

Systematic Review



Structural Changes of Lumbar Muscles in Non-Specific Low Back Pain

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Background: Lumbar muscle dysfunction due to pain might be related to altered lumbar muscle structure. Macroscopically, muscle degeneration in low back pain (LBP) is characterized by a decrease in cross-sectional area and an increase in fat infiltration in the lumbar paraspinal muscles. In addition microscopic changes, such as changes in fiber distribution, might occur. Inconsistencies in results from different studies make it difficult to draw firm conclusions on which structural changes are present in the different types of non-specific LBP. Insights regarding structural muscle alterations in LBP are, however, important for prevention and treatment of non-specific LBP.

Objective: The goal of this article is to review which macro- and/or microscopic structural alterations of the lumbar muscles occur in case of non-specific chronic low back pain (CLBP), recurrent low back pain (RLBP), and acute low back pain (ALBP).

Study Design: Systematic review.

Setting: All selected studies were case-control studies.

Methods: A systematic literature search was conducted in the databases PubMed and Web of Science. Only full texts of original studies regarding structural alterations (atrophy, fat infiltration, and fiber type distribution) in lumbar muscles of patients with non-specific LBP compared to healthy controls were included. All included articles were scored on methodological quality.

Results: Fifteen studies were found eligible after screening title, abstract, and full text for inclusion and exclusion criteria. In CLBP, moderate evidence of atrophy was found in the multifidus; whereas, results in the paraspinal and the erector spinae muscle remain inconclusive. Also moderate evidence occurred in RLBP and ALBP, where no atrophy was shown in any lumbar muscle. Conflicting results were seen in undefined LBP groups. Results concerning fat infiltration were inconsistent in CLBP. On the other hand, there is moderate evidence in RLBP that fat infiltration does not occur, although a larger muscle fat index was found in the erector spinae, multifidus, and paraspinal muscles, reflecting an increased relative amount of intramuscular lipids in RLBP. However, no studies were found investigating fat infiltration in ALBP. Restricted evidence indicates no abnormalities in fiber type in the paraspinal muscles in CLBP. No studies have examined fiber type in ALBP and RLBP.

Limitations: Lack of clarity concerning patient definitions, exact LBP symptoms, and applied methods.

Conclusions: The results indicate atrophy in CLBP in the multifidus and paraspinal muscles but not in the erector spinae. No atrophy was shown in RLBP and ALBP. Fat infiltration did not occur in RLBP, but results in CLBP were inconsistent. No abnormalities in fiber type in the paraspinal muscles were found in CLBP.

Key words: Low back pain, non-specific, chronic, recurrent, acute, muscle structure, fat infiltration, cross-sectional area, fiber type, review

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Lumbar muscle degeneration is a common feature in low back pain (LBP) (1,2). Macroscopically this muscle degeneration is characterized by a decrease in cross-sectional area (CSA) (1,3-7) and an increase in the amount of fat content (2,8-10) of the lumbar paraspinal muscles. Although changes in muscle size and fat infiltration of the lumbar muscles are frequently reported in LBP literature, inconsistencies in results make it difficult to draw firm conclusions whether structural changes are present in different types of non-specific LBP. This could be due to the generalization of previous observations across different types of LBP (specific vs non-specific LBP, and acute vs recurrent vs chronic LBP), while it is likely that each type of LBP is characterized by its own clinical picture and etiology.

In addition to macroscopic changes, it has been proposed that microscopic changes as well can occur in patients with non-specific LBP. For instance, micro-traumata of the deep muscular tissues can arise when the motion of the vertebra exceeds its physiological boundaries, which occurs when the demand for spinal muscle control is high (11-14). These micro-traumata could form a pain source during an episode of acute LBP (ALBP) or recurrent LBP (RLBP). Furthermore, it has been reported that patients with severe chronic LBP (CLBP) have a higher portion of type IIX (fast twitch glycolytic, previously called type IIB) at the expense of type I (slow twitch oxidative) fibers (15). In healthy people, the paraspinal muscles have been shown to contain more type I fibers, compared to other musculoskeletal muscles (16). Hence, the changes in fiber type, as seen in severe CLBP, could lead to lowered fatigue resistance of the paraspinal muscles which in turn results in higher vulnerability of the lumbar spine (16). However, not all studies have been able to reveal differences in fiber type characteristics of non-specific LBP patients (17).

As shown by Falla and Farina (18), pain can affect muscle structure by compromising muscle function. Compromised muscle function due to pain can consequently lead to altered muscle structure (18). This theory could explain why macroscopic muscle degeneration in non-specific LBP is often established in paraspinal muscles, and in particular the multifidus muscle, as these muscles play an important role in providing lumbar stability (19). On the other hand, muscular inhibition and atrophy might be a direct consequence of pain, as pain-related nerve inhibition reduces lumbar muscle activity in order to prevent tissue damage (20). Indeed, some studies have found evidence that structural changes are strongly associated with the presence

of (non-)specific LBP (8,21-23), whereas others could not find an association between the occurrence of (non-)specific LBP and structural changes in paraspinal muscles (24-28). To date, it is unclear whether structural changes of the lumbar musculature are the cause or consequence of non-specific LBP. Insights regarding the fact whether structural muscle alterations occur and how the lumbar muscles specifically change in case of LBP are, however, important for the prevention and treatment of non-specific LBP.

For the reasons described above, a systematic review of the existing literature was performed to examine whether and which type of macro- and/or microscopic structural alterations of the lumbar muscles occur in case of non-specific LBP. In order to prevent ambiguities, this review will solely focus on the non-specific LBP population, and will present the results separately for ALBP, RLBP, and CLBP.

METHODS

Eligibility Criteria

This systematic review is conducted according to the PRISMA-guidelines (<http://www.prisma-statement.org/>). A PICOS-approach was applied to formulate the research question: Patient (P), Intervention (I), Comparison (C), Outcome (O), and Study design (S). This systematic review attempted to select those articles which described "Which structural alterations (O) occur in lumbar muscles (P) of patients suffering from non-specific LBP" (I). Studies were included if they reported changes in CSA, fat infiltration, and fiber type distribution of the lumbar muscles in human adults suffering from non-specific LBP, compared to healthy controls which are pain-free (C). For this purpose, only case-control studies (S) were included.

Search Strategy

A systematic search on the existing literature was conducted in August 2014. Two electronic databases were screened for articles: PubMed and Web of Science. The following key words were used to search the databases for eligible articles: low back pain, acute low back pain, recurrent low back pain, chronic low back pain, non-specific low back pain, low backache, low back ache, lower back pain, and lumbago. These synonyms were combined with the following search terms regarding outcome using the Boolean-term "AND" in order to make the search as complete as possible: muscle atrophy, cross-sectional area, muscle size, muscular size,

muscular thickness, muscle thickness, muscular atrophy, muscle atrophy, muscle atrophies, adipose tissue, fat infiltration, fatty infiltration, fat deposition, intramuscular fat, fat tissue, fatty tissue, muscle fiber, fiber type, fiber size, fiber density, muscle structure, muscular structure, muscle morphology, muscular morphology, muscle composition, and muscular composition.

In addition, a hand search was conducted by screening the reference lists of all eligible articles and relevant reviews. The last author (L.D.), an expert in the area of LBP and the examination of structural properties of the spinal muscles, was asked to review the list of studies retrieved by the search strategy and to identify any missing relevant studies.

Study Selection

After removing duplicates, title and abstract of the remaining articles were screened regarding fulfillment of the selection criteria. Afterwards full texts of the remaining articles were screened against these criteria to ensure eligibility.

To be included, an article had to fulfill the following criteria: (1) case-control study (patients with non-specific ALBP, RLBP, or CLBP compared to healthy participants); (2) only living human adults (≥ 18 years old); (3) evaluating at least one of the following outcomes of LBP: CSA, fat infiltration, fiber type; (4) of the lumbar muscles. Only full texts written in English, Dutch, French, and German were included in this review. Exclusion criteria were (1) lumbar surgery; (2) spinal stenosis; (3) disk herniation, as these were considered as reasons for specific LBP.

Risk of Bias

The "checklist for assessing risk of bias of studies examining side effects and etiology" presented on the website of the Dutch Cochrane Centre (<http://dcc.cochrane.org/>) was used. This checklist contains 4 evaluation criteria: 1) adequate definition of participant groups; 2) absence of selection bias; 3) blindness of intervention and outcome; 4) identification for possible confounders. The assessment of risk of bias was executed by 2 independent, blinded researchers (D.G. & J.V.O.). The results were compared and differences were discussed in case of disagreement. The risk of bias score was not decisive for inclusion in this review, but was taken into account when presenting the results.

Afterwards a level of evidence (LOE) was assigned to each article, based on study design and risk of bias, using the guidelines of the EBRO-platform (Evidence-

based guideline development in the Netherlands, www.cbo.nl). In order to draw correct conclusions, the level of conclusion will be determined based on the levels of evidence of the different studies per topic.

Data Extraction

Information was extracted regarding participant characteristics, definition of patient group, evaluation technique, outcome measure, lumbar test site and participant position, and study results.

RESULTS

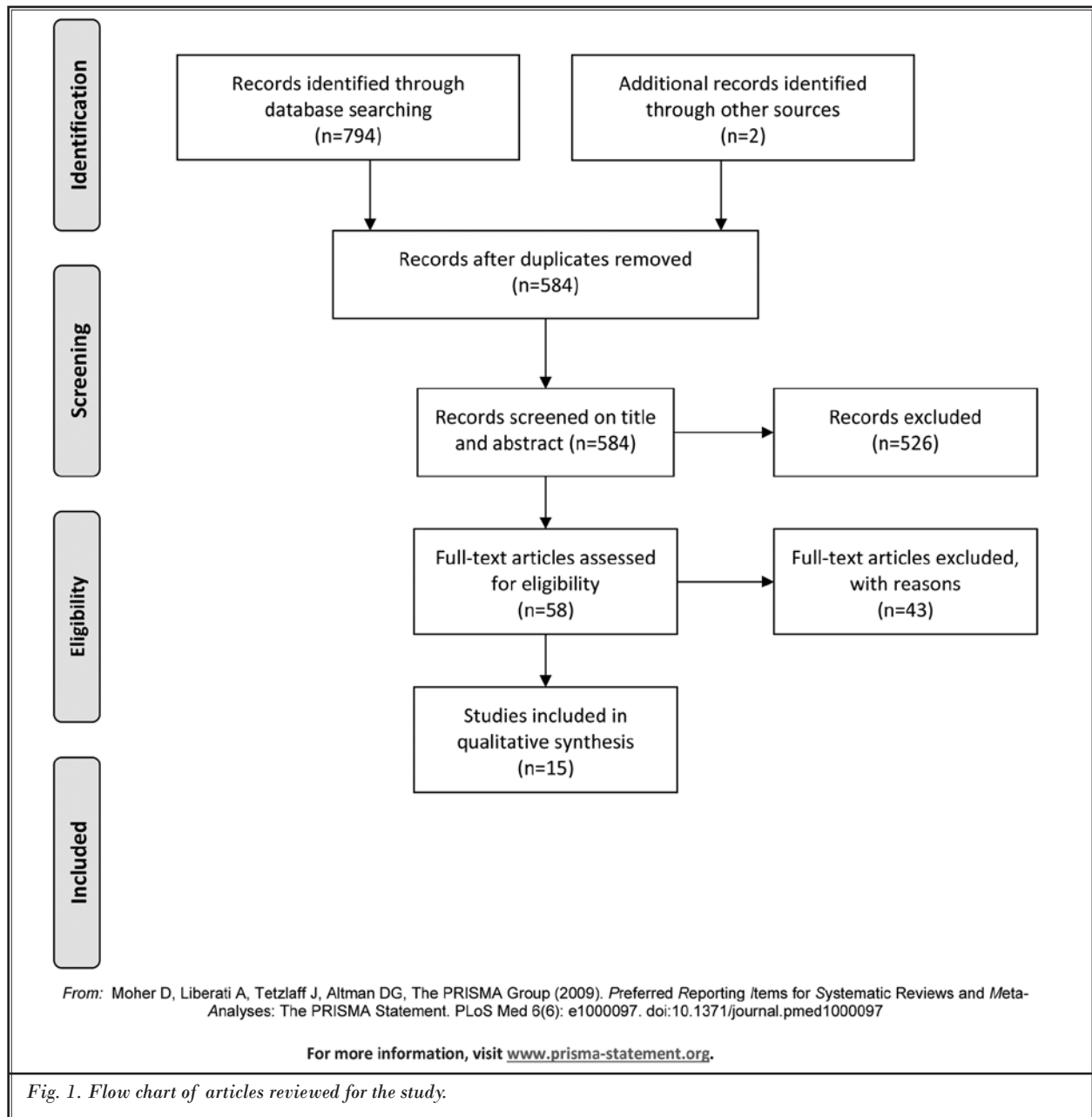
Study Selection

The systematic search resulted in 794 articles. Additionally 2 articles were found through hand searching. After removing duplicates, 584 articles remained and were screened for inclusion based on title and abstract and, if necessary, on full text. After this complete screening, 15 articles remained. The complete screening procedure and the exact reasons for exclusion during each screening phase are represented in the flowchart (Fig. 1).

Study Characteristics

Since the intention was to compare structural characteristics between non-specific LBP patients and healthy controls, only case-control studies were admitted. Clearly defined CLBP patients were found in 9 studies (1,4,8,17,22,27,29-31), whereas specifically defined RLBP patients were seen in 2 studies (29,32) and one study investigated clearly defined ALBP (3). Four studies however, reported only LBP with varying definitions and no clear defined duration (28,33-35). One of these subdivided LBP into "previous LBP" and "current LBP" (34). Another study split the patient group into a group without hip-pain and a group with hip-pain (33). Three articles included only patients with unilateral complaints (3,32,35), whereas 11 did not clearly mention if patients suffered from unilateral or bilateral LBP (1,8,17,22,27-31,33,34). Only one article subdivided the patient group into a bilateral and a unilateral LBP group (4).

Fourteen studies evaluated CSA in lumbar muscles (1,3,4,8,22,27-35), whereas 5 studies evaluated fat infiltration (1,8,29,32,33), and one study examined the lumbar muscle fibers types (17). From all studies, 6 applied ultrasound imaging (USI) (3,4,8,27,30,31,35), 4 applied magnetic resonance imaging (MRI) (28,32-34), and 3 applied computed tomography (CT) (1,22,29) to



evaluate CSA and/or fat content of the lumbar muscles. The study investigating fiber type used percutaneous spinal muscle biopsies which were obtained using the conchotome technique (17). The examined muscles varied among all articles: 12 studies investigated the isolated multifidus muscle (1,3,4,8,22,27,30-35), 5 studies investigated the isolated erector spinae muscle (1,29,32-34), and 4 studies examined the complete paraspinal muscles (1,17,22,28). Fourteen articles inves-

tigated both left and right side of the lumbar muscles (1,3,4,8,22,26-35) but in only 8 studies, was it examined whether there were differences between both sides (3,4,27,30-33,35). Only one study did not clearly mention if the measurements were taken on one or both sides of the lumbar musculature (17). All characteristics extracted from the included articles are presented in the evidence table (Table 1).

Structural Changes of Lumbar Muscles in Non-specific Low Back Pain

Table 1. Evidence table.

Study (year)	Characteristics patient group; control group	Definition patient group	Evaluation technique	Outcome measure	Test site & position subjects	Results
Chan et al (2012)	CLBP (12m; 22-52y; mean age 36.6±2.9) HC (12m; 21-34y; mean age 25.2±1.1)	CLBP: ODI ≥20%	US	CSA Fat area	MF At L4, bilateral In prone position; 25°: forward stooping; 45° forward stooping; upright standing	CSA CLBP < HC in all positions (P <0.001) Fat area CLBP > HC (P <0.001)
Crossman et al (2004)	CLBP (35m; 18-55y; mean age 41±11) HC (32m; 18-55y; mean age 38±10)	CLBP: continuous or recurrent LBP >6 months	Muscle biopsy	Type I fiber content	PS	No histomorphometric group differences: Fiber types by percent number: CLBP = HC Mean fiber narrow diameter: CLBP = HC Relative area occupied by type I: CLBP = HC Fiber size type I or type II: CLBP = HC Admixture of type I & type II fibers in CLBP & HC Size type I fibers > type II in CLBP & HC; in CLBP (P <0.01)
Danneels et al (2000)	CLBP (17m; 15f; 25-55y; mean age 36.91±10.26) HC (13m; 10f; 25-55y; mean age 37.34±9.78)	CLBP: ≥1 year	CT	CSA Fat deposits	PS (MF, longissimus & iliocostalis) Isolated MF Isolated ES (longissimus & iliocostalis) At upper endplate L3; upper & lower endplate L4, bilateral In prone position	CSA PS CLBP = HC at upper L3 & L4, with and without fat (P > 0.05) CLBP < HC at lower L4 (with fat P =0.048; without fat P =0.036) CSA MF CLBP = HC at upper L3 & L4, with and without fat: (P > 0.05) CLBP < HC at lower L4 (with fat P =0.009; without fat P =0.012) CSA ES CLBP = HC at upper L3 P =0.79; upper L4 P =0.707; Lower L4 P =0.25 Fat: no group differences (P > 0.05)
D'hooge et al (2012)	RLBP, unilateral, in remission (6m; 7f; mean age 32.09±11.52) HC (6m; 7f; mean age 32.09±11.52)	RLBP: history of ≥2 previous episodes (≥24h pain) of LBP followed by ≥1 month pain free; onset >6 months; interference in ADL	MRI	Total CSA Lean muscle CSA Fat CSA MFI	MF ES At upper endplate L3; upper & lower endplate L4, bilateral In supine position	Total CSA MF & ES RLBP = HC at any level (MF P =0.337; ES P =0.627) Lean muscle CSA MF & ES RLBP = HC at any level (MF P =0.276; ES P =0.752) Fat CSA MF & ES RLBP = HC (P = 0.640) MFI MF & ES RLBP > HC bilaterally (at upper endplate L4 P =0.014; at lower endplate L4 P =0.017) LBP = HC at upper endplate L3 (P = 0.380)
Gildea et al (2013)	LBP (13) LBP + hip (10) HC (8) TOTAL (31; 14m; 17f; mean age 23.7±3.6)	LBP(+ hip): pain in lower back (+buttock or hip)	MRI	CSA Fat content	MF ES At L2-L5 (at level of the intervertebral discs), bilateral In supine position	CSA MF Group differences (P = 0.049) LBP < HC at L3, L4, L5 on both sides (P <0.024) LBP+ hip < HC at L3 on both sides & at L4 on right side (P <0.027) No differences at L2 (P > 0.44) CSA ES No differences (P = 0.10) Fat MF <10% fat content in all groups Fat ES Not evident

Table 1 (cont). Evidence table.

Study (year)	Characteristics patient group; control group	Definition patient group	Evaluation technique	Outcome measure	Test site & position subjects	Results
Hides et al (1994)	ALBP (16m; 10f; 17-46y; mean age m 29.2; mean age f 33.6) HC (21m; 30f; 19-32 y; mean age m 25.0; mean age f 25.3)	ALBP: suffering first episode of LBP, unilateral	US	CSA	MF At L2-L5/L2-S1 (ALBP); at L4 (HC), bilateral In prone position	HC between side differences (at L4) < ALBP (at all levels) (P <0.001) ALBP: difference in atrophy between symptomatic & other levels (P <0.05) ALBP: No atrophy below symptomatic level HC: No difference in levels (P > 0.05)
Hides et al (2008a)	CLBP (23m; 27f; mean age 46.8±13.2) HC (27m; 13f; mean age 28.4±5.7)	CLBP (central/bilateral & unilateral): pain at T12-gluteal fold; >3 months	US	CSA	MF At L2-L5, bilateral In prone position	CLBP < HC (P = 0.001) Asymmetry unilateral CLBP > HC (L4 P =0.003; L5 P =0.001) Asymmetry unilateral CLBP > bilateral CLBP (L4 P =0.004; L5 P =0.016) At L2-L3 no differences
Hides et al (2008b)	LBP, unilateral (10m; mean age 21.9±2.5) HC (16m; mean age 21.4±2.0)	LBP: current or previous LBP interfering with sports performance	US	CSA	MF At L2-L5, bilateral In prone position	LBP < HC at both sides, at all levels
Hultman et al (1993)	CLBP (20m; mean age 49±6) ILBP(35m; mean age 50±3) HC (18m; mean age HC 50±3) TOTAL (148; 49-51y)	ILBP: ≥1 episodes; ≥2 months pain free episode CLBP: ≥3 years; sick leave ≥ 3 months in previous year	CT	CSA RD	ES At L3, bilateral In supine position	CSA Mean values CLBP < HC < ILBP CLBP < ILBP (P = 0.037) CLBP = HC (P > 0.05) ILBP = HC (P > 0.05) RD Mean values CLBP < HC < ILBP CLBP < ILBP (P = 0.000) CLBP < HC (P <0.05) ILBP = HC (P > 0.05)
Kamaz et al (2007)	CLBP (36f; 30-58y; mean age 43.2±6.9) HC (34f; 31-61y; mean age 44.4±7.7)	CLBP: ≥1 year	CT	CSA	PS (MF, iliocostalis, longissimus) Isolated MF At upper & lower endplate L4 In prone position	CSA PS CLBP = HC at upper endplate L4 (P = 0.137) CLBP < HC at lower endplate L4 (P = 0.010) CSA MF CLBP < HC at upper endplate L4 (P = 0.002) CLBP < HC at lower endplate L4 (P = 0.001)
Lee et al (2006)	CLBP (16m; 34-47y; mean age 39.9) HC (19m; 35-47y; mean 41.7)	CLBP: ≥1 year	US	CSA	MF At L4 & L5, bilateral In upright standing; 25° forward stooping; 45° forward stooping; prone position	LBP < HC at L4 & L5 (generally) LBP < HC at L4 upright (P <0.05) Asymmetry in CLBP at L4, not in HC No difference at L5 in standing No difference at L4 or L5 in prone, 25° or 45°
McGregor et al (2002)	PREVIOUS LBP (13; mean age 23.2±5.3) CURRENT LBP (5; mean age 22.0±1.8) HC (4; mean age 21.0±2.2) TOTAL (22; mean age 22.6±4.3)	PREVIOUS: time off training CURRENT: preventing full training	MRI	CSA	ES MF At L4-L5 & L5-S1 disc interspace, bilateral In rowing position	CSA MF Previous/current LBP > HC (most prominent in previous LBP) (P <0.0001) Previous LBP > current LBP (P <0.001) CSA ES Previous/current LBP > HC at L4-L5 (P <0.001) Previous LBP = current LBP at L4-L5 (P > 0.05) Previous/current LBP < HC at L5-S1 (tendency) Previous LBP < HC L5-S1 (P <0.05)

Table 1 (cont). Evidence table.

Study (year)	Characteristics patient group; control group	Definition patient group	Evaluation technique	Outcome measure	Test site & position subjects	Results
Scott et al (2014)	CLBP (20; 14m; 6f; mean age 31.9±7.2) HC (20; 14m; 6f; mean age 31.3±7.6)	CLBP: ≥3 months	RUSI	CSA	MF At L5 In prone position; sitting on stable surface; sitting on labile surface	CLBP = HC at all positions Asymmetry CLBP = HC
Wallwork et al (2009)	CLBP (17; 8m; 9 f; 18-60y; mean age 41.9±13.7) HC (17; 8m; 9 f; 18-45y; mean age 33.9±11.2)	CLBP: ≥3 months	US	CSA	MF At L2-L5 In prone position	CLBP < HC at L5 (P = 0.001) CLBP > HC at L2 (P = 0.047) Asymmetry CLBP = HC (P > 0.05)
Yarjanian et al (2013)	LBP (10; 4m, 6f; mean age 62.00±8.58) HC (10; 5m; 5f; mean age 65.00±6.72)	LBP: non-radiating LBP without stenosis	MRI	Functional CSA (muscle isolated from fat)	PS At L5-S1 disc level, bilateral	LBP = HC (P = 0.80)

ADL = activities of daily living; ALBP = acute low back pain; CLBP = chronic low back pain; CSA = cross-sectional area; f = females; HC = healthy controls; ILBP = intermittent low back pain; m = males; MFI = muscle fat index; LBP = low back pain; >ES = lumbar erector spinae; MF = multifidus muscle; MRI = Magnetic resonance imaging; PS = Paraspinal; RD = radiological density; RLBP = recurrent low back pain; RUSI = rehabilitative ultrasound imaging; US = ultrasound imaging; VS = versus; y = years

Risk of Bias

The methodological quality of all included articles is presented in Table 2. In 75% of the cases, both researchers agreed. The remaining items were discussed until agreement was reached. From all included studies, one scored 0/4 (3) and one scored 1/4 (27) which was considered as a high risk of bias, whereas 3 studies scored 2/4 which was considered as a moderate risk of bias (4,8,34). Six studies scored 3/4 (17,28-32), and 4 studies scored 4/4 (1,22,33,35) which were respectively considered as a limited and low risk of bias. Since all studies were case-controls, all articles received a B level of evidence.

Outcome Measures

CSA

Chronic Low Back Pain

Seven studies investigated lumbar muscle atrophy in the multifidus in CLBP (1,4,8,22,27,30,31). Six of these studies found a lowered CSA in the multifidus compared to healthy persons, for at least one lumbar level (1,4,8,22,30,31). At level L4, 3 studies found a lower CSA in CLBP (4,8,30). Two other studies made a distinction

between the upper and lower endplate of L4 (1,22). One of these found a lowered CSA both at the upper and lower endplate of L4 (22), whereas Danneels et al (1) demonstrated that the multifidus, both with and without fat, was smaller only at the lower endplate, but not at the upper endplate. At L5, one study reported a lower CSA in the multifidus in CLBP (31), whereas 2 others found no differences (27,30). At lumbar levels L2-L3, no differences were seen between CLBP and healthy controls (1,4). One study even found a larger multifidus at higher lumbar levels in CLBP compared to healthy persons (31). Two studies noted asymmetry at lower levels in CLBP (4,30). According to Hides et al (4), asymmetry was larger in unilateral CLBP compared to healthy participants and to bilateral CLBP, indicating possible unilateral atrophy in unilateral CLBP (4). On the contrary, one study found no differences in asymmetry between healthy participants and CLBP (31).

Two studies separately reported on differences in CSA for the isolated erector spinae muscle but could not establish any differences between CLBP and healthy controls (1,29).

Only 2 studies investigated CSA in the complete paraspinal muscle and could establish a lowered CSA in CLBP compared to healthy participants at the lower

Table 2. Scoring.

	Study	CBO score							Total CBO score	LOE	LOC	
		1	2	3	4	5	6	7				
CSA	CLBP	Chan et al (2012)	0	1	0	/	/	/	1	2/4	B	2
			0	1	0	/	/	/	1			
		Danneels et al (2000)	1	1	1	/	/	/	1	4/4	B	
			1	1	1	/	/	/	1			
		Hides et al (2008a)	1	0	0	/	/	/	1	2/4	B	
			1	0	0	/	/	/	1			
		Kamaz et al (2007)	1	1	1	/	/	/	1	4/4	B	
			1	1	1	/	/	/	1			
		Lee et al (2006)	1	1	?	/	/	/	1	3/4	B	
			1	1	?	/	/	/	1			
		Scott et al (2014)	0	0	?	/	/	/	1	1/4	B	
			0	0	?	/	/	/	1			
		Wallwork et al (2009)	1	0	1	/	/	/	1	3/4	B	
			1	0	1	/	/	/	1			
	RLBP	D'hooge et al (2012)	1	0	1	/	/	/	1	3/4	B	
			1	0	1	/	/	/	1			
		Hultman et al (1993)	1	1	?	/	/	/	1	3/4	B	
			1	1	?	/	/	/	1			
	ALBP	Hides et al (1994)	0	0	0	/	/	/	0	0/4	B	
			0	0	0	/	/	/	0			
Undefined LBP	Gildea et al (2013)	1	1	1	/	/	/	1	4/4	B		
		1	1	1	/	/	/	1				
	Hides et al (2008b)	1	1	1	/	/	/	1	4/4	B		
		1	1	1	/	/	/	1				
	McGregor et al (2002)	1	0	?	/	/	/	1	2/4	B		
		1	0	?	/	/	/	1				
	Yarjanian (2013)	1	0	1	/	/	/	1	3/4	B		
		1	0	1	/	/	/	1				
FAT CONTENT	CLBP	Chan et al (2012)	0	1	0	/	/	/	1	2/4	B	
			0	1	0	/	/	/	1			
		Danneels et al (2000)	1	1	1	/	/	/	1	4/4	B	
			1	1	1	/	/	/	1			
		Hultman et al (1993)	1	1	?	/	/	/	1	3/4	B	
			1	1	?	/	/	/	1			
	RLBP	D'hooge et al (2012)	1	0	1	/	/	/	1	3/4	B	
			1	0	1	/	/	/	1			
		Hultman et al (1993)	1	1	?	/	/	/	1	3/4	B	
			1	1	?	/	/	/	1			
	Undefined LBP	Gildea et al (2013)	1	1	1	/	/	/	1	4/4	B	
			1	1	1	/	/	/	1			
FIBER TYPE	CLBP	Crossman et al (2004)	1	1	?	/	/	/	1	3/4	B	
			1	1	?	/	/	/	1			

endplate, but not at the upper endplate of L4 (1,22). At more cranial levels, also no differences in CSA could be established (1).

Recurrent Low Back Pain

Two studies investigated CSA in erector spinae muscles at levels L3-L4, but none of them could establish differences in CSA between RLBP and healthy controls (29,32). One study established a decreased CSA in the erector spinae muscle of CLBP compared to RLBP at level L3 (29).

Only one study searched for differences in CSA in multifidus in RLBP, but could not establish any difference in total muscle CSA or lean muscle CSA compared to healthy controls at any level. Also no pain-side related differences were seen (32).

Acute Low Back Pain

Only one article studied atrophy in the multifidus in ALBP compared to healthy controls. The between side differences in healthy participants (at L4) appeared smaller in comparison with ALBP (at all levels). A significantly larger asymmetry between symptomatic (L5) and asymptomatic (L2-L4) levels were reported in ALBP, whereas no differences between levels occurred in healthy controls. Below symptomatic levels, no atrophy was noted both in ALBP and healthy persons (3).

Undefined Low Back Pain

Three articles discussed CSA in the multifidus muscle (33-35) of which 2 established a smaller CSA in LBP compared to healthy persons (33,35). One of these 2 latter studies detected a smaller CSA at both sides, at all lumbar levels (L2-L5) (35), whereas the other could only find differences at L3-L4 and L5 level, but not at L2 (33). Conversely, a third study established a larger CSA in the multifidus in (previous and current) LBP compared to healthy controls. Moreover, CSA in previous LBP was larger compared to current LBP (34).

Two articles considered differences in CSA in the lumbar erector spinae and found conflicting results (33,34). One of these studies could not find any differences between healthy controls and LBP at all lumbar levels (L2-L5) (33), whereas in the study of McGregor et al (34) a significant larger CSA was found in the healthy participants versus previous LBP at L5-S1. Contradictory, in this latter study, the erector spinae appeared larger in both previous and current LBP, compared to healthy controls at L4-L5. No differences were found between previous LBP and current LBP at L4-L5 (34).

Only one study investigated muscle functional CSA in the complete paraspinal muscle at level L5-S1 but no differences were found when comparing non-radiating LBP to healthy controls (28).

In summary, moderate evidence of atrophy can be found in CLBP (conclusion strength 2) since 6/7 studies indicated the multifidus muscle is smaller when compared to healthy controls (1,4,8,22,30,31). A lowered CSA in the paraspinal muscles in CLBP was only seen at the lower endplate of L4 (1,22) but no atrophy was found in the erector spinae muscle in CLBP (1). Moreover moderate evidence occurred in RLBP and ALBP (conclusion strength 2) in which no atrophy was shown in any lumbar muscle (3,29,32). Conflicting results were seen in the undefined LBP group (conclusion strength >3). One study found multifidus to be larger in LBP (34) whereas 2 others found multifidus to be smaller in LBP compared to healthy controls (33,35). In the erector spinae, one study could not find any difference for CSA (33) whereas another found the erector spinae to be smaller in the LBP group at level L5-S1, but conversely larger at L4-L5 (34). The sole study investigating paraspinal muscles could not establish atrophy in undefined LBP (28).

Fat Content

Chronic Low Back Pain

Two studies in this review investigated fat infiltration in CLBP in the isolated multifidus muscle, providing conflicting results (1,8). One study established differences in fat content between healthy controls and CLBP at L4 (8), whereas the other researchers could not detect any difference between groups (1).

Inconsistent results for the isolated erector spinae were also found in 2 studies (1,29). On the one hand, Hultman et al (29) found a significant difference between CLBP and healthy controls at L3, whereas Dannels et al (1) could not establish differences in fat content.

Only one study investigated the total paraspinal muscle, but could not demonstrate differences between healthy persons and CLBP (1).

Recurrent Low Back Pain

Two studies investigated fat infiltration in the erector spinae in RLBP and could not find any differences compared to healthy controls (29,32). An increase in fat content was however detected in CLBP compared to

RLBP (29).

One study investigated the multifidus and the total paraspinal muscle in unilateral RLBP patients during remission but could not find differences compared to healthy controls. Conversely, the authors of this study indicated that the muscle fat index (reflecting the amount of fat content in lean muscle CSA) was larger in RLBP compared to healthy participants for all muscles at the upper and lower endplate of L4, but not at upper endplate of L3. No pain-side related differences were found (32).

Acute Low Back Pain

No studies investigating fat content in lumbar muscles of non-specific ALBP were found through our search strategy.

Undefined Low Back Pain

One study, which did not define the LBP group, was not able to establish differences in fat content nor in multifidus or erector spinae between the patient group and healthy controls (33).

Results concerning fat infiltration in CLBP are conflicting (conclusion strength 3). Studies provided contradictory results for the isolated multifidus (1,8) and for erector spinae (1,29). The sole study investigating paraspinal muscles, did not find fat infiltration in CLBP (1). On the other hand, there is moderate evidence fat infiltration does not occur in RLBP (conclusion strength 2) since no fat infiltration in the erector spinae, multifidus, or paraspinal muscles was found in RLBP (29,32). Conversely a larger muscle fat index for erector spinae, multifidus, and paraspinal muscles was found in RLBP, reflecting an increased relative amount of intramuscular lipids (32). In undefined LBP, no differences in multifidus and erector spinae were demonstrated (33) (conclusion strength 3). No studies were found investigating fat content in ALBP, so no conclusions can be made for this population.

Fiber Type

Chronic Low Back Pain

Only one study examined the fiber type content in paraspinal muscles. No histomorphometric differences were found between healthy controls and CLBP, suggesting no significant atrophy of either fiber type in CLBP. Type I fibers size was slightly larger than type II fiber size, both in CLBP and healthy controls, but only significant in the CLBP group (17).

Recurrent Low Back Pain and Acute Low Back Pain

No studies investigating fiber type in lumbar muscles of patients with ALBP or RLBP were found.

In summary, restricted evidence to date indicates that patients with CLBP show no abnormalities in paraspinal muscle fiber types (conclusion strength 3). As no studies have examined whether alterations in fiber type occurs in ALBP and RLBP, no conclusions can be made for these populations.

DISCUSSION

Results

The main objective of this systematic review was to determine the evidence on structural changes in lumbar muscles in patients with non-specific LBP. Moreover, this review intended to summarize differences in muscle size (CSA), fat infiltration, and muscle fiber characteristics in persons with non-specific CLBP, RLBP, or ALBP compared to healthy controls.

The present study revealed different outcomes for CSA in different LBP groups. In CLBP, moderate evidence is provided that the multifidus is smaller in CLBP compared to healthy controls at different levels (1,4,8,22,30,31), while results about CSA in paraspinal muscles and the erector spinae muscle were less conclusive (1,22,29). These results are similar to the review of Fortin and Macedo (5) which investigated muscle morphology in patients with specific and non-specific LBP and found that both multifidus and paraspinal muscles were smaller in CLBP compared to healthy controls. According to Bierry et al (36), the multifidus is predominantly affected by atrophy in LBP, given that the multifidus is exclusively innervated by the medial ramus of the dorsal root of the spinal nerve, without segmental nerve supply, which is present in other spinal muscles. After pain onset, a combination of reflex inhibition and disturbance in coordination of trunk muscles occurs changes in the multifidus structure (1,19). Therefore, muscle training focused on multifidus activation is often considered as a key feature in the clinical approach of LBP (19,37).

According to levels of lowered CSA in CLBP, results were similar amongst studies: lowered CSA was mainly found in more caudal lumbar levels (1,4,8,30,31) whereas at more cranial lumbar levels no conclusive results could be established (1,4,31). The review of Fortin and Macedo (5) established multifidus atrophy in CLBP was even larger in L5 compared to L4. An explana-

tion for this can be found in the fact that the multifidus muscle becomes larger at lower levels (4). At the level L3, the multifidus is about one-sixth of the total paraspinal muscle; whereas, the multifidus muscle is one-third of the paraspinal muscle at the lower endplate of L4 (1). Due to a larger muscular mass in lower areas of lumbar muscles, clear atrophy can be rather expected in the lower lumbar areas. In the current review, however, 2 studies could not find any atrophy in the multifidus muscles in CLBP at L5 (27,30), but one of these studies included professional athletes who were attending physiotherapy. Being at different stages in rehabilitation might imply that some patients normalized their multifidus structures. In rehabilitation, muscle training on the multifidus should preferably be focused on the lower levels, instead of general lumbar region.

In RLBP and ALBP no differences could be shown in lumbar muscle size between patients and healthy controls (3,29,32). Possibly earlier reductions in muscle size during an episode of LBP resolve in remission. This assumption is found in a correlation between CSA and "time that elapsed since the last LBP episode" in the dissertation of D'Hooge et al (32). To make this assumption more clear, a study should investigate muscle structure, as well during a pain flare as in pain remissions during different points in time. This is the only way to examine the direct influence of clinical LBP on muscle structure and the effect of pain remission. Notable is the difference in CSA in the erector spinae between RLBP and CLBP, indicating CSA is lowered in CLBP compared to RLBP (29). This result supports our hypothesis of differences in characteristics and etiology between LBP groups.

Studies investigating ambiguous LBP groups could not find conclusive results towards CSA in lower back muscles (28,33-35). Like Crossman et al (17) proposes, 2 groups of LBP might appear: LBP patients who stay active despite their discomfort and LBP patients reducing their physical activity as a protection mechanism resulting in deconditioning. The amount of physical activity despite LBP complaints might influence the muscle structure characteristics. Studies should take this into account when comparing groups and either match participant groups for daily activity levels or report when group differences exist regarding this confounding factor. Given the importance of well-functioning lower back muscles with regard to spinal functioning, rehabilitation of LBP complaints should contain general physical activity to ensure patients don't get inactive and deconditioned. Special attention should be paid

to multifidus activation exercises, since the multifidus is the most sensitive to atrophy.

Besides activity levels as a confounding factor of fat content in the lumbar musculature, also body mass index (BMI) and subcutaneous fat levels might influence fat infiltration. More specifically, paraspinal muscle density has been shown to decrease when BMI increases (24). Some articles in this review reported that an increased fat infiltration in LBP is not related to BMI or other body composition parameters (8,22,29), whereas others just did not take this parameter into account.

The amount of fat content in lumbar muscles is considered as a sign of atrophy (2). In CLBP a significant increase in fat infiltration compared to healthy controls was found in 2 studies (8,29), whereas another was unsuccessful in confirming these findings (1). Chan et al (8) found an increased fatty infiltration in CLBP, but the control group was much younger (25 years) compared to the patient group (37 years). The significant increase in muscle fat content in this patient group can possibly be explained rather by age difference than by LBP. Another included article investigated very young persons (< 32 years) and could not find differences in fat infiltration between an undefined LBP group and healthy controls (33). These results also suggest the duration of LBP in young persons might be too short to cause structural changes. The role between fat content and age has been confirmed by McLoughlin et al (25), who found that fat infiltration is related to age and is not a sign of atrophy in the lumbar muscles. Other research supports the idea that an increase in fat content is caused by age (1,22,33,38) or by disuse (1,22) of the lumbar muscles rather than by the lumbar pain itself. So age differences could lead to misinterpretation of results concerning fat infiltration in lumbar muscles, therefore age should be taken into account as a confounding factor when investigating fat content.

Both studies investigating fat content in RLBP in remission reported no macroscopic fat depositions in RLBP compared to healthy controls, speculating fat content was not reduced or was restored during the remission period (29,32). D'Hooge et al (32) on the other hand also reported an increased muscle fat index (which reflects increased relative amounts of intramuscular lipids) in lean muscle tissue in the absence of alterations in muscle size or macroscopic fat infiltration. These results mainly presume that the quality of the muscle structure might be decreased during remission periods, contributing to recurrence of LBP, rather than muscle

size being decreased. A decrease in CSA associated with an increase in fat infiltration in the multifidus in CLBP patients compared to healthy participants, implies an increased infiltration of non-contractile material in lumbar muscles (8). As a consequence, lumbar muscle quality drops in LBP without visual changes in absolute muscle size. Studies incapable of finding differences in CSA might be masking a reduction in relative muscle size. Results in studies only measuring CSA without paying attention to fat infiltration, need careful interpretation, especially when confounders like age and BMI are not taken into account.

No studies in this review reported on fat infiltration in non-specific ALBP. If the fat content is supposed to be a result of aging, long-lasting inactivity, or long lasting LBP, it is not expected in persons experiencing ALBP, although a relationship with fat infiltration was discovered by Mcloughlin et al (25). Longitudinal research could further unravel the relationship (cause or consequence) between fat infiltration and the etiology of LBP.

According to fiber type characteristics, this review could not establish changes in non-specific CLBP. Crossman et al (17) found similar results regarding ranges of type I and II fiber dimension and distributions in healthy persons compared to CLBP, suggesting no abnormalities in paraspinal muscle fibers in CLBP symptom generation. However the review of Mannion (16) suggests the degree of abnormalities in musculature most likely depends on age, duration of symptoms, and physical (in)activity prior to and after the onset of LBP. Crossman et al (17) matched both groups for age, but no information on physical activity was mentioned. D'Hooge et al (39) on the other hand, found lower T2-rest values for multifidus, but not for erector spinae, in non-specific RLBP in remission. These authors suggest a higher proportion of glycolytic fibers (type II) in multifidus muscles, which might lead to a reduced capability of the multifidus in stabilizing the spine because of fatigue. Few studies concerning fiber type characteristics in lumbar muscles of LBP patients are available. Based on the solitary study of Crossman et al (17), a sound conclusion on fiber characteristics in non-specific CLBP cannot be made. Hence, future studies examining fiber size, and type and composition of the lumbar muscles in all non-specific LBP populations are warranted.

Study Limitations and Suggestions for Further Research

The current evidence should be interpreted in light

of the study limitations of the individual studies. First of all, some studies did not clearly define the included patient population (CLBP, RLBP, or ALBP) or included a mixture of LBP patients. This made it difficult to incorporate the results of these studies when drawing conclusions for specific types of non-specific LBP (28,33-35). Besides this, a lot of different definitions were applied to identify RLBP and CLBP, which might influence results and hamper conclusions. Future studies should define their study population sufficiently, and moreover, a global consensus regarding the definition for specific groups of non-specific LBP is wanted.

Lack of clarity about LBP to be unilateral or bilateral was also common in the included studies, however the side of complaints might play an important role regarding structural changes. In addition, some studies pooled outcomes of muscles from the left and right body side when no significant differences were found between both. In other studies, left and right were examined separately, even when nothing was mentioned about side differences or the affected side, which might lead to improper conclusions. According to Bierry et al (36) atrophy ought to be concentrated ipsilateral to the side of pain and at the level of pain. These results were also found by Hides et al (3), in ALBP and in cricketers with general LBP (35). Also in CLBP, studies have shown rather local muscle changes (1,4,31). Other studies conversely provide evidence of more generalized changes in LBP populations (26,32,33,35). The review of Fortin and Macedo (5) revealed significant differences in symptomatic and asymptomatic sides in CLBP patients. Generally one would expect complaints in persons with CLBP to be more widespread and generalized in the lumbar muscles, whereas in ALBP, symptoms are more focal. Hence, it is recommended that when patients experience unilateral complaints each side should be examined separately. In case of bilateral complaints, mean values of the right and left side should be averaged only in case of no significant side differences, which should also be reported.

Furthermore the position in which patients were examined differed among studies. Some evaluations took place in upright position, others with the patients in a prone or supine position. When in a supine position, which is often the case when MRI is applied, muscles might experience small amounts of flattening because of the body weight. In an upright position, the human body needs a minimum of muscular activity to stabilize the spine, which might affect the lumbar muscle size. Thus when comparing results from an upright position with results from a prone or supine position, the differ-

ence in position could lead to bias.

The different applied techniques (USI, CT, and MRI) to investigate CSA and fat infiltration in this review might also have an influence upon the conclusions which were made. Like Mengiardi et al (10) put forward, magnetic resonance spectroscopy could reveal increased metabolic fat content, whereas conventional MRI using a semi quantitative visual grading system could not reveal these differences. CT scans, on the other hand, have a poor ability to differentiate soft tissue types and therefore might not be favorable to investigate muscle characteristics (8) or the applied MRI-sequence might not have been sensitive enough for fat evaluation in lumbar muscles (40). Besides these issues, most applied techniques for calculating fat content rely on qualitative visual analysis which is liable to interpretation and image windowing. Other more recent techniques such as opposed-phase magnetic resonance (26), Dixon (41,42), and proto magnetic resonance spectroscopy (10) are able to quantify fat fraction in tissues and are less sensitive for detection bias. Also blinding of the assessor for participant status is key to avoid the assessor of being prejudiced and influential for the results. However, not all studies took this methodological issue into account.

A last limitation can be found in the designs of the included studies. A cross-sectional design, restrains us from drawing definite conclusions regarding temporal patterns and causality between structural characteristics and LBP. We are not aware of prospective studies investigating structural muscle changes in non-symptomatic LBP patients, although these studies are warranted to gain more insight into the etiology of LBP and the related muscle structure alterations.

CONCLUSION

This systematic review provided evidence for the

presence of macroscopic changes in lumbar muscle structures of CLBP. There is moderate evidence for atrophy of the multifidus muscle in CLBP patients, whereas atrophy of the paraspinal and erector spinae muscles in CLBP is less clear. Especially a loss of muscle size is seen in the lower lumbar levels, but not in the more cranially lumbar levels. An increase in fat infiltration in CLBP, on the other hand, seems more likely to be due to age or by disuse of lumbar muscles, rather than to LBP itself. Thus far, microscopic changes do not seem to affect the lumbar muscles of CLBP, as patients have similar fiber characteristics as healthy people. No clear signs of macro- or microstructural changes of the lumbar musculature were established in RLBP and ALBP, but more research is warranted to confirm these conclusions.

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Author contributions

This research question was constructed by all authors. Mrs. Dorien Goubert conducted the search strategy for the literature search, ensured the selection for relevant articles, and wrote the first draft of the manuscript. The assessment for methodological quality was done both by Mrs. Dorien Goubert and Mrs. Jessica Van Oosterwijck. Mrs. Jessica van Oosterwijck, Mrs. Mira Meeus, and Mr. Lieven Danneels provided revision and final approval of the manuscript.

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