

Intermittent pain in patients with chronic low back pain is associated with abnormalities in muscles and fascia

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We investigated the relationship between paravertebral muscles and perimuscular connective tissues of the thoracolumbar fascia region and the four types of pain in patients suffering from chronic low back pain. A total of 17 patients with chronic low back pain participated in this study. Ultrasound imaging method was used to measure the thickness and echogenicity of the paravertebral muscles and perimuscular connective tissues. The measurement site considered in this study was located lateral to the midpoint between L2–3 and L4–5 spines. In addition, age, gender, BMI, numerical rating scale and the short-form McGill pain questionnaire 2 (includes questions with respect to continuous pain, intermittent pain, neuropathic pain and affective descriptors) were used for assessment. Statistical analysis was performed using correlation analysis and multiple regression analysis. A significant association was observed between paravertebral muscle echogenicity at L2–3 and the numerical rating scale ($r=0.499$), between paravertebral muscle echogenicity at L4–5 with numerical rating scale ($r=0.538$) and intermittent pain ($r=0.594$), and between perimuscular connective tissue thickness at L2–3 and numerical rating scale ($r=0.762$). We observed

that the factor influencing perimuscular connective tissue thickness at L2–3 and L4–5 was intermittent pain ($\beta=0.513$, $\beta=0.597$, respectively). It was also observed that some of the imaging findings were associated with age and BMI. In conclusion, we observed that paravertebral muscle echogenicity and perimuscular connective tissue thickness in patients with chronic low back pain were associated with pain, especially intermittent pain. *International Journal of Rehabilitation Research* 45: 33–38 Copyright © 2021 Wolters Kluwer Health, Inc. All rights reserved.

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Introduction

There is a high prevalence of chronic low back pain (CLBP) around the world [1] where about 90% of CLBP cases are nonspecific, but the pathogenesis of CLBP is not fully understood [2]. However, recent studies have shown that most cases of CLBP can be diagnosed by X-rays, MRI, computed tomography and neurological and physical examinations [3–6]. In addition, patients with CLBP have atrophy of the paravertebral muscles (PVM) [7–9], fatty infiltration and fibrosis of PVM [9–11], along with increased thickness and echogenicity of the perimuscular connective tissue (PMCT) of the thoracolumbar fascia [12–14]. Imaging findings of the PVM and PMCT can help in the diagnosis and treatment of CLBP.

On the other hand, several reports deny any association between the changes in PVM and CLBP [8,15,16]. As only a few studies have been conducted, it is not possible to determine if there is an association between PMCT and CLBP.

One of the reasons for the disagreements among previous studies on the association between PVM and CLBP

and between PMCT and CLBP is the inadequate CLBP assessment methods as most of the previous studies assessed the pain intensity using only a visual analog scale. However, CLBP patients have many types of pain such as continuous pain, intermittent pain, neuropathic pain, affective descriptors, among others. Therefore, our study plan incorporated a detailed assessment of CLBP for each type of pain to provide new insights. Furthermore, because the imaging findings of PVM and PMCT have been associated with age, gender and body composition [13,15,16], we analyzed the imaging findings of PVM and PMCT in detail by simultaneously examining their association with age, gender and body composition.

The present study investigated the relationship between the imaging findings of PVM and PMCT with the type of pain, age, gender and body composition in patients with CLBP.

Methods

The design was a prospective, cross-sectional study. The protocol of this study was approved by the Ethical

Review Committee of Mie University Hospital in accordance with the Helsinki Convention (approval No.: H2019-146). We obtained written informed consent from all the study participants.

Participants

Patients who had an outpatient visit between November 2019 and November 2020 were recruited as participants for this study. The participants were aged ≥ 20 years and had CLBP for at least 6 months. Exclusion criteria were as follows: previous severe back or low limbs injury or surgery; lower extremity radiating pain; a strong suspicion of neuropathic pain (painDETECT score of 19 or higher [17,18]). Initially, 22 participants were recruited for the current study, but after applying the exclusion criteria, a total of 17 participants were recruited for this study.

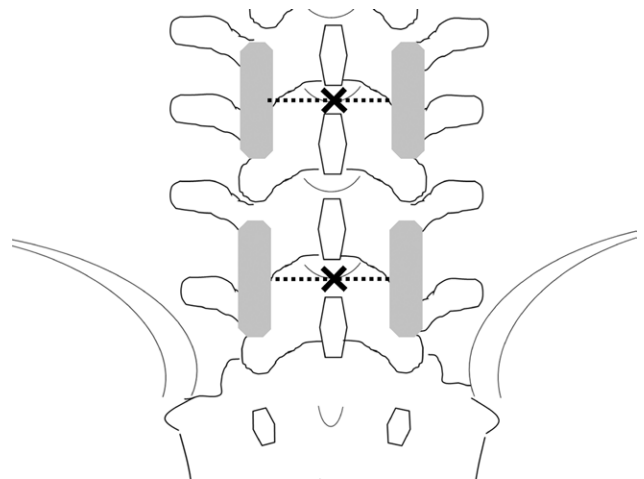
Measurement items

The numerical rating scale (NRS) was used to assess the average pain intensity in a span of 4 weeks. The short-form McGill pain questionnaire 2 (SF-MPQ-2) was used to assess each of the four types of pain: continuous pain (six items), intermittent pain (six items), neuropathic pain (six items) and affective descriptors (four items) [19]. The age and gender details were obtained from the participant's medical record information. The height and weight were measured, and the BMI was also calculated in this study.

Ultrasound imaging

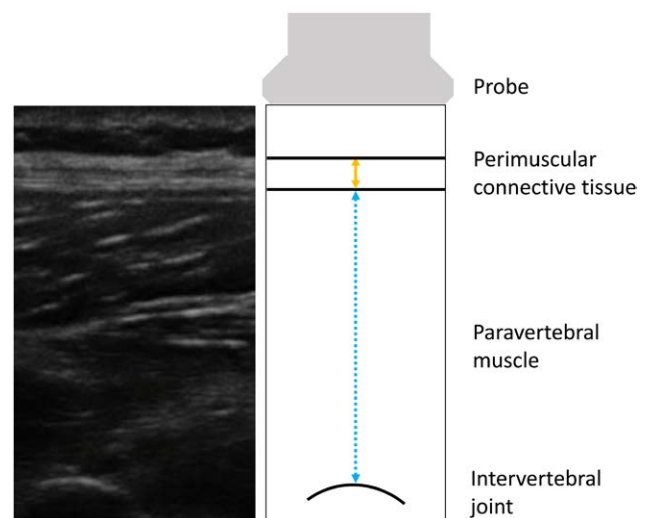
Ultrasound imaging (USI) examinations were conducted using the SonoSite S-Series S-Nerve. The measurement position was supine and the assessor was positioned next to the participants. The probe (HFL 13-6 MHz, 38-mm broadband linear array) was placed in the long axis directly above the L2-3 and L4-5 lumbar intervertebral joints and 2 cm lateral to the midpoint of each spinous process, which was carried out in reference to the previous studies [12,13] (Fig. 1). When acquiring ultrasound images, great care was taken with the patients to minimize pressure on the tissue. The measurements were taken three times at the same location and the average value was calculated. Values obtained from the right and left sides of the spine were averaged because preliminary analyses showed no difference for the sides. The PVM thickness was defined as the distance of the vertical line from the intervertebral joint to the base of PMCT, which is the point of change from low echogenicity to high echogenicity. The PMCT thickness was defined as the distance of the vertical line from the base of the PMCT to the top of the PMCT, which is the point of change from high echogenicity to low echogenicity (Fig. 2). The PVM and PMCT echogenicity were measured on the vertical line used in the thickness measurements. The echogenicity was divided by the echogenicity of the bone in the intervertebral joint.

Fig. 1



The location of the probe of ultrasound imaging. The upper mark was between L2 and L3, and the lower mark was between L4 and L5. The probe was placed 2 cm outside the mark in the vertical direction.

Fig. 2



An example of the ultrasound imaging of the perimuscular connective tissues and paravertebral muscles.

Statistical analyses

Spearman's rank correlation coefficient was applied to examine the association between the variables of USI and the variables of age, gender, BMI, NRS and SF-MPQ-2.

Multiple regression analysis was applied to examine the variables that were most related to USI, considering USI as the dependent variable and age, gender, BMI and SF-MPQ-2 as independent variables, using the step-wise method. NRS was excluded to reduce the risk of multicollinearity. Multicollinearity among variables was

assessed using the variance inflation factor. All statistical analyses were conducted using the IBM SPSS Statistics Ver.25. The threshold for significance was $P < 0.05$.

Results

The characteristics of the participants are shown in Table 1.

On average, the participants were middle-aged and of normal weight (age range: 42.6 ± 16.9 years, BMI: 23.5 ± 3.1). Seven of the 17 participants were women. The participants reported moderate pain (NRS: 5.4 ± 1.6).

The result of correlation analysis between paravertebral muscles and each variable is shown in Table 2.

Significant association was detected between the PVM thickness at L2–3 and BMI ($r=0.654$); between PVM echogenicity at L2–3 and NRS ($r=0.499$) and between PVM echogenicity at L4–5 with NRS ($r=0.538$) and intermittent pain ($r=0.594$).

The results of correlational analysis between the perimuscular connective tissues and each variable are indicated in Table 3.

A significant association was reported between the PMCT thickness at L2–3 and NRS ($r=0.762$) and between PMCT echogenicity at L2–3 and BMI ($r=0.512$).

The results of multiple regression analysis are given in Table 4.

The factors affecting PVM thickness at L2–3 were BMI ($\beta=0.632$; 95% confidence interval (CI)= 0.411 – 2.113 ; $P=0.006$). The factors affecting the PVM thickness at L4–5 were age ($\beta=-0.612$; 95% CI= -0.306 to -0.052 ; $P=0.012$). The factor influencing the PMCT thickness at L2–3 and L4–5 was intermittent pain ($\beta=0.513$; 95% CI= 0.03 – 0.068 ; $P=0.035$ and $\beta=0.597$; 95% CI= 0.013 – 0.087 ; $P=0.011$). The factor influencing the PMCT echogenicity at L2–3 was BMI ($\beta=0.560$; 95% CI= 0.017 – 0.163 ; $P=0.019$). For any dependent variable, only one

item was extracted at a time. There was only a little risk of multicollinearity.

Discussion

The results of this study depicted an association between USI and intermittent pain in patients suffering from CLBP. To the best of our knowledge, this is the first study of USI focused on intermittent pain. In the present study, we described the hyperechoic region of PVM as ‘fatty/fibrosis infiltration’ [13], because fat and fibrosis cannot be assessed separately in USI [20].

We found a correlation between fatty/fibrous infiltration of PVM and pain, especially intermittent pain. Intermittent pain in SF-MPQ-2 refers to six types of pain such as shooting pain, stabbing pain, sharp pain, cracking pain, electric-shock pain and piercing [19]. These are temporary types of pain, including sudden pain not triggered by any factor and pain induced by certain movements or posture maintenance.

Patients with CLBP are reported to have a different pattern of changes in their muscle cross-sectional area while changing postures as compared with that of a healthy individual [21]. As the fatty/fibrosis infiltration of PVM progresses, the muscles are replaced by noncontractile tissue, which results in insufficient muscle action. As a result, there is an increased risk of mechanical stress on the lumbar structures, causing the patient to experience frequent intermittent pain. Conversely, intermittent pain may also promote fatty/fibrosis infiltration of the PVM. The area of pain inhibits the activity of alpha motor neurons in the anterior horn of the spinal cord to protect the damaged tissue [22]; this phenomenon is called reflex inhibition. The inability of the PVM to function correctly leads to fatty/fibrosis infiltration. Additionally, when patients want to avoid movements and postures that cause intermittent pain, they choose immobility. Chronic disuse leads to accelerated fatty/fibrosis infiltration of the PVM [23]. Therefore, in the present study, the causal relationship between PVM fatty/fibrosis infiltration and intermittent pain is unclear.

We found an association between PMCT thickening and intermittent pain.

The thoracolumbar fascia is a dense connective tissue with numerous tightly packed collagen fibers. It connects the transversus abdominis, vastus lateralis and internal oblique muscles to the spine, and transmits the force between the spine, pelvis and lower extremities [24]. The thoracolumbar fascia forms a compartment by enclosing the psoas major muscle in the anterior and middle layers and the PVM in the middle and posterior layers. This compartment helps in movement generation during flexion and extension of the lumbar spine [25].

It is known that the shear strain in PMCTs of patients with CLBP is 20% lower than that of the healthy subjects

Table 1 Characteristics of participants [N or mean \pm SD (median)]

Age	42.6 \pm 16.9 (39.0)
Gender (female)	7
BMI	23.5 \pm 3.1 (23.6)
Numerical rating scale	5.4 \pm 1.6 (6.0)
Short-form McGill pain questionnaire 2	
Continuous pain	14.6 \pm 10.7 (12.0)
Intermittent pain	10.9 \pm 9.8 (7.0)
Neuropathic pain	10.6 \pm 11.2 (7.0)
Affective descriptors	8.2 \pm 8.3 (6.0)
Paravertebral muscle thickness at L2–3 (mm)	24.37 \pm 6.27 (22.27)
Paravertebral muscle thickness at L4–5 (mm)	24.23 \pm 4.94 (23.83)
Paravertebral muscle echogenicity at L2–3	0.42 \pm 0.24 (0.34)
Paravertebral muscle echogenicity at L4–5	0.50 \pm 0.33 (0.43)
Perimuscular connective tissue thickness at L2–3 (mm)	2.67 \pm 0.68 (2.40)
Perimuscular connective tissue thickness at L4–5 (mm)	2.39 \pm 0.81 (2.06)
Perimuscular connective tissue echogenicity at L2–3	1.23 \pm 0.50 (0.97)
Perimuscular connective tissue echogenicity at L4–5	1.52 \pm 0.87 (1.31)

Table 2 Results of correlational analysis between paravertebral muscles and each variable

	Paravertebral muscle thickness		Paravertebral muscle echogenicity	
	L2-3	L4-5	L2-3	L4-5
Age	-0.204	-0.451	-0.047	-0.296
Gender	0.098	-0.293	0.293	0.439
BMI	0.654 ^a	0.358	0.309	0.076
Numerical rating scale	0.045	-0.216	0.499 ^a	0.538 ^a
Continuous pain	-0.165	-0.290	-0.009	0.079
Intermittent pain	0.057	-0.230	0.452	0.594 ^a
Neuropathic pain	0.167	-0.002	0.206	0.327
Affective descriptors	-0.268	-0.374	-0.015	-0.030

^a*P*<0.05.**Table 3 Results of correlational analysis between perimuscular connective tissues and each variable**

	Perimuscular connective tissue thickness		Perimuscular connective tissue echogenicity	
	L2-3	L4-5	L2-3	L4-5
Age	0.208	0.233	-0.405	-0.304
Gender	0.098	0.146	0.293	-0.049
BMI	0.265	-0.059	0.512 ^a	0.409
Numerical rating scale	0.762 ^a	0.080	0.080	0.274
Continuous pain	0.164	-0.069	-0.132	-0.169
Intermittent pain	0.336	0.124	0.197	0.036
Neuropathic pain	0.253	-0.290	0.136	0.192
Affective descriptors	0.152	0.200	-0.007	-0.316

^a*P*<0.05.**Table 4 Results of multiple regression analysis**

Dependent variable	Explanatory variable	Regression coefficient	95% CI	<i>P</i> value
Paravertebral muscle thickness at L2-3	BMI	0.632	0.411-2.113	0.006
Paravertebral muscle thickness at L4-5	Age	-0.612	-0.306 to -0.052	0.012
Perimuscular connective tissue thickness at L2-3	Intermittent pain	0.513	0.03-0.068	0.035
Perimuscular connective tissue thickness at L4-5	Intermittent pain	0.597	0.013-0.087	0.011
Perimuscular connective tissue echogenicity at L2-3	BMI	0.560	0.017-0.163	0.019

Seven explanatory variables were considered: age, gender, BMI, continuous pain, intermittent pain, neuropathic pain and affective descriptors. This table shows only the variables that were entered by the stepwise method among the seven explanatory variables, excluding those that were not listed. As no variables were entered for paravertebral muscle echogenicity at L2-3 and L4-5 and perimuscular connective tissue echogenicity at L4-5, they are not given in this table. CI, confidence interval.

[26], and it is likely that PMCT thickening interferes with force transmission and moment generation. As a result, we speculate that the inappropriate loads that are repeatedly applied to the lumbar region increase the chances for intermittent pain. However, the cause for the association of PVM fatty/fibrosis infiltration and intermittent pain could not be determined in this study. Thus, conversely, the chronicity of the intermittent pain may cause PMCT thickening. In this case, contracture due to immobility and mechanical stress on the PMCT due to abnormal movement patterns are possible factors for PMCT thickening.

Furthermore, PMCT in patients with CLBP may have disorganized morphology and may have a multilayered structure [12,27]. In this study, a multilayered disordered morphology was observed in some of the participants. Because we measured the distance between the top and bottom of the PMCT, any disruption in morphology was also recorded as PMCT thickening. If we could distinguish between PMCT thickening and disruption of

PMCT morphology, the relationship between CLBP and PMCT might have been clearer.

We also found that there is a relationship between age and PVM thickness in the lower lumbar spine and between low body weight and PVM thickness in the upper lumbar spine. Because the PVM of the lower lumbar region has a high percentage of lumbar multifidus and the PVM of the upper lumbar region has a high percentage of erector spinae [28], there may be an association between aging and lumbar multifidus and between low body weight and erector spinae. In addition, previous studies also indicated muscle atrophy in the PVM due to age-related sarcopenia [9]. Considering that the lumbar degenerative diseases (such as lumbar spinal canal stenosis, spondylolisthesis and lumbar disc herniation) increase in prevalence with age and are more common in the lower lumbar region, the association between age and reduced lumbar PVM thickness may involve lumbar degenerative diseases as a covariate.

We conducted a multiple regression analysis with four characteristics of age, gender, BMI and pain to determine the factors that were strongly associated with USI findings. PMCT thickness was strongly associated with intermittent pain, and PVM thickness was strongly associated with age and BMI; in contrast, PMCT echogenicity was strongly associated with BMI. It could indicate that PVM thickness and PMCT echogenicity may have some association with chronic pain.

Limitations

The following limitations of this study should be noted.

First, there was an insufficient number of participants because this study was conducted at a single institution, and we were unable to recruit more participants due to clinical limitations. More participants might have provided different results.

Second, there is a potential risk of bias such as selection bias as the study was limited to outpatients who were able to come to the hospital and information bias due to the lack of blinding of the participants. In addition, confounding factors may not have been assessed because there were only a few participants who could be convened for this study, so the evaluation items for our survey were narrowed down. However, CLBP may have a multifactorial effect where the duration of pain, medical history, medication history, treatment history, physical functioning, psychological factors, social factors, the activity of daily living, quality of life, etc. may be considered as confounding factors. Additional studies are expected to be conducted in the future, where such limitations would be considered in the research.

Conclusion

In conclusion, our results suggested that PVM fatty/fibrosis infiltration and PMCT thickening in patients with CLBP are associated with pain, especially with intermittent pain.

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Conflicts of interest

There are no conflicts of interest.

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