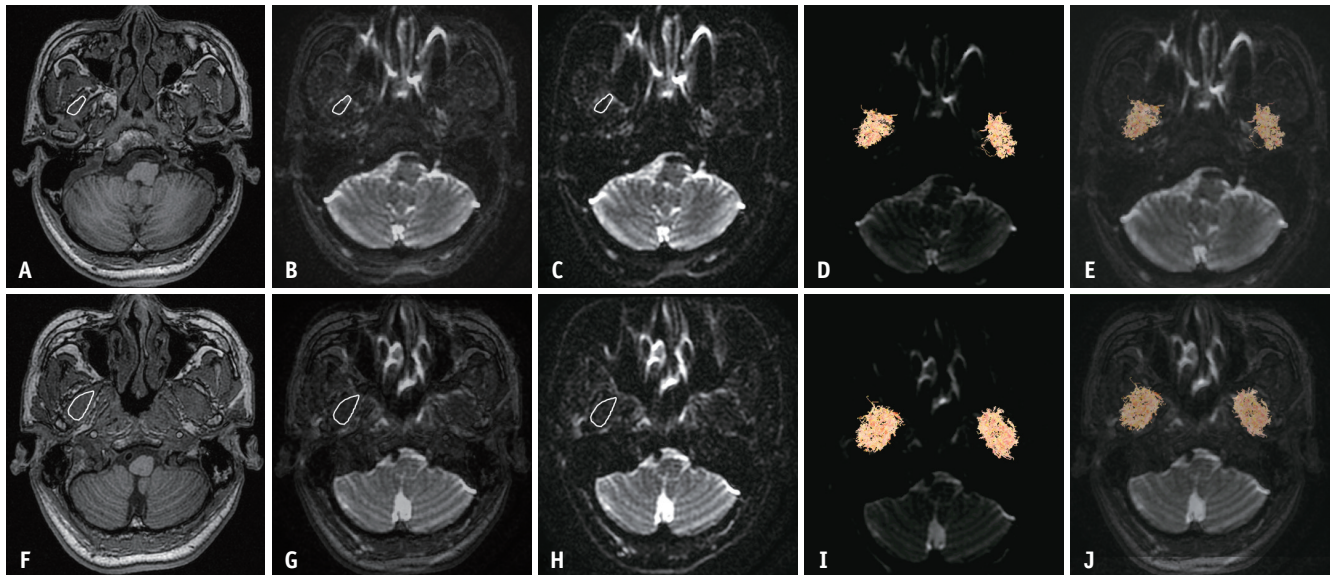The measurement of ADC, FA, λ1, λ2, and λ3 between the two readers was in good agreement (ICC > 0.75). The

Fig. 2. The method for setting ROI at SHLPM (A-E) and IHLPM (F-J).
A-J. The overlapping region of SHLPM and IHLPM in overlapped images **(B, G)**, acquired by fusing three-dimensional brain volume images **(A, F)** and DTI B0 images **(C, H)** (both at the plane of a maximum axial cross-section of the muscle), were used as ROIs. Then the ROI was placed on DTI B0 images **(C, H)**. The diffusion tensor tractography images (axial) of SHLP **(D)** and IHLP **(I)** were fused with the overlapped images **(B, G)** respectively to provide detailed anatomy **(E, J)**. DTI = diffusion tensor imaging, IHLPM = inferior head of the lateral pterygoid muscle, ROI = region of interest, SHLPM = superior head of the lateral pterygoid muscle

Table 2. Difference in Diffusion Parameters (ADC, FA, λ1, λ2, and λ3) of SHLPM and IHLPM among Volunteers and TMD Patients

Muscle	Parameters	Volunteer (n = 40)	TMD (Total, n = 177)	ND (n = 68)	ADWR (n = 16)	ADWOR (n = 93)
SHLPM	ADC	1.505 ± 0.010	1.588 ± 0.080*	1.530 ± 0.035[†]	1.583 ± 0.021[‡]	1.632 ± 0.082[§]
	FA	0.469 ± 0.033	0.462 ± 0.041	0.476 ± 0.038	0.470 ± 0.024	0.450 ± 0.042[§]
	λ1	2.270 ± 0.067	2.387 ± 0.108*	2.327 ± 0.087[†]	2.392 ± 0.057[‡]	2.429 ± 0.108[§]
	λ2	1.430 ± 0.032	1.502 ± 0.085*	1.442 ± 0.054	1.499 ± 0.033[‡]	1.546 ± 0.084[§]
	λ3	0.815 ± 0.059	0.877 ± 0.104*	0.821 ± 0.071	0.858 ± 0.041[‡]	0.921 ± 0.112[§]
IHLPM	ADC	1.508 ± 0.015	1.557 ± 0.063*	1.517 ± 0.038	1.570 ± 0.033[‡]	1.583 ± 0.067[§]
	FA	0.470 ± 0.031	0.466 ± 0.030	0.476 ± 0.026	0.467 ± 0.030	0.459 ± 0.031[§]
	λ1	2.283 ± 0.062	2.347 ± 0.086*	2.303 ± 0.068	2.371 ± 0.075[‡]	2.374 ± 0.087[§]
	λ2	1.423 ± 0.029	1.473 ± 0.062*	1.435 ± 0.040	1.486 ± 0.031[‡]	1.499 ± 0.066[§]
	λ3	0.818 ± 0.055	0.851 ± 0.079*	0.814 ± 0.058	0.853 ± 0.062[‡]	0.878 ± 0.084[§]

Data are mean ± standard deviation. *$p < 0.050$ for the comparison between TMD and volunteer, [†]$p < 0.050$ for the comparison between ND and volunteer, [‡]$p < 0.050$ for the comparison between ADWR and volunteer, [§]$p < 0.050$ for the comparison between ADWOR and volunteer. FA is unit-less, all other diffusion tensor imaging-derived parameters values are in units of 10^{-3} mm²/sec. ADC = apparent diffusion coefficient, ADWOR = anterior disc displacement without reduction, ADWR = anterior disc displacement with reduction, FA = fractional anisotropy, IHLPM = inferior head of the lateral pterygoid muscle, ND = normal disc position, SHLPM = superior head of the lateral pterygoid muscle, TMD = temporomandibular joint disorder

average of the two readers' measurements was used for further data analysis. Age and sex were not significantly different between volunteers and all TMD patients (age: $p = 0.898$ and sex: $p = 0.092$).

As shown in Table 2, compared to volunteers, all patients with TMD, and ADWR and ADWOR subgroups had significantly higher ADC, $\lambda 1$, $\lambda 2$, and $\lambda 3$ in both the SHLPM and IHLPM ($p < 0.050$). In contrast, the ND subgroup had significantly higher ADC and $\lambda 1$ ($p < 0.001$). Meanwhile, a significant difference in FA in the SHLPM and IHLPM was only found between volunteers and the ADWOR groups ($p = 0.014$ and $p = 0.037$, respectively). Among the three TMD subgroups (Fig. 3), except for $\lambda 3$ and FA in the ADWR

subgroup, ADWR and ADWOR had significantly higher ADC, $\lambda 1$, $\lambda 2$, and $\lambda 3$ and lower FA values than those of the ND subgroup ($p < 0.050$). However, there was no significant difference in any of the diffusion parameters between the ADWR and ADWOR subgroups.

Compared to the NOA subgroup, the OA subgroup had a significantly higher $\lambda 3$ ($p = 0.001$) and significantly lower FA ($p < 0.001$) in the IHLPM (Table 3).

DISCUSSION

Our previous study [6] confirmed the potential application of DTI in assessing LPM function in jaw movement. We
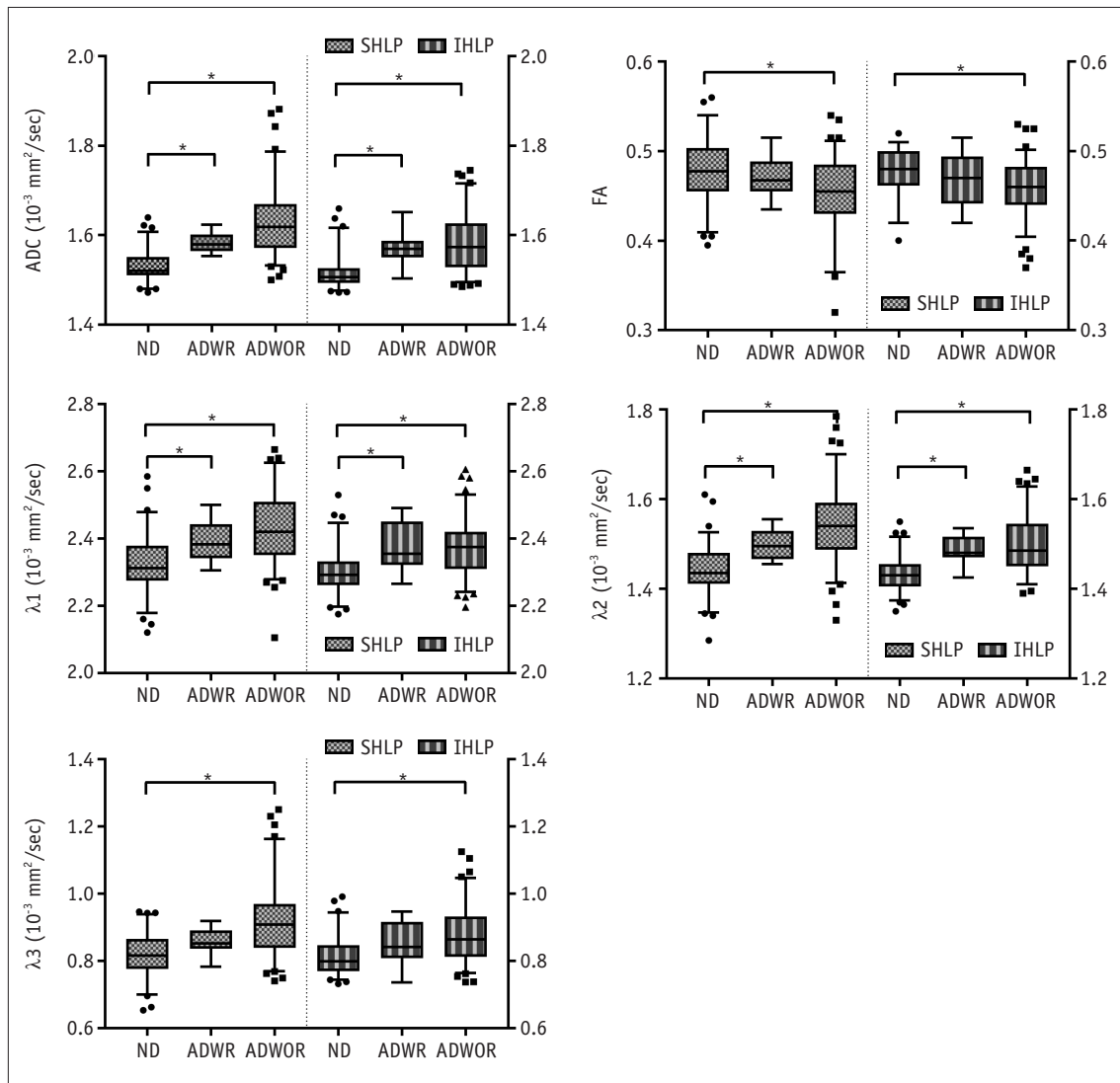

Fig. 3. The diffusion parameters (ADC, FA, $\lambda 1$, $\lambda 2$, and $\lambda 3$) of SHLPM and IHLPM in temporomandibular joint disorder with different status of disc position. Error bars reflect 95% confidence intervals (*$p < 0.050$). ADC = apparent diffusion coefficient, ADWOR = anterior disc displacement without reduction, ADWR = anterior disc displacement with reduction, FA = fractional anisotropy, IHLPM = inferior head of the lateral pterygoid muscle, ND = normal disc position, SHLPM = superior head of the lateral pterygoid muscle

Table 3. Difference in Diffusion Parameters (ADC, FA, λ1, λ2, and λ3) of SHLPM and IHLPM between ADWOR Patients with (OA) and without OA (NOA)

Muscle	Parameters	NOA (n = 58)	OA (n = 35)
SHLPM	ADC	1.624 ± 0.077	1.645 ± 0.090
	FA	0.455 ± 0.041	0.442 ± 0.042
	λ1	2.423 ± 0.104	2.439 ± 0.117
	λ2	1.542 ± 0.082	1.553 ± 0.088
	λ3	0.909 ± 0.108	0.941 ± 0.117
IHLPM	ADC	1.573 ± 0.064	1.599 ± 0.070
	FA	0.467 ± 0.028	0.444 ± 0.032*
	λ1	2.377 ± 0.091	2.370 ± 0.082
	λ2	1.490 ± 0.061	1.514 ± 0.071
	λ3	0.855 ± 0.074	0.915 ± 0.088*

Data are mean ± standard deviation. FA is unit-less, all other diffusion tensor imaging-derived parameters values are in units of 10^{-3} mm^2/sec. *p < 0.050 for the comparison between NOA and OA in ADWOR. ADC = apparent diffusion coefficient, ADWOR = anterior disc displacement without reduction, FA = fractional anisotropy, IHLPM = inferior head of the lateral pterygoid muscle, NOA = non-osteoarthritis, OA = osteoarthritis, SHLPM = superior head of the lateral pterygoid muscle

also confirmed the dual role of the SHLPM during jaw opening and intercuspal clenching; however, the IHLPM only plays a role in jaw opening, leading to the hypothesis that the SHLPM is more prone to pathological changes due to overuse. Based on previous findings, our present study further evaluated diffusion variables of the LPM in patients with TMD with different disc displacement status, suggesting the presence of the hypertonic status of the LPM in varying degrees in different stages of TMD.

In TMD, differences in diffusivity were observed in both the SHLPM and IHLPM compared to that in the volunteers. Previous DTI studies [15-17] have confirmed that three eigenvalues offer insights into the size of the apparent diffusion in three orthogonal directions and correlate with muscle fiber architecture. The significantly increased eigenvalues of both the SHLPM and IHLPM in patients with TMD in our study indicate the hypertonic status of this muscle. Moreover, the ADC and FA were derived from the three eigenvalues [18]. Thus, the increased ADC observed in patients with TMD is a comprehensive reflection of the three eigenvalues, indicating the hypertonic status of the LPM. As the FA is associated with the degree of diffusion anisotropy, such as the degree to which the diffusion profile is aligned [19], changes in FA correlate with changes in muscle microstructure. Since changes in muscle structure have been regarded as a subsequent change in the later

stages of TMD [1,10], the FA changes in patients with TMD as a whole may be diluted by the inclusion of patients with early stage TMD (ADWR and ND). This may explain the lack of significant difference in FA between patients with TMD and healthy volunteers in our study.

In TMD, higher eigenvalue were only observed in λ1 and ADC of the SHLPM in ND, with all three eigenvalues in the SHLPM and IHLPM significantly higher when TMD progressed to ADWR and ADWOR. This indicates the unsynchronized diffusivity changes in the SHLPM and IHLPM in the early stage of TMD, i.e., the precursory role of the SHLPM's hyperfunction in the early stage and the secondary change in the IHLPM at an advanced stage. This finding confirmed our hypothesis that the SHLPM is more likely to be overused and undergo pathological changes in TMD. In addition, the early signs of LPM dysfunction can be identified by unsynchronized diffusivity changes in λ1 in the two heads of the LPM. Some researchers [9,10] suggested a delicate balance of forces imposed on the anterior band of a disc by the SHLPM and the posterior band via the retrodiscal tissue. The involuntary SHLPM activity in TMD without disc displacement may disrupt the balance and likely force the disc further forward [20]. The fibers of retrodiscal tissue begin to rupture and stretch with time, resulting in an anterior shift of the disc [1,9], slackening the connection between the SHLPM and anterior band of the disc [21]. Under these conditions, the SHLPM loses control over the disc during mouth closing, and the IHLPM then becomes activated as compensation [1,21]. Moreover, a significantly lower FA in both heads of the LPM than that in volunteers was only observed in the ADWOR subgroup, indicating the change in fiber alignment of the LPM in the later stages of TMD.

Among the three TMD subgroups, ADC and the three eigenvalues of both heads of the LPM underwent generally increased with the aggravation of TMD, which is consistent with the findings of Liu et al. [22]. Moreover, the ADWR and ADWOR subgroups had significantly higher ADC, λ1, and λ2 than those in the ND subgroup. In addition, the ADWOR subgroup had significantly higher λ3 and lower FA values. Since λ3 has been proven to correlate with the physiological cross-sectional area [16] and FA correlates with changes in muscle microstructure, the differences in diffusivity in the ADWOR subgroup indicate the structural changes of the LPM in TMD with the most severe anterior disc displacement. Gerwin et al. [23] reported that hyperactive muscles initiate a continuous cycle of localized muscle contraction and block blood flow to the muscle, causing ischemia and

hypoxia, resulting in myocyte swelling and increased muscle diffusivity. A recovery process and regeneration will then occur, resulting in decreased diffusivity [24]. The ischemia and regeneration process in chronic disc displacement might explain the slightly but not significantly higher ADC and three eigenvalues and lower FA in the LPM in the ADWOR subgroup compared to those in the ADWR subgroup.

Previous studies [10,25] have concluded that TMJ OA leads to weakening and atrophy of the muscle, especially the SHLPM. However, we observed significantly higher λ3 and significantly lower FA of the IHLPM in OA, which was associated with the hypertonic status of the muscle. These findings demonstrate that the absence of muscle atrophy or diffusivity changes induced by hypertonic status surpassed the changes induced by atrophy in OA.

The present study has several limitations. First, DTI was only performed in the jaw rest position because of the intolerability to keep the mouth open during a relatively long MRI scan time. Second, compared to the sizes of the ADWR and ND subgroups, the size of the ADWR subgroup was relatively small. Further studies are required to include more patients with ADWR and analyze the differences in diffusivity in the LPM of patients with TMD in different jaw positions.

In conclusion, DTI successfully detected changes in diffusion parameters in the LPM of patients with TMD, indicating LPM dysfunction in TMD. Furthermore, the unsynchronized diffusivity changes in the LPM of different subgroups of TMD can be a potential indicator to identify the severity of LPM hyperfunction in various stages of TMD.

Availability of Data and Material

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

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Simin Liu, Chu Pan. Data curation: Simin Liu. Formal analysis: Simin Liu. Investigation: Changhua Wan, Haosen Li. Methodology: Weiwie Chen, Chu Pan. Project administration: Chu Pan. Resources: Changhua Wan, Haosen Li. Software: Simin Liu. Supervision: Chu Pan. Visualization: Changhua Wan. Writing—original draft: Simin Liu. Writing—review & editing: Weiwie Chen, Chu Pan.

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