



Myofascial Pain and Treatment

Structural remodelling of the lumbar multifidus, thoracolumbar fascia and lateral abdominal wall perimuscular connective tissues: A cross-sectional and comparative ultrasound study

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ABSTRACT

Introduction: With low back pain (LBP), remodelling of the lumbar soft tissues involves both trunk muscles and neighbouring passive connective tissues. The aim of the present study was to compare three quantitative measures of these tissues, using ultrasound imaging (USI), among healthy controls and individuals with LBP.

Methods: USI measures from 30 healthy subjects and 34 patients with non-acute LBP were compared between groups and sexes. The measures employed were (1) lumbar multifidus echogenicity (fatty/fibrosis infiltration) at three vertebral levels; (2) posterior layer thickness of the thoracolumbar fascia, and (3) thickness of the perimuscular tissues surrounding the external oblique, internal oblique and transversus abdominis (TrA).

Results: USI measures of (1) multifidus echogenicity showed statistically significant changes between vertebral levels and sexes (females > males; $p = 0.02$); (2) differences in thoracolumbar fascia thickness approached statistical significance between groups (LBP > controls; $p = 0.09$) and sexes (females < males; $p = 0.07$); and (3) perimuscular tissue surrounding the TrA was significantly thinner ($p \leq 0.001$) in patients with LBP compared to controls.

Discussion: The thinner perimuscular tissues surrounding the TrA in patients with LBP is a new finding, concurring with previous findings with regard to the lower activation of this deep muscle as well as more recent findings on other perimuscular tissue.

Conclusion: Overall, USI measures were sensitive to different potential changes (pain status, sex, vertebral level), and this is useful in studying the remodelling of various soft tissues of the trunk.

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1. Introduction

The study of trunk muscle anatomy and function is central to understanding injury mechanisms and impairments of the lumbar

spine (Steele et al., 2014; van Dieen et al., 2003). Perimuscular connective tissues (PMCT), however, have been largely overlooked, despite their direct and indirect roles in conveying mechanical forces (Driscoll, 2018). There is increasing interest in the remodelling of PMCT (Hodges et al., 2015; Langevin et al., 2009, 2011; Whittaker et al., 2013), in addition to the biomechanical function of these passive soft tissues and their relationship with trunk muscle function (Vleeming et al., 2014).

Ultrasound imaging (USI) may be a practical tool to accelerate research on lumbar PMCT. USI has previously been used to study the posterior layer of the thoracolumbar fascia (Bishop et al., 2016;

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Langevin et al., 2009, 2011), with one study showing greater tissue thickness in patients with low back pain (LBP) (Langevin et al., 2009). Similarly, Whittaker et al. (2013) found a 22% greater thickness of the anterior and lateral abdominal PMCT in individuals with lumbopelvic pain versus healthy controls. It would be of interest, however, to evaluate the PMCT separating each of the lateral abdominal wall muscles. The transversus abdominis (TrA) is the one most closely connected to the middle layer of the thoracolumbar fascia, followed by internal obliques (IO) and, occasionally, external obliques (EO) (Willard et al., 2012), with each muscle having a different stiffening effect on the thoracolumbar fascia (Vleeming et al., 2014). Furthermore, TrA more consistently shows motor control changes with clinical or experimental pain (Hodges et al., 2003; Hodges and Richardson, 1996), which may, in turn, affect the surrounding PCMT. Some patients have difficulty in voluntarily contracting TrA (Ferreira et al., 2010) or in activating this muscle automatically at an appropriate latency, i.e. just before the voluntary production of a trunk disturbance (Hodges et al., 2003; Hodges and Richardson, 1996).

Previous findings on animal models, and lower and upper limb muscles, have also validated the use of USI to estimate muscle adipose (Reimers et al., 1993) and fibrous content (Arts et al., 2012; Pillen et al., 2009), and have revealed a relationship with muscle strength (Cadore et al., 2012; Fukumoto et al., 2012). Similar techniques could be applied to the lumbar multifidus (LM), which is prone to remodelling (D'hooge et al., 2013; Danneels et al., 2000; Mengiardi et al., 2006) due to reflex inhibition (Hodges et al., 2006). Such degenerative remodelling of muscles may be better characterized by the measuring of fatty/fibrosis infiltration than by changes in the cross-sectional area (CSA) (D'hooge et al., 2012; Fortin et al., 2016; Urrutia et al., 2018), because early replacement of muscle with fat may not alter CSA, with decreased CSA occurring only later (Hodges et al., 2015). In previous research, magnetic resonance imaging (MRI) and computed tomography (CT-Scan) have shown greater muscle fatty infiltration in the lumbar multifidus (LM) of patients with low back pain (LBP) than in healthy controls (Hicks et al., 2005; Hultman et al., 1993; Mengiardi et al., 2006). Whether these findings can be replicated with USI remains to be tested. Given these imaging technologies cannot differentiate adipose from fibrous content and that adipose/fibrous relative contribution to LM remodelling remains unknown, the terms intramuscular fatty/fibrosis infiltration will be used hereafter with regard to the present findings.

The main aim of this study was to compare USI measures of LM muscle fatty/fibrosis infiltration, and thickness of thoracolumbar fascia and PMCT of the lateral abdominal wall muscles, between healthy controls and individuals with non-acute LBP. To validate USI measures of LM muscle fatty/fibrosis infiltration, comparisons between males and females were conducted, as sex differences are generally observed for these measures (Molinari et al., 2015), including those involving the LM (Crawford et al., 2016; Kader et al., 2000; Kjaer et al., 2007; Le Cara et al., 2014; Paalanne et al., 2008). It was hypothesized that patients with LBP and females have more LM muscle fatty/fibrosis infiltration than healthy controls and males, respectively (H1); that patients have a thicker posterior thoracolumbar fascia than controls (H2); and that patients have a thicker PMCT surrounding the TrA than controls (H3).

A secondary aim was to test whether adjusting for different body fat metrics (USI measures of subcutaneous thickness, percentage fat, BMI) in the analyses of covariance (ANCOVA) would change the statistical findings, given that previous studies have acknowledged that, compared to other specific measures, using BMI might not be an accurate estimate of body fat (Crawford et al., 2016; Hebert et al., 2014; Kjaer et al., 2007). The results and discussion corresponding to this secondary aim are presented in the [Supplementary File](#).

2. Methods

The present clinical trial has been recorded in the International Standard Registered Clinical/soCial sTudy Number (ISRCTN) registry (ID: ISRCTN94152969).

The following section summarizes the more detailed methods recently published on USI measures of the LM (Lariviere et al., 2018a) and abdominal wall (Lariviere et al., 2018b) muscles. The same USI assessments were performed on the same participants on the same day, with a focus on LM thickness at different vertebral levels, as well as thickness of the EO, IO and TrA muscles at rest and during contraction. The present study focuses on the complementary USI measures of LM echogenicity, as well as thoracolumbar fascia and PMCT thickness measured at rest, just before standardized muscle contraction. The measures described in this study were taken prior to the 8-week lumbar stabilization exercise program described in the studies cited above; they did not change significantly following this treatment program.

2.1. Participants

All participants between 18 and 65 years of age were recruited through newspaper advertisements and physiotherapy clinics (Montreal, Canada), and assessed from July 2012 to August 2016 (Table 1). Inclusion criteria were as follows: patients had LBP in the lumbar or lumbosacral region, with or without radicular pain, for at least four weeks (non-acute phase), and a minimum score of 12% on the Oswestry Disability Index (ODI). General exclusion criteria included the following: surgery on the pelvis or spinal column; a known specific lumbar pathology or scoliosis; systemic or degenerative disease; the initiation of an exercise program in the last three months; or pregnancy. Other additional exclusion criteria for patients with LBP were the presence of one positive neurological sign in two out of three of the following test categories: (a) reduced Achilles and patellar tendon reflexes; (b) reduced strength in lumbosacral myotomes; (c) reduced sensation in lumbosacral dermatomes. Exclusion criteria for the control subjects were back pain in the preceding year, or a history of back pain lasting more than one week. To participate in neuromuscular testing, all healthy controls had to have a body mass index (BMI) ≤ 30 kg/m², since the amount of subcutaneous tissue and fat is a limiting factor for these tests. Consequently, only the recruited patients who also met this criterion were retained for neuromuscular testing. Given that this was not an intervention study, the assessors were not blind to any participant group. All subjects gave informed consent to the experimental procedure, which had been approved by the Ethics Committee of the Centre of Interdisciplinary Research in Rehabilitation of Greater Montreal (Ethics Registration Number: CRIR-738-0512).

Subject characteristics, including the clinical profile of the patients with LBP and the description of the corresponding measures, are shown in Table 1. As expected, differences were observed between the sexes (height, weight, %Fat). The patients with LBP were on average 6 years older than the healthy controls, had a significantly higher BMI, and reported a significantly lower physical activity level.

2.2. USI assessment

All quantitative USI examinations were conducted using a Phillips HD11 1.0.6 ultrasound machine (Philips Medical Systems, Bothell, WA). A 5–2 MHz curvilinear array transducer (model C5–2; 75° field of view; 6.5 cm footprint) was used to image lumbar spine structures in the parasagittal plane (Fig. 1), while a 12–5 MHz 50-mm linear array transducer (Model L12–5) was used to image the

Table 1
Demographic and clinical profiles [Mean (SD)].

Variable	Control Subjects		Patients with LBP		P values ^a	
	Males (n = 15)	Females (n = 15)	Males (n = 16)	Females (n = 19)	GROUP	SEX
Age (years)	39.3 (14.3)	39.8 (13.7)	44.1 (13.5)	47.8 (11.9)	.03	.69
Height (cm)	178.0 (8.4)	164.2 (6.1)	172.0 (6.2)	163.1 (5.8)	<u>.07</u>	<.001
Weight (kg)	77.1 (10.7)	62.9 (10.9)	76.0 (12.9)	71.4 (9.9)	.202	<.001
BMI (kg/m ²)	24.4 (3.2)	23.3 (3.6)	25.6 (3.8)	26.8 (3.0)	<.001	.94
%Fat	21.0 (6.9)	32.8 (6.3)	23.6 (6.6)	36.8 (3.8)	<u>.05</u>	<.001
STT _{L45} (mm)	5.0 (1.9)	7.4 (3.3)	5.3 (2.9)	11.1 (4.7)	<u>.06</u>	<.001
STT _{ABD} (mm)	5.4 (1.8)	6.7 (2.6)	6.0 (1.7)	8.8 (3.7)	<u>.07</u>	<.001
PAL-sport	3.0 (0.9)	3.1 (0.8)	2.5 (0.9)	2.4 (1.1)	.02	.88
PAL-leisure	3.2 (0.7)	3.3 (0.7)	2.6 (0.5)	2.8 (0.8)	<.001	.47
NPRS (/10)	/	/	5.0 (1.6)	4.8 (1.0)	/	.67
ODI (%)	/	/	27.5 (9.0)	30.9 (10.2)	/	.25
FABQ _{PA} (/24)	/	/	18.1 (3.9)	15.0 (6.8)	/	.16
PCS (/52)	/	/	27.1 (10.6)	21.2 (12.6)	/	.13

Significant *p* values are identified in bold characters, while trends ($.05 < p < .10$) are underlined; BMI: body mass index; %Fat: percentage of body fat as estimated with age, sex and four skin-fold measures (Durnin and Womersley, 1974); STT_{L45} and STT_{ABD}: Ultrasound measure of subcutaneous tissue thickness at L4/L5 and over abdominals, respectively; PAL-sport and PAL-leisure: Physical activity level – sport and leisure subscales (Baecke et al., 1982); NPRS: numeric pain rating scale (Childs et al., 2005); ODI: Oswestry Disability Index (Fairbank et al., 1980); FABQ_{PA}: Fear-avoidance beliefs questionnaire – physical activity subscale (Waddell et al., 1993); PCS: pain catastrophizing scale (Sullivan et al., 1995).

^a None of the GROUP × SEX interactions reached statistical significance, but trends were observed for weight ($p = .08$) and STT_{L45} ($p = .06$).

PMCT of the abdominal wall in the longitudinal plane (Fig. 2).

USI measures were collected at rest on an exam table, in supine (ventrolateral abdominal wall) and prone (dorsal soft tissue), just before performing a standardized task to assess muscle activation (Larivière et al., 2018a,b). Subjects were instructed to keep their head straight; at the end of an exhalation phase (start of the 10-s image recording), the subject was instructed to rest 3-s before performing the corresponding standardized task. For each side of the dorsal trunk, and for each side of the ventrolateral abdomen, three 10-s ultrasound video clips were collected, with approximately 1 min of rest between trials.

For the LM echogenicity measures quantifying LM muscle fatty/fibrosis infiltrations, the settings of the ultrasound scanner remained unchanged (gain: 70; depth: 8 cm) for all subjects and trials (Molinari et al., 2015).

2.3. Data analysis and statistics

The different USI measures of the dorsal trunk and ventrolateral abdominal wall soft tissues are illustrated and explained in Figs. 1

and 2, respectively. For the present study, the measurements of interest were carried out at rest, using the first frame of the 10-s video. Averaged scores over the three trials were first computed for each measure. Scores for the left and right sides were averaged, as preliminary analyses confirmed no effects for side. The sum of PMCT_{ST/EO} (ST: subcutaneous tissue), PMCT_{EO/IO}, PMCT_{IO/TrA} and PMCT_{TrA/IA} (IA: intra-abdominal content) was also computed, to create PMCT_{SUM}, for comparison with a previous study (Whittaker et al., 2013).

All statistical analyses were done with NCSS software (version 10.0 for Windows), using a significance level (alpha) of 0.05 and the GLM procedure for ANOVAs and ANCOVAs, as described next. Marginal effects ($0.05 < p < .10$) were also identified. Since some variables showed abnormal distributions, all variables were systematically transformed (Van Albada and Robinson, 2007) to normalize their distributions, as verified with the Wilk-Shapiro test, thus allowing the use of parametric statistical analyses.

All USI measures were compared between healthy controls and patients with LBP (GROUP factor), and between sexes (SEX factor), using two-way ANOVAs (2 GROUP × 2 SEX). Cohen's *d* effect sizes

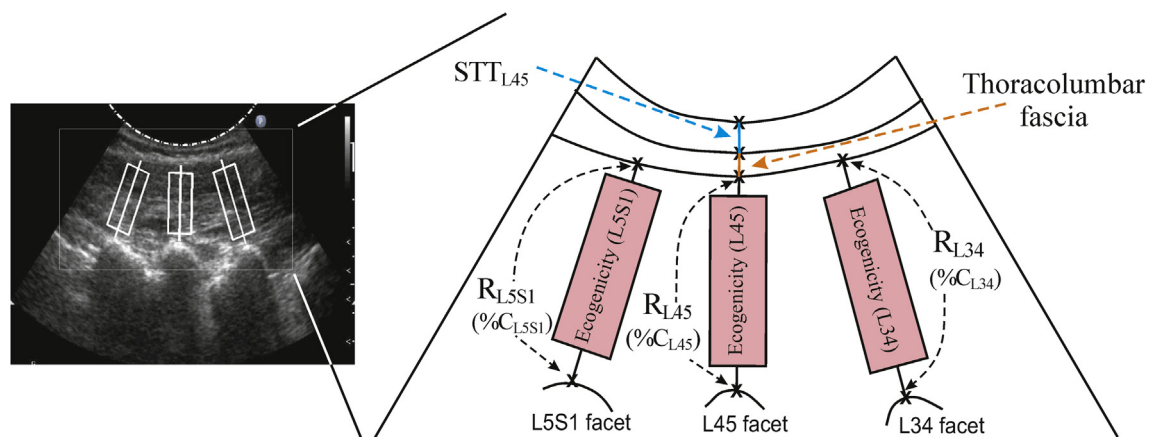


Fig. 1. From Larivière et al. (2020). USI measures (thickness) of the LM at rest (e.g. R_{L5S1}) and during the contraction (in parentheses; e.g. $\%C_{L5S1}$) as previously defined (Larivière et al., 2018a), as well as the new measures for the current study (STT_{L45} thickness; thoracolumbar fascia thickness, LM echogenicity at the L5S1, L45 and L34 facets). LM echogenicity was measured inside the regions of interest identified with shaded rectangles (width: 1 cm; height: 80% of LM thickness) positioned in the middle of the marks used to define LM thickness at rest (Larivière et al., 2018a); the grey-scale analysis to compute echogenicity is detailed elsewhere (Nadeau et al., 2016). STT_{L45}: subcutaneous tissue thickness at the L45 vertebral level (in blue); thoracolumbar fascia: posterior layer of the thoracolumbar fascia thickness at the L45 vertebral level (in orange); R and %C: lumbar multifidus thickness at rest, and as a percentage change during contraction. (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

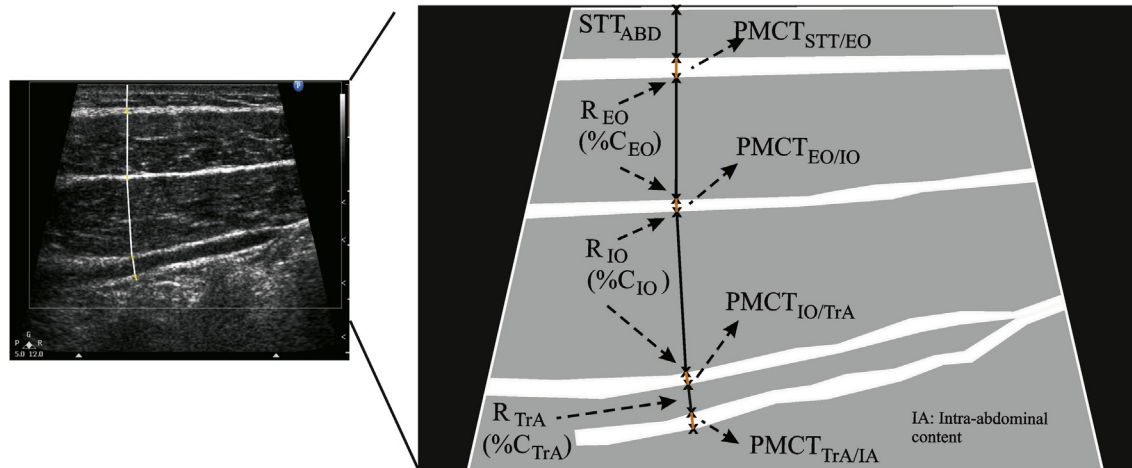


Fig. 2. From Larivière et al. (2020). USI measures of the lateral abdominal wall muscles at rest (e.g. R_{EO}) and during the contraction (in parentheses; e.g. $\%C_{EO}$) as previously defined (Larivière et al., 2018b), as well as new measures for the current study (STT_{ABD} , PMCT). Muscle thickness was defined as the distance between the inside edges of each muscle border, while PMCT thickness was defined as the distance between the outside edges of each connective tissue represented in white (thickness measures in orange on the right). Inside edges of muscles corresponded to the outside edges of the PMCT planes, thus allowing computation of PMCT thickness using the pixels already identified for muscle thickness. STT_{ABD} : subcutaneous tissue thickness over the lateral abdominal wall. PMCT: perimuscular connective tissue between STT_{ABD} and EO (ST/EO), between EO and IO (EO/IO), between IO and TrA (IO/TrA) and between TrA and intra-abdominal area (TrA/IA) are illustrated, while the sum of these four measures was also computed (PMCT_{SUM}). R and %C: EO, IO and TrA thickness at rest, and as a percentage change during contraction (Larivière et al., 2018b). (For interpretation of the references to colour in this figure legend, the reader is referred to the Web version of this article.)

were computed and interpreted as follows: d around 0.2 is interpreted as ‘low’, 0.5 as ‘average’ and 0.8 as ‘strong’.

ANCOVAs were completed to determine if ANOVA effects remained after controlling for age and body fat, as is common for these types of measures (Fukumoto et al., 2012; Goodpaster et al., 2001; Hebert et al., 2014; Kjaer et al., 2007; Langevin et al., 2009; Le Cara et al., 2014; Storheim et al., 2017; Valentin et al., 2015; Whittaker et al., 2013). The same covariates were applied, irrespective of the dependent variables, because confounder/moderator/mediator variables are unknown for thoracolumbar fascia and PMCT measures. Preliminary analyses also included weight and physical activity level (PAL-sport was correlated to some USI outcomes; $r = -0.25$ to -0.38) as covariates, in addition to age and body fat, but the findings remained basically the same.

With regard to the body fat covariate, the STT USI measures (STT_{L45} and STT_{ABD}) were used, as previously carried out for the thigh (Goodpaster et al., 2001), because they are more specific to each muscle group (LM and abdominals, respectively). The percentage of body fat (%Fat), as predicted by four skin folds, age and sex (Durnin and Womersley, 1974), was also investigated along with BMI, to test whether the use of different body fat covariates makes a difference. The corresponding results are detailed in the Supplementary File. It was concluded that STT USI measures are likely more appropriate than %Fat and BMI as covariates.

3. Results

Except for echogenicity, only main effects are described. Only the ANOVA for echogenicity, and no ANCOVA, showed significant GROUP \times SEX interaction for USI measures.

Patients with LBP showed a trend for higher STT_{L45} and STT_{ABD} relative to controls, while these measures were significantly higher in females than in males (Table 1).

3.1. Back structures (LM echogenicity, thoracolumbar fascia)

An ANOVA for repeated measures first showed that there was a significant difference ($p < .001$) in echogenicity of LM at different vertebral levels (L5S1, L45, L34). Post hoc comparisons (Tuckey

Kramer) showed significantly higher LM echogenicity scores at the L5S1 vertebral level (78, SD 21) compared to the two upper levels ($d = 0.68$ between L5S1 and L34); higher echogenicity scores were also found at L45 (76, SD 19) compared to L34 (66, SD 17), with a moderate effect size ($d = 0.55$). Hereafter, the average score across vertebral levels will be used as a dependent variable to allow ANCOVAs (not possible on repeated factors). The significant GROUP \times SEX interaction (Table 2; Fig. 3C) highlighted that significantly higher scores of LM echogenicity were observed in females, but more so for females with LBP (95, SD20) than for males with LBP (68, SD21), leading to a strong effect size ($d = 1.36$). Adjusting for the covariates (STT_{L45} , Age) eliminated the interaction, but SEX remained significant (Table 3).

The thoracolumbar fascia thickness was significantly higher in patients with LBP than in healthy controls, and was not affected by SEX, as detailed in Table 2 and Fig. 3B. Adjusting for covariates (STT_{L45} , Age) eliminated the GROUP effect ($p = .09$), but produced a marginal effect of SEX (females $<$ males; $p = .07$).

3.2. Abdominal structures (PMCT_{SUM}, individual PMCT)

The sum of all PMCT scores (PMCT_{SUM}) did not show a GROUP effect, but was thicker in females, as further detailed in Table 2 and Fig. 3E. Adjusting for covariates (STT_{ABD} , Age) led to a marginal GROUP effect ($p = .06$; Healthy $>$ LBP; adjusted means: $5.0 > 4.6$ mm) and eliminated the effect of SEX ($p = .90$; Table 3).

With regard to the individual abdominal connective tissue thickness measures (PMCT), significant GROUP effects (Table 2; $p < 0.001$) were observed for PMCT_{IO/TrA} and PMCT_{TrA/IA} (Fig. 3H and I): patients with LBP had lower connective tissue thickness than the control group, with strong effect sizes ($d = 0.83$ – 0.98). For SEX, males showed significantly lower PMCT_{STT/EO} scores than females [1.5 (SD, 0.8) $<$ 2.7 (SD, 1.5) mm; $d = 0.98$]. When accounting for covariates (STT_{ABD} , Age), the GROUP effects remained, as well as the SEX effects for PMCT_{STT/EO} (males $<$ females), but a new SEX difference reached statistical significance for PMCT_{EO/IO} (males $>$ females) and just failed to reach significance for PMCT_{IO/TrA} and PMCT_{TrA/IA} (Table 3).

Table 2

Statistical results (*P* values) corresponding to the comparisons between control subjects and patients with LBP (GROUP factor), between males and females (SEX factor), and to the corresponding interaction.

Variable	ANOVA Results (<i>p</i> and <i>d</i> values, means)		
	GROUP (G)	SEX (S)	G × S
Back Structures			
ECHO	.16	< .001 ($\delta < \varnothing$); <i>d</i> = 1.15 65(SD, 14) < 82(SD, 16)	.04
TLF _{L45}	.02 (C < LBP); <i>d</i> = 0.58 3.3 (SD, 0.8) < 4.0 (SD, 1.1) mm	.90	.13
Abdomen Structures			
PMCT _{SUM}	.573	.04 ($\delta < \varnothing$); <i>d</i> = 0.60 4.3 (SD, 1.2) < 5.3 (SD, 2.0) mm	.31
PMCT _{STT/EO}	.243	< .001 ($\delta < \varnothing$); <i>d</i> = 0.98 1.5 (SD, 0.8) < 2.7 (SD, 1.5) mm	.40
PMCT _{EO/IO}	.353	.18	.79
PMCT _{IO/TrA}	< .001 (C > LBP); <i>d</i> = 83 1.0 (SD, 0.2) > 0.8 (SD, 0.2) mm	.17	.35
PMCT _{TrA/IA}	< .001 (C > LBP); <i>d</i> = 98 0.9 (SD, 0.2) > 0.7 (SD, 0.2) mm	.14	.32

STT_{ABD} and STT_{L45}: Subcutaneous tissue thickness (mm) over the lateral abdominal wall and at the L45 vertebral level, respectively; ECHO: Echogenicity (unitless) averaged over the three vertebral levels; TLF_{L45}: thoracolumbar fascia thickness (mm) at the L45 vertebral level; PMCT: Perimuscular Connective Tissues summed across all measures (PMCT_{SUM}), between STT_{ABD} and EO (STT/EO), between EO and IO (EO/IO), between IO and TrA (IO/TrA), between TrA and intra-abdominal content (TrA/IA); EO and IO: external and internal obliques; TrA: Transversus Abdominis; C: healthy controls; LBP: patients with low back pain.

Significant *p* values are identified in bold characters, while trends ($.05 < p < .10$) are underlined. δ : males; \varnothing : females; *d* = Cohen's effect size; SD = standard deviation.

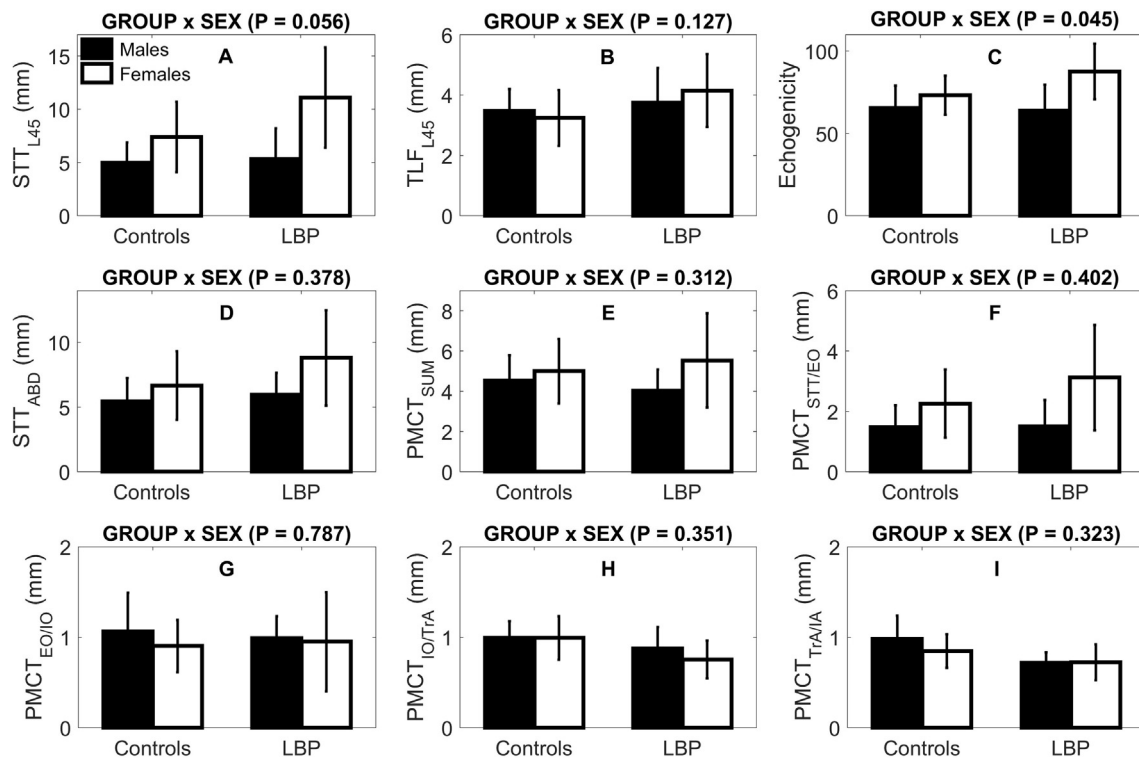


Fig. 3. Illustration of the mean scores corresponding to (A) the subcutaneous tissue thickness at L45 (STT_{L45}), (B) thoracolumbar fascia thickness at L45 (TLF_{L45}), (C) lumbar multifidus echogenicity across all vertebral levels, (D) the subcutaneous tissue thickness of the abdominal wall (STT_{ABD}), (E) the sum of perimuscular connective tissue thicknesses at all depths of the abdominal wall (PMCT_{SUM}), and abdominal PMCT thickness at four different depths, namely between (F) STT_{ABD} and EO (PMCT_{STT/EO}), (G) EO and IO (PMCT_{EO/IO}), (H) IO and TrA (PMCT_{IO/TrA}) and (I) TrA and intra-abdominal content (PMCT_{TrA/IA}).

4. Discussion

The main findings of the present study were that (1) LM echogenicity measures were responsive to sex (hypothesis partially supported) but not to pain status (H1 partially supported); (2) the thoracolumbar fascia thickness just failed to reach statistical significance with regard to group ($p = 0.090$) and sex ($p = 0.067$) factors (H2 rejected); and (3) PMCT surrounding the TrA muscle

was significantly thinner in patients with LBP relative to controls (H3 partially supported).

4.1. Echogenicity of the lumbar multifidus at different vertebral levels

Our data showed no difference in echogenicity of LM between patients with LBP and healthy controls, which is contrary to reviews

Table 3
Statistical results (*p* values) corresponding to the ANCOVAs, controlling for STT* and age.

Variable	Adjusted means				Main effects and interaction				
	Controls - ♂	Controls - ♀	Patients - ♂	Patients - ♀	STT*	Age	GROUP (G)	SEX (S)	G × S
Back structures									
ECHO	71	75	66	81	< .001	<.001	.75	.02	.14
TLF _{L45} (mm)	3.9	3.2	4.1	3.5	<.001	.52	.09	.07	.43
Abdomen structures									
PMCT _{SUM} (mm)	5.0	5.0	4.3	4.9	< .001	.37	.06	.90	.55
PMCT _{STT/EO} (mm)	1.8	2.3	1.8	2.6	< .001	.84	.87	<.001	.75
PMCT _{EO/IO} (mm)	1.1	0.9	1.0	0.9	< .001	.17	.18	.01	.94
PMCT _{IO/TrA} (mm)	1.0	1.0	0.9	0.7	.14	.24	<.001	.07	.28
PMCT _{TrA/IA} (mm)	1.0	0.8	0.7	0.7	.01	.03	< .001	.05	.37

* STT_{L45} for back and for STT_{ABD} for abdomen. STT_{L45} and STT_{ABD}: Subcutaneous tissue thickness at L45 and over the lateral abdominal wall, respectively; ECHO: Echogenicity at different vertebral levels; TLF_{L45}: thoracolumbar fascia at the L45 vertebral level; PMCT: Perimuscular Connective Tissues between STT_{ABD} and EO (STT/EO), between EO and IO (EO/IO), between IO and TrA (IO/TrA) and between TrA and intra-abdominal area (TrA/IA); EO and IO: external and internal obliques; TrA: Transversus Abdominis.

concluding that there is more muscle fatty infiltration in patients with LBP (Cooley et al., 2018; Kalichman et al., 2017), although this is not a universal finding (Bailey et al., 2019; Kalichman et al., 2010). This may be explained by the heterogeneity of patients with non-specific LBP. Increased muscle fatty infiltration is associated with muscle disuse over time (Goubert et al., 2017; Hamrick et al., 2016; Paalanne et al., 2011), likely secondary to reflex inhibition in the LM (Hodges et al., 2006). It has been previously reported that the patients in the current study showed decreased bilateral activation of LM at the L5/S1 level, but not at the L4/L5 and L3/L4 vertebral levels, and no atrophy at rest (Larivière et al., 2018a). This suggests limited inhibition of LM. It is not surprising, therefore, that these patients show no clear evidence of LM remodelling based on echogenicity. LM fatty infiltration, however, is generally located within the deeper portions of the LM (Kader et al., 2000; Kjaer et al., 2007; Mooney et al., 1997; Woodham et al., 2014). This might be better visualized with a transverse view of the entire LM, rather than with the longitudinal view used in our study. Whether there is a correlation between the magnitudes of deep fatty infiltration and fatty infiltration that would be more homogeneously distributed across the LM muscle remains to be tested (Keller et al., 2003). It seems that fat is seen in small collections within a muscle whereas fibrous tissue is reported to be more evenly distributed (Arts et al., 2012). Consequently, it is not excluded that our measure of echogenicity (with its defined region of interest) may be more sensitive to differences in fibrous content than to differences in fat content.

Echogenicity of LM was greater in females than in males, which is in line with previous MRI/CT Scan studies of the back (Crawford et al., 2016; Kader et al., 2000; Kjaer et al., 2007; Le Cara et al., 2014; Paalanne et al., 2011) and other muscles (Goodpaster et al., 2001). Age was identified as a significant covariate in the ANCOVA, which is also in line with the known detrimental effect of age on fatty infiltration (Kalichman et al., 2017; Urrutia et al., 2018), explaining up to 22% and 33% of total variance in LM for males and females, respectively (Shahidi et al., 2017). Differences were also observed between different vertebral levels, which is in line with the findings of Kjaer et al. (2007), who observed LM muscle fatty infiltration primarily at the L5 level, to a lesser extent at the L4 level and virtually none at the L3 level. These visual observations of MRI images were later substantiated with the quantification of scanner images (Crawford et al., 2016; Niemelainen et al., 2011). A possible explanation is that muscle degeneration, including fatty infiltration, occurs adjacent to injuries to the intervertebral discs (Hodges and Danneels, 2019), with intervertebral disc degeneration being more frequent at lower levels (Albert et al., 2011; Teichtahl et al., 2016). A recent review substantiated that fatty infiltration is associated with the degenerative findings of different spinal passive

tissues, including intervertebral discs, facet joints, spondylolisthesis, spinal stenosis and ligaments (Kalichman et al., 2017). The same review, however, also discussed the fact that fatty infiltration is modulated by sex, age and vertebral levels, which creates a challenge in separating pathological changes from normal changes. In line with this reasoning, a recent study has shown that sex, age and inter-vertebral disc degeneration are independently associated with paraspinal muscle fatty infiltration, although BMI and physical activity were not accounted for in their statistical model (Urrutia et al., 2018).

Collectively, our findings suggest that USI echogenicity measures were responsive to some known variations of LM muscle fatty/fibrosis infiltrations (related to age, sex and vertebral level). Whether they were sufficiently responsive to the effects of interventions remains to be tested. To date, the few randomized control trials on this topic suggest that exercise may at least halt - and may even decrease - muscle fatty infiltration (Addison et al., 2014), although the latter seems to require at least 12 weeks of exercise. Physical activity has also been shown to attenuate LM fibrosis secondary to intervertebral disc degeneration in mice (James et al., 2019). To the authors' knowledge, no such trials have been conducted for human back muscles, although some preliminary results predict a positive outcome, at least with regard to fatty infiltration (Mooney et al., 1997; Woodham et al., 2014).

A final point with regard to USI echogenicity measures is the choice of the transducer. As recommended (Stokes et al., 2007), a 5-2 MHz curvilinear array transducer was used to image lumbar spine structures, a curvilinear array allowing imaging LM on at least three vertebral levels in the parasagittal plane (as performed here) or its full cross-sectional area in the transverse plane. Stokes et al. (2007) also mentioned that the depth of LM is more suited to 5 MHz for image clarity than lower or higher frequencies, such as 3 MHz or 7–10 MHz, respectively. We do not know whether the use of another transducer providing a higher resolution, such as the one used to image abdominal structures (12-5 MHz 50-mm linear array transducer), would provide a better greyscale analysis to measure echogenicity. A more accurate measure of echogenicity would possibly change the present findings in terms of sensitivity.

4.2. Thickness of the posterior layer of the thoracolumbar fascia

The posterior layer of the thoracolumbar fascia was 18% thicker in patients with LBP than in healthy controls, which more or less replicates the significant 25% increase observed by Langevin et al. (2009). The latter study observed a significantly ($p < 0.01$) thicker fascia in patients with LBP, though adjusted for BMI. When covariates (STT_{L45}, age) were accounted for in our data, the GROUP effect

was eliminated ($p = .09$) and SEX almost reached significance ($p = .07$), although Langevin et al. (2009) did not observe SEX difference. Interestingly, our own results with BMI as a covariate were still not significant, but using %Fat as a covariate led to a significant GROUP effect (Supplementary File). It appears that the GROUP effect in our population is borderline and that having recruited a few more patients showing thicker fascia (or showing more evidence of disuse, as discussed below) would have provided a clearer picture.

A tentative explanation would be that the lower physical activity level in patients with LBP, based on PAL-sport and PAL-leisure measures (Table 1), may not only explain the marginally higher thickness of adipose tissues observed in patients with LBP, as measured with %Fat ($p = .05$), STT_{L45} ($p = .06$) and even STT_{ABD} ($p = .07$), but may also explain the fatty infiltrate of the thoracolumbar fascia, as previously observed (Langevin et al., 2009). The decrease of the LM bilateral activation at the L5S1 level, as discussed above, may further support this hypothesis, although the reflex inhibition of LM were apparently not affecting its activation at other vertebral levels (Larivière et al., 2018a). These various findings are in line with results showing that injury to thoracolumbar fascia and movement restriction can both affect thoracolumbar fascia properties (Bishop et al., 2016). It might be possible, therefore, that thoracolumbar fascia thickness is a function of both pathological and normal physiological processes (influenced by sex, age, physical activity), as seen for muscle fatty infiltration. A study (Wilke et al., 2019) looking at the effect of age found higher thickness of this fascia in older participants, as well as a positive correlation with BMI (Kendall's tau-b correlation = 0.45; $p < 0.05$), which is in line with our findings on LM fatty infiltration.

4.3. Thickness of the perimuscular connective tissues of the lateral abdominal wall

The thickness of all of the abdominal wall connective tissues (PMCT_{SUM}) showed no difference in terms of GROUP or SEX. However, analyses carried out on individual PMCT measures showed SEX differences for PMCT layers surrounding the EO, and GROUP differences for PMCT layers surrounding the TrA. The latter finding is new and extends previous results on the TrA, such as lower activation (Ferreira et al., 2010) and delayed anticipatory postural adjustments (Hodges et al., 2003; Hodges and Richardson, 1996), as well as more recent findings with regard to changes in the thickness of other perimuscular tissues (Bishop et al., 2016; Langevin et al., 2009, 2011; Whittaker et al., 2013).

Females showed lower thicknesses of the PMCT_{EO/IO} ($p = .01$) and PMCT layers surrounding the TrA (marginal differences), which was expected as females have a smaller body size and smaller muscles. However, this would not explain why females have a thicker PMCT_{STT/EO}. Considering that PMCT_{STT/EO} is the most superficial layer, just beside subcutaneous tissue (fat), a tentative explanation would be that this fat, which is more important in females (Table 1), infiltrates this layer further than it does in males.

Contrary to what was previously observed in patients with lumbopelvic pain (Whittaker et al., 2013), the thickness of the abdominal wall connective tissue (PMCT_{SUM}) was not affected by the presence of pain (GROUP factor). However, e PMCT_{IO/TrA} and PMCT_{TrA/IA} layers. Interestingly, contrary to findings regarding the posterior layer of the thoracolumbar fascia (Langevin et al., 2009) and the sum of lateral abdominal wall PMCT (Whittaker et al., 2013), the present study showed lower thicknesses in patients with LBP relative to healthy controls, with strong effect sizes. This partially supports our third hypothesis, as only connective tissue surrounding the TrA muscle was involved. This was anticipated, but not in the direction expected. Whether these contradictory findings can be attributed to the source of pain is unknown, as patients with

lumbar and lumbosacral pain were both included in the present study.

Whittaker et al. (2013) hypothesized that the thicker abdominal PMCT measured in patients with lumbopelvic pain might be secondary to an altered motor control strategy involving a reduced contribution of the RA over time, as substantiated by its atrophy (at the umbilicus level). Considering that connective tissues remodel in response to mechanical stress (Tillman and Cummings, 1992), they further proposed an increased role for connective tissues (PMCT and linea alba) to dissipate trunk loads and to contain intra-abdominal pressure. However, more recently, Singh et al. (2016) showed that, compared to healthy controls, the RA CSA of patients with LBP was larger at L3-L4 and L4-L5, and smaller at L5-S1. This may suggest that different effects on PMCT and linea alba tissue can also occur at different vertebral levels. Our own USI measures of the lateral abdominal wall muscle thickness at rest (e.g. REO, RIO, RTrA) and during activation (e.g. %CEO, %CIO, %CTrA) did not show GROUP main effects (Larivière et al., 2018b). At first glance, these muscle function parameters do not appear to contribute to the decreased thickness of the PMCT surrounding TrA. However, the USI assessment of each abdominal wall muscle "activation" (thickness change) is affected by forces exerted by neighbouring muscles, via shared PMCT, causing complex deformation patterns (Brown and McGill, 2010). There is epimuscular myofascial force transmission between neighbouring muscles (Huijing, 2009; Yoshitake et al., 2018) and possibly more so between TrA and IO (Brown and McGill, 2009), as these muscles have fibres running obliquely to one another. Consequently, it is likely that these PMCT are subjected to remodelling due to the continuous conversion of mechanical stress to bio-chemical response (Driscoll and Blyum, 2011).

4.4. Is there a link between these USI parameters?

The following speculations are based on the premise that the marginal GROUP difference ($p = .09$) observed for the thickness of the posterior layer thoracolumbar fascia is due to a lack of statistical power, as previously suggested. With regard to GROUP effects, the decreased bilateral activation at the L5S1 level (%_{L5S1-L}; %_{L5S1-R}) previously substantiated in these patients (Larivière et al., 2018a), as well as their decrease in physical activity over time (Table 1), might be the causes of the increased ($p = .09$) thickness of the posterior layer thoracolumbar fascia observed in the individuals with LBP (Bishop et al., 2016), as previously discussed. However, is it possible that this effect is linked to the decreased thickness of PMCT surrounding the TrA? Vleeming et al. (2014) revealed the presence of a co-dependent mechanism involving the balanced tension between deep abdominal (TrA and IO) and deep lumbar spinal (LM) muscles. They hypothesized that the dorsal and ventral muscle co-contraction enables the application of tension to the respective aponeurotic components of the thoracolumbar fascia, which in turn increases the stability of the lumbar spine. Their findings indicate that in the presence of weakness or dysfunction of these deep trunk muscles, this lumbar stability mechanism could be compromised by unbalancing the anterior and posterior tensions affecting the thoracolumbar fascia. Consequently, it is possible that the reduced LM activation previously substantiated (Larivière et al., 2018a) was accompanied by a reduced TrA activation (undetected) and associated PMCT so as to avoid such an unbalance. Consequently, the PMCT thickness surrounding TrA might have decreased due to a long-term decrease in deep trunk muscle activation. The link between these parameters definitely needs further investigation.

4.5. Limitations

When not adjusting for Age and STT_{L45}, the significant GROUP × SEX interaction ($p = 0.045$) highlighted significantly higher scores of LM echogenicity in females and, in particular, females with LBP. While this finding concurs with [Kjaer et al. \(2007\)](#), these authors adjusted for several covariates, including BMI. As shown in the [Supplementary File](#), when we adjust for BMI, the interaction changed a little ($p = 0.063$), but when adjusting for STT_{L45}, it disappeared ($p = 0.144$). Adjusting for different body fat metrics, therefore, may lead to different conclusions. In the present study, STT_{L45} was selected as the best covariate (instead of BMI or % fat), as in the case of previous research on the thigh ([Goodpaster et al., 2001](#)) and as further justified in the [Supplementary File](#). Caution must be exercised, therefore, when comparing results between studies that have, or have not, adjusted for different covariates.

This study has other limitations. Echogenicity parameters should be validated with gold standard measures (MRI or CT SCAN). The present PMCT USI measures corresponded only to the epimysium layer surrounding the abdominal muscles and to the posterior layer of the thoracolumbar fascia. More specific measures, requiring MRI and CT-Scan technologies, would be required to see if these findings could be extended to the endo- and perimysium, as well as to the middle layer of the thoracolumbar fascia and the aponeurosis attaching the lateral abdominal muscles to this thoracolumbar fascia layer. The echogenicity USI parameter cannot differentiate between fat and fibrosis content so the present findings must be interpreted accordingly. The responsiveness of these USI parameters to treatment needs to be tested to observe whether measurable changes correlate with changes in clinical outcomes. However, the duration of this treatment might need to be elongated as our own 8-week (16 session) lumbar stabilization exercise program did not make any changes to these parameters (data not published). Finally, measurements of fascia mechanical properties would have been useful to better explain the mechanisms underlying the observed changes.

5. Conclusion

Overall, the USI measures considered in the present study were sensitive to different potential changes or states, showing at least some potential for studying the remodelling of LM and PMCT (including the thoracolumbar fascia) surrounding the lumbar spine. Lumbar multifidus echogenicity was responsive to the vertebral level and sex, supporting its validity in measuring muscle fatty/fibrosis infiltration, while the thickness measure of the posterior layer of the thoracolumbar fascia approximated previous findings. The thinner perimuscular tissues surrounding the TrA in patients with LBP is a new finding, and might be related to a redistribution of mechanical stress across muscles and passive tissues. The study of remodelling passive and active soft tissues of the lumbar spine is in its infancy, and should be further explored, including any changes observed following appropriate intervention.

6. Clinical relevance

- The echogenicity parameter extracted from ultrasound images of the lumbar multifidus was responsive to vertebral level and sex, supporting its validity in measuring muscle fatty/fibrosis infiltration. Perimuscular tissue surrounding the transversus abdominis muscles is significantly thinner, relative to controls, in patients with LBP.

- The USI measures are useful in study the remodelling of lumbar soft tissues and are feasible for clinical use (with training); as such, they should be used to advance research on this topic.
- These original findings must be replicated in different populations before drawing any conclusions as regards their potential clinical use.

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Institutional review board

The ethical committee of the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal (CRIR) has approved the study protocol (registration number: CRIR-738-0512).

CRediT authorship contribution statement

Christian Larivière: Conceptualization, Methodology, Validation, Formal analysis, Investigation, Resources, Writing - original draft, Supervision, Project administration, Funding acquisition. **Richard Preuss:** Conceptualization, Methodology, Writing - review & editing, Funding acquisition. **Dany H. Gagnon:** Conceptualization, Methodology, Software, Writing - review & editing, Funding acquisition. **Hakim Mecheri:** Methodology, Software, Validation, Formal analysis, Writing - review & editing. **Sharon M. Henry:** Conceptualization, Methodology, Writing - review & editing, Funding acquisition.

Declaration of competing interest

No financial and personal relationships with other people or organizations inappropriately influenced (bias) our work.

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Appendix A. Supplementary data

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