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Factors Associated With the Ultrasound Characteristics of the Lumbar Multifidus: A Systematic Review Peer-reviewed author version

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- 2 systematic review.
- 3
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- 22 Abstract
- 23 *Objective*
- 24 The first aim of this review was to investigate the association between age, sex, height,
- 25 weight, physical activity level, posture, lumbar level and body side, and structural
- 26 characteristics (cross-sectional area (CSA), thickness, linear dimensions and echo intensity)
- 27 of the lumbar multifidus (LM) measured by ultrasound (US). Secondly, differences between
- healthy subjects and patients with chronic low back pain (CLBP) were investigated.
- 29 *Type*
- 30 Systematic review.
- 31 Literature Survey
- 32 Pubmed, Embase and Web of Science were searched until September 2018.
- 33 Methodology
- 34 Studies were included if (a) full text was available in English, Dutch or French, (b) subjects
- 35 were aged over 18 years and were asymptomatic or had nonspecific CLBP and (c) the
- 36 relation between structural characteristics of the LM, measured by US, and at least one of
- 37 the above-mentioned factors was described, and/or a comparison between a CLBP and
- 38 control group was made. Data was extracted independently by two reviewers. Quality of
- 39 studies was assessed using an adapted version of the Downs and Black checklist.
- 40 Synthesis
- 41 Twenty-seven studies were included. Thickness and CSA of the LM do not correlate with age.
- 42 Males have a larger LM size than females. Thickness and CSA of left and right LM are highly
- 43 correlated in healthy subjects. More significant side-to-side differences are present in
- 44 subjects with CLBP than in those without. Muscle size increases from proximal to caudal
- 45 lumbar levels. The presence of CLBP is associated with muscle size and function.

46	Concl	usions

47	The association between the factors age, sex, height, weight, physical activity level, posture,
48	lumbar level, body side, and presence of CLBP, and the US characteristics of the LM is
49	discussed. These factors should be taken into account in future research on structural
50	muscle characteristics, or for example when correlating with functional behavior or
51	investigating the effect of a targeted intervention.
52	Level of evidence
53	I
54	Key words: Low back pain, multifidus, paraspinal muscles, ultrasound
55	
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57	

58 Introduction

59 Low back pain (LBP) is the main contributor to disability worldwide, with important personal, professional and socioeconomic implications.^{1–3} In up to 85% of patients with LBP, pain 60 cannot be attributed to a specific cause and is considered to be nonspecific.^{4,5} Macintosh et 61 al. previously suggested a role for the lumbar multifidus (LM) in the etiology of LBP.^{6,7} The 62 LM is the largest and most medial of the lumbar back muscles, consisting of a repeating 63 series of fascicles originating from the laminae and spinous processes of the lumbar 64 65 vertebrae with a consistent pattern of caudal insertions.⁷ Functional impairments, such as decreased proprioception,^{8–10} and decreased strength and endurance of the lumbar 66 musculature,^{11–13} have been identified in people with LBP. Moreover, the relation between 67 these functional impairments and the development of LBP was demonstrated in several 68 studies.^{10,14,15} However, the role of structural alterations of the LM in LBP, such as changes in 69 70 thickness and cross-sectional area (CSA), is less understood. A recent review indicated a negative relationship between CSA of the LM and LBP,¹⁶ while other reviews showed only a 71 72 weak or even no association between lumbar muscle characteristics (morphometry, fat infiltration) and clinical outcomes in LBP.^{17–19} By extending our knowledge regarding 73 74 structural characteristics of the lumbar muscles, we might gain more insight into the 75 underlying mechanisms of LBP.

76

Previous studies indicated that ultrasonography (US) is a reliable and valid technique for the evaluation of CSA, thickness and linear dimensions (depth and length) of the LM.^{20,21} Echo intensity (EI) refers to the ability to reflect or transmit ultrasound waves in the context of surrounding tissue, whereby the structure can be characterized as hyper-echoic or hypoechoic, representing lighter or darker pixels on the screen, respectively.²² Echo intensity is

considered to be an indicator of the ratio of adipose and connective tissue to muscle,^{23–25} as 82 a higher EI is highly correlated with a higher level of adipose tissue using a muscle biopsy²⁴ as 83 well as with a higher intramuscular fat content using MRI.²⁵ Ultrasonography is noninvasive, 84 radiation free, widely available and inexpensive. Moreover, real time imaging allows a 85 dynamic evaluation which is a unique advantage compared to other imaging techniques. 86 87 Because of these features, the use of US in musculoskeletal conditions has significantly increased over the last years.^{26,27} To optimize the applicability of US for the evaluation of LM 88 89 structural characteristics, it is essential to understand the factors associated with these measurements. Sex differences may play a role, as global skeletal muscle mass is greater in 90 men than women.²⁸ Independent of sex, global skeletal muscle mass decreases with age, 91 especially above the age of 50 years and with an increasing rate above 65 years.^{29,30} 92 Weight^{31,32} and physical activity^{33,34} have an influence on abdominal muscle size; hence, an 93 impact on lumbar muscle size might be presumed. The influence of posture should also be 94 taken into account. Only investigating lumbar muscle characteristics in a recumbent position 95 might not be sufficient to distinguish between subjects with and without LBP.^{35,36} 96 Additionally, cadaver studies by Macintosh et al.⁷ and Amonoo-Kuofi et al.³⁷ suggest a 97 98 lumbar muscle size difference related to spinal level. Lastly, symmetry of lumbar muscle structure might be of relevance. For example, localized muscle atrophy has been 99 demonstrated in the presence of disc or nerve root injury,^{38,39} as well as in acute/subacute 100 unilateral LBP.40 101

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Therefore, the first objective of this study was to provide a literature overview of the
association between age, sex, height, weight, physical activity level, posture, lumbar level,

- and body side, and the intrinsic structural characteristics (CSA, thickness, linear dimensions
- and EI) of the LM measured by US. Secondly, differences between healthy subjects and
- 107 patients with chronic low back pain (CLBP) were summarized.

110 Methods

The review was performed following the Preferred Reporting Items for Systematic Reviews
 and Meta-Analyses (PRISMA) guidelines.⁴¹ The protocol was registered in the PROSPERO
 database (CRD42018083743,

http://www.crd.york.ac.uk/PROSPERO/display record.php?ID=CRD42018083743). Studies 114 were identified by searching the electronic databases Pubmed, Embase and Web of Science 115 and scanning reference lists of the relevant articles. No restrictions were imposed regarding 116 117 publication dates. The last search was applied on September, 18 2018. The following search terms were used for all databases: ("spine muscle" or "multifidus" or "lumbar muscle" or 118 "paraspinal muscle" or "paravertebral muscle") AND (ultrasound or ultrasonography or 119 120 echography). When full text was not available, attempts to acquire it were made by 121 contacting the authors. Table 1 shows the applied in- and exclusion criteria.

122

After removal of duplicates, assessment for eligibility was performed independently by two 123 124 reviewers (S.R. and E.R). Disagreements were resolved by consensus or by consulting a third 125 reviewer (A.D.G.). Using a basic spreadsheet, data was extracted by one reviewer (S.R.) and 126 checked by a second reviewer (E.R.): author, publication year, population characteristics (number of subjects, age, sex, anthropometric parameters and LBP-related characteristics), 127 measurement position, frequency and shape of the US probe, assessed lumbar level, 128 129 structural characteristics of the LM assessed by US (thickness (mm), CSA (cm²), EI (grey level intensity on an arbitrary units scale)), and outcome measures (measure of association or 130 comparison between control and CLBP group). Risk of bias was assessed by two reviewers 131 (S.R. and E.R.) by using an adapted version of the Downs and Black checklist (Appendix).⁴² 132

133 This tool was identified as one of the two most useful instruments for the assessment of non-randomized studies⁴³ and is recommended by the Cochrane collaboration for this 134 purpose.⁴⁴ The original tool was adapted for non-interventional studies, and has been used 135 before.^{45,46} Related questions (items 4, 8, 9, 13, 14, 17, 19, 23, 24 and 26) were omitted. 136 137 Case-series studies and case studies were not assessed on items related to a control group 138 (items 21 and 22). We maintained item 15 related to blinding of the observer measuring the 139 outcomes, as this was possible when different subject groups were investigated. Item 27 140 concerning the power of the study was adapted to: "Was a sample size calculation done? (yes = 1, no = 0)". Consequently, the number of questions varied between study designs and 141 the results on risk of bias were presented as a percentage score (Table 2). Inter-rater 142 agreement for risk of bias assessment was measured by calculating the Kappa statistic using 143 144 IBM SPSS Statistics Version 25. The following classification was used to interpret this agreement: poor (0.00), slight (0.01-0.20), fair (0.21-0.40), moderate (0.41-0.60), 145 substantial (0.61–0.80) and almost perfect (0.81–1.00).⁴⁷ No articles were excluded based on 146 bias assessment. Interpretation of the strength of reported correlations was done following 147 the rule of thumb of Hinkle et al.: little if any (0.00-0.30), low (0.30-0.50), moderate (0.5-148 0.70), high (0.70-0.90) and very high (0.90-1.00).48 149

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Results

153	See Figure 1 for a flowchart of study selection. 1666 articles were identified through
154	database searching, and no additional articles were found from the reference list search. A
155	total of 27 articles were included. Results of assessment of risk of bias are shown in Table 2.
156	Total risk of bias scores ranged from 53 to 80% between studies. Scores from both reviewers
157	were equal in 94% of the cases (431/459). The agreement between both reviewers was
158	almost perfect (Kappa= 0.89; 95% confidence interval= 0.85 to 0.93, p< 0.0005). In Table 3
159	the extracted data and results of individual studies are provided.
160	
161	Age
162	Five studies included age in their analysis. ^{49–53} No significant association was found between
163	age and CSA of the LM at L4, 50 L5 50 nor at L2 to L5 49 in healthy subjects nor patients with
164	CLBP. Stokes et al. reported a smaller shape ratio, which is a ratio of linear measurements
165	(anteroposterior divided by lateral dimensions), at L5 in younger compared to older healthy
166	persons. ⁵⁰ No difference in symmetry was seen between age groups. ⁵⁰ For thickness at rest,
167	no association with age was reported for the LM at L4 in women without LBP. ^{51,52} Two
168	studies analyzed the relation between EI of the LM and age in healthy subjects, one showing
169	a moderate positive correlation, ⁵³ the other showing no significant association. ⁵²
170	
171	Sex
172	Associations with sex were investigated in eight studies. ^{49,50,53–58} Four studies found a
173	significantly larger CSA of the LM in males compared to females at L2, ^{49,57} L3, ^{49,57} L4 ^{49,50} and
174	L5 ^{50,58} in subjects with and without CLBP, although two of these studies could not confirm

these findings for certain lumbar levels.^{49,57} No significant difference in symmetry of CSA was

observed between sexes in an asymptomatic population⁵⁰ nor in patients with CLBP.⁴⁹ In 176 healthy subjects, Stokes et al. reported a smaller shape ratio in females compared to 177 males.⁵⁰ A larger muscle **thickness** in males compared to females was demonstrated in 178 healthy subjects at L4-5 at rest^{53,56} and during contraction⁵⁶, as well as in patients with CLBP 179 at L5 at rest.⁵⁴ Two studies did not show a sex effect on thickness change during contraction 180 of the LM at L2 to L5 in subjects with and without CLBP⁵⁷ or at L4-5 in healthy subjects.⁵⁶ Cai 181 et al. found a smaller thickness change in male runners with CLBP compared to healthy 182 subjects, but not in females.⁵⁵ Importantly, when taking into account anthropometric 183 parameters, the sex difference in CSA was no longer significant in the study of Stokes et al.⁵⁰ 184 but remained significant in two other studies on CSA⁵⁸ and thickness.⁵⁶ Yoshiko et al. 185 reported a lower EI of the LM in healthy males compared to females.⁵³ 186

187

188 Anthropometric parameters

In four studies, anthropometric parameters were analyzed in healthy subjects.^{50,58–60} Hides 189 et al. found positive correlations between CSA at L4 and weight, height and weight x 190 height.⁵⁹ In males, these correlations were stronger than in females.⁵⁹ A strong positive 191 correlation between CSA and weight was seen at L4 by Stokes et al., in females only.⁵⁰ A 192 193 moderate positive correlation was confirmed at L4 and L5 by Nuzzo et al. in an all-male population.⁶⁰ In contrast, Watson et al. found a moderate negative relationship between 194 percent body fat and CSA at L5.⁵⁸ Two studies did not find a relation between body mass 195 index (BMI) and CSA at L4^{50,59} and L5,⁵⁰ nor between height and CSA.⁵⁰ Nuzzo et al. 196 197 demonstrated a moderate positive correlation between weight and thickness at rest of the LM at L4 and L5.⁶⁰ 198

199

200 Physical activity level

Only two studies analyzed physical activity level.^{51,57} Wallwork et al. reported a positive 201 association between weekly physical activity level and CSA of the LM at L3, L4 and L5 (not at 202 L2), without any difference between subjects with or without CLBP.⁵⁷ No significant 203 association was found with muscle thickness at rest and during contraction.⁵⁷ In the elderly 204 205 (age 86.9 ± 6.2 years), a smaller thickness at rest of the LM at L4 was observed by Ikezoe et 206 al. in women who were dependent (chronically bedridden) compared to those able to perform activities of daily living independently.⁵¹ The LM was also thinner in the dependent 207 elderly group compared with young women, but no differences in muscle thickness were 208 seen between the young and independent elderly group.⁵¹ 209 210 Posture 211 Three studies investigated the influence of posture.^{61–63} Coldron et al. did not report a 212 significant difference in the **CSA** of the LM at L5 between prone and side lying in healthy 213 subjects.⁶² In healthy subjects, two studies observed an increase in CSA of the LM at L4 from 214 prone lying to upright standing and a gradual decrease in CSA from 25° to 45° forward 215 stooping.^{61,63} These differences in CSA were not significant at L5.⁶³ 216 217

218 Lumbar level

Four studies included lumbar level in their analysis.^{20,49,50,64} Three studies on healthy subjects observed a significant difference in **CSA** of the LM between lumbar levels ranging from L2 to S1, with greater CSA at caudal levels.^{20,49,50} Correlations between CSA at L4 and L5 were high and significant in healthy subjects in the study of Stokes et al.⁵⁰ In females, a smaller shape ratio was reported at L5 compared to L4, because of a larger lateral dimension of the LM at

L5.⁵⁰ Dar et al. found no significant difference in **thickness** at rest or thickness change during
 contraction between L4-5 and L5-S1 in healthy subjects.⁶⁴

226

227 Symmetry

Fifteen studies investigated the difference between left and right side of the 228 body.^{20,48,49,53,55–58,63-69} Several studies found a high correlation between left and right **CSA** of 229 the LM in healthy subjects at L5,^{58,65} L2 to L5,⁴⁹ S1⁶⁸ and L2 to S1,²⁰ and in patients with CLBP 230 at L5,⁶⁵ with side-to-side differences smaller than 5%. However, in two studies a larger 231 asymmetry in CSA was observed in healthy subjects at L4 and L5.^{50,67} No influence of sex, age 232 or vertebral level on symmetry of the CSA was reported by Stokes et al.⁵⁰ Side-to-side 233 234 differences larger than 10% were also seen by Hides et al. in subjects with unilateral CLBP at L4 and L5 but not at L2 and L3.⁴⁹ Side-to-side differences in patients with central or bilateral 235 pain were lower.⁴⁹ Smaller asymmetry was found in CSA than in shape.^{50,59} For **thickness** at 236 rest, side-to-side differences were reported to be around 5% in healthy subjects⁵⁶ and 237 around 10% in patients with CLBP.⁵⁴ There was no significant asymmetry in resting thickness 238 in subjects with unilateral CLBP in prone or standing at L4-5 and L5-S1,⁷⁰ nor in subjects with 239 and without CLBP at L4-5.⁶⁹ Dar et al. described a significant side-to-side difference in 240 thickness change during contraction at L5-S1, but not at L4-5, in a subgroup of healthy 241 subjects.⁶⁴ A small but significant asymmetry in thickness change was observed by Wallwork 242 et al. from L2 to L5 in subjects with and without CLBP.⁵⁷ This asymmetry was not confirmed 243 by Sweeney et al. in subjects with CLBP at L4-5 or L5-S1.⁷⁰ 244

245

246 Chronic low back pain

In fourteen studies, the influence of CLBP was analyzed.^{49,55,71–74,57,61,63,65–67,69,70} 247 Asymptomatic subjects had a larger CSA of the LM compared with subjects with CLBP at L4 248 and L5,^{49,57,61,63,72,73} although findings were not significant for all levels⁵⁷ or in all positions.⁶³ 249 In unilateral CLBP, a significant asymmetry in CSA was noted at L4 and L5,⁴⁹ as well as a 250 strong relation between pain scores and the ratio of the CSA of the unaffected and affected 251 side at L5.⁶⁶ However, Zhang et al. did not report a difference in CSA of the LM between 252 unaffected and affected sides,⁷³ nor was a difference in CSA confirmed between subjects 253 with and without CLBP at L2,⁴⁹ L3⁴⁹ or L5.⁶⁵ At L2, Wallwork et al. even observed a slightly 254 larger CSA in subjects with CLBP compared to healthy controls.⁵⁷ Lee et al. reported a 255 different change in CSA of the LM at L4 and L5 in different postures in patients with CLBP 256 257 compared to healthy controls.⁶³ The largest CSA was observed in upright standing in healthy subjects, while in patients with CLBP the maximal CSA occurred at 25° forward stooping.⁶³ 258 Yet, this group difference was not confirmed by Chan et al.⁶¹ In the study of Rostami et al., 259 the difference between contracted and resting CSA of the right LM at L4 was significantly 260 smaller in patients with CLBP compared to controls.⁷² Wallwork et al. confirmed this finding 261 at L5, but not at L2, L3 and L4.⁵⁷ Regarding thickness of the LM, four studies showed no 262 significant differences between subjects with and without CLBP at rest at L4,^{67,74} L4-5,^{68,69} 263 L5⁶⁷ or L5-S1⁷⁰, nor at L4-5 during maximal contraction lifting the head, upper trunk and 264 contralateral arm against static resistance.⁶⁹ Zhang et al. reported a smaller thickness at rest 265 and during contraction in subjects with CLBP compared with healthy controls.⁷³ A smaller 266 thickness change during contraction of the LM was found in subjects with CLBP compared 267 268 with healthy controls at L4⁷³ and L4-5.^{55,69,71} On the other hand, Sweeney et al. found a larger thickness change at L5-S1 (not at L4-5) in subjects with CLBP during a contralateral 269

- arm lift in standing, but not in prone position.⁷⁰ The **fat area** at L4 was higher in subjects with
- 271 CLBP in the study of Chan et al.⁶¹
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- 273

274 **Discussion**

The main objective of this systematic review was to provide an overview of the association of predefined factors with the intrinsic structural characteristics of the LM defined by US, in subjects with and without CLBP.

278

Ultrasound-assessed thickness and CSA of the LM did not correlate with age in subjects with 279 nor without CLBP.^{49–52} In terms of shape at L5, a more ovoid muscle in the anteroposterior 280 direction was associated with older age.⁵⁰ Prior studies using magnetic resonance imaging 281 (MRI) have reported inconsistent associations between LM size and age, probably due to 282 methodological differences in outcomes (CSA versus volume), regions of interests, and study 283 samples. Age-related muscle atrophy has been frequently demonstrated for upper and 284 lower limbs, ^{28,75,76} as well as for superficial abdominal muscles. ^{51,77} In deep trunk muscles 285 such as the LM or deep abdominal muscles, age-related atrophy is less obvious.^{51,78} This 286 might be explained by the fact that deep trunk muscles predominantly contain type I 287 fibers,^{79–81} in which less age-related atrophy occurs in comparison with type II muscle 288 fibers.^{82–84} Qualitative age-related differences such as increased fatty infiltration were 289 previously reported in several studies using MRI^{85,86} or computed tomography (CT).⁸⁷ By 290 291 contrast, opposite findings regarding the association between age and EI were reported in the current review.^{52,53} 292

293

Ultrasound-assessed thickness and CSA of the LM were found to be larger in males than
females.^{49,50,54,56–58} There may be a more ovoid LM muscle shape in females than males.^{50,59}
However, few studies took into account weight, percent body fat or BMI as covariates for
sex-related differences.^{50,56,58} Although none of the included studies could confirm a

relationship between CSA of the LM and BMI,^{50,59} there were moderate to strong positive 298 correlations with weight.^{50,59,60} By contrast, Watson et al. found a moderate negative 299 correlation between percent body fat and CSA of the LM at L5.⁵⁸ They hypothesized that a 300 sedentary lifestyle might lead to an increase in body fat deposition and muscle fat 301 infiltration, as well as disuse atrophy of the LM.⁵⁸ On MRI, Crawford et al. reported a higher 302 303 fat infiltration in paravertebral muscles including the LM in women compared to men, after controlling for BMI.⁸⁶ Correspondingly, in the current review, a higher EI was reported in 304 women than in men.⁵³ 305

306

Furthermore, the influence of physical activity level on weight and body fat should not be 307 308 overlooked. A direct relationship between physical activity level and CSA and thickness of the LM was reported in two studies, although both had a high risk of bias (Table 2).^{51,57} 309 Ikezoe et al. suggested that the muscle mass of the LM might be maintained by small muscle 310 contraction during daily physical activities, given the fact that independent elderly women 311 had a larger LM thickness compared to chronically bedridden women.⁵¹ This statement is 312 supported by Cholewicki et al. who previously documented electromyographically that only 313 314 1-3% of the maximum voluntary contraction of the LM is needed to maintain segmental stability around a neutral spine position.⁸⁸ On MRI, Hides et al. noted a decrease in CSA of 315 316 the LM after eight weeks of bed rest, most likely because of removal of normal axial gravitational loading as a stimulus for muscle activity.⁸⁹ Moreover, it is possible that specific 317 sport-related physical demands lead to hypertrophy of the LM as seen in elite athletes 318 319 (weightlifters⁹⁰ and rowers⁹¹) compared to normal healthy controls, even in the presence of 320 LBP. Important to note is that analyses were mostly based on self-reported physical activity,

which tends to overestimate the activity level. In addition, patients with LBP are even more likely to underestimate sedentary time.⁹²

324	Ultrasound measurement of the CSA of the LM can be performed in prone or side lying
325	position, as no significant difference between either position was demonstrated. ⁶² Two
326	studies investigated the CSA of the LM in four positions. ^{61,63} Even though the risk of bias was
327	high in both studies (Table 2), they both reported an increase in CSA of the LM in standing
328	compared to a prone lying position. ^{61,63} This increase in CSA might reflect the exerted force
329	of the LM to stabilize the lumbar region in standing position. ⁶³ The CSA of the LM decreased
330	in a stooped position compared to standing, ^{61,63} which might be explained by an eccentric
331	type of contraction in stooping.
332	
333	For lumbar level, several studies reported an increasing CSA of the LM caudally from L2 to
334	S1. ^{49,50,59} These findings are in line with the cadaver study of Amonoo-Kuofi in 1983,
335	documenting a larger LM at caudal levels. ³⁷ No difference in thickness change of the LM was
336	observed between L4-5 and L5-S1, ⁶⁴ but the risk of bias in this one study examining the
337	association between lumbar level and thickness change was high (Table 2).
338	
339	Correlation between left and right side CSA and thickness of the LM is high in healthy
340	
	subjects at L2 to S1.20,40,50,00,00 Side-to-side differences in shape of the LIVI were larger

might be a less sensitive parameter to investigate asymmetry. Most studies on healthy

subjects reported approximately 5% asymmetry in CSA and thickness of the LM.^{49,58,59,68}

Based on previous studies, an asymmetry in CSA of > 10% was suggested as potentially

abnormal.⁴⁹ But this criterion of 10% asymmetry in CSA might not be applicable for all
populations, as asymmetry up to 40% has been reported in healthy subjects, based on
US^{59,67} and MRI images.⁹³ Moreover, asymmetry may be normal in some groups, for example
because of predominant unilateral use of muscles in sports.⁵⁹ Other factors (e.g.
handedness, physical activity) influencing asymmetry were investigated, but results were
inconsistent.⁹⁴ On the contrary, some studies indicate that LM asymmetry may be related to
occurrence of injuries in cricket⁹⁵ and football.⁹⁶

352

Subjects with CLBP have a smaller CSA of the LM on US, as demonstrated in several studies 353 included in this review, ^{49,57,61,63,72} and confirmed in studies using CT and MRI.^{97,98} However, 354 355 this difference between subjects with and without CLBP might not be present at the upper lumbar levels^{49,57} or in specific populations such as elite athletes.⁶⁵ In subjects with CLBP, 356 asymmetry in CSA of the LM seems to be more pronounced compared to healthy 357 subjects.^{49,63} Asymmetry of the LM was also seen on MRI in patients with chronic unilateral 358 LBP.⁹⁹ On the other hand, Fortin et al. found no association between LBP history and LM 359 asymmetry on MRI.⁹⁴ Muscle atrophy in subjects with CLBP might be the result of inhibition 360 361 of muscle activity because of perceived pain or because of the incapacity of a muscle or ligament to recover to its initial resting length due to long-lasting strain.⁶¹ But curiously, no 362 363 significant differences in LM thickness in rest were found between subjects with and without CLBP.^{67,69,70,74} Thus, thickness measures of the LM might be insufficient to detect size 364 differences as they do not account for medial to lateral expansion. A larger fat area of the 365 366 LM was reported in subjects with CLBP compared to asymptomatic controls, however, only the L4 level was investigated.⁶¹ This implicates a larger proportion of noncontractile tissue in 367

the LM and possibly a reduction in muscle quality which could contribute to differences inmuscle function.

370

It is suggested that subjects with LBP have altered neuromuscular control resulting in 371 different muscle activation.^{9,100,101} Several studies in this review confirmed lower activation 372 ratios in subjects with CLBP.^{55,57,69,71,72} On the contrary, Sweeney at al. reported a larger 373 374 thickness change in subjects with CLBP, however, only during a contralateral arm lift in standing.⁷⁰ Moreover, Lee et al. hypothesized that the LM is not able to respond to the 375 postural demand in subjects with CLBP, particularly in upright positions, as they found an 376 altered LM CSA in standing and stooping positions in subjects with CLBP compared to those 377 378 without.⁶³ However, this group difference in change in CSA of the LM in different positions was not confirmed in the study of Chan et al.⁶¹ 379

380

381 Methodological considerations and implications for future research

382 This systematic review has several limitations. No inter-rater agreement was calculated for data extraction. Because of the heterogeneity of the included studies, the results were 383 384 summarized qualitatively. Across the included studies, several factors increasing the risk of bias were present (Table 2). First, study populations were sometimes small, and clear 385 386 definitions of the patient and control groups were frequently not available. Definition and 387 aspects (duration, intensity, location) of LBP differed between studies or were not 388 mentioned. Information about participant recruitment was mostly insufficient, making it 389 more difficult to compare results. In most studies the investigator was not blinded for LBP 390 status of the study participant, possibly increasing the risk of bias. Moreover, potential 391 confounding factors such as age, BMI or activity level were often not taken into account. Sex 392 differences should be related to weight and other anthropometric parameters for a correct interpretation of findings. More research is needed to determine the association between 393 anthropometric parameters and the structural characteristics of the LM, especially in 394 395 populations with a higher BMI. The role of physical activity level in the structure and 396 function of the LM is still unclear and should be further investigated using objective 397 measurements of physical activity. Furthermore, US protocols varied between studies, with 398 some investigating left and right sides separately, and some pooling the results for both 399 sides. However, side-to-side differences of the LM may be present in case of unilateral LBP,^{40,99} which implies both sides should be examined separately. Several studies 400 investigated only one lumbar level, which limits interpretation of the findings. As 401 characteristics of the LM differ between lumbar levels, investigating more than one level is 402 403 recommended to be able to understand the differences related to LBP. Most studies analyze 404 CSA or thickness to assess muscle size or symmetry, but do not determine EI as a reflection 405 of fatty infiltration. However, greater infiltration with fatty or fibrous tissue can influence 406 muscle quality without altering muscle size. Further investigating the change of EI in subjects 407 with CLBP versus healthy subjects can provide more insight in the structural muscle 408 alterations in CLBP.

409

The clinical relevance of LM shape has yet to be explored. Hypertrophy is only possible in the lateral or posterior direction because medial and anterior borders are defined by bony structures. Larger muscles thus tend to be more triangular, which cannot be deduced from the shape ratio. In patients with acute LBP, a rounder shape of the LM was seen at the affected level.⁴⁰ This might be caused by a change in muscle tone or presence of a muscle spasm.^{40,50}

Conclusion

417	In this systematic review, several factors associated with the US characteristics of the LM are
418	identified. A relation between age and LM size is not confirmed. Males have a larger
419	thickness and CSA of the LM than females. The correlation between the left and right LM
420	size is high in healthy subjects. More significant side-to-side differences are present in
421	subjects with CLBP than in those without. An increase in LM size is seen from proximal to
422	caudal lumbar levels. The presence of CLBP is associated with muscle size and function. The
423	role of physical activity and body weight in characteristics of the LM is unclear. Muscle El
424	was not sufficiently investigated to reach any conclusions. The above-mentioned factors
425	should be taken into account in future research on structural characteristics of the lumbar
426	muscles, the relation with functional behavior or the effect of a targeted intervention.
427	
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429	This research did not receive any specific grant. All authors declare no conflict of interest.
430	

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751 **Table 1. Inclusion and exclusion criteria.**

752

	Inclusion	Exclusion
Population	- Humans > 18 years old	- Animals
	- Patients with nonspecific CLBP	- Patients with other disorders
	(duration > 3 months) or healthy,	(neurological, deformation, etc.)
	pain-free subjects	or CLBP due to a specific cause
Instrument	- Ultrasonography of the lumbar	- Only non-ultrasound imaging
and site	multifidus	method
		- Only non-multifidus muscles
Outcome	Structural characteristics of the	- Effect of intervention (treatment
	lumbar multifidus (CSA, thickness,	including surgery, application of
	anteroposterior/lateral dimensions,	load or resistance) [‡]
	echo intensity)	- Relation with prognostic factors
	Association with one of the	
	influencing factors (age, sex,	
	anthropometric parameters,	
	physical activity level, posture,	
	lumbar level, body side)	
	AND/OR	
	Comparison between CLBP and	
	control group	
Type of report	- Clinical report	- Systematic review, meta-analysis,
	- Full-text	letter to editor
	- In English, Dutch or French †	- No full text available, abstract only
		- Other languages
	1	1

753

754 CLBP: chronic low back pain, CSA: cross-sectional area

⁷⁵⁵ [†] No foreign language articles were included in the final analysis.

⁷⁵⁶ [‡] Only baseline data of intervention studies was included, if a measure of association or

757 comparison between CLBP and control group was present at this baseline assessment.

ltem	Aboufazeli ⁷¹	Berglund ⁵⁴	Cai ⁵⁵	Chan ⁶¹	Coldron ⁶²	Dar ⁶⁴	Djordjevic ⁶⁹	Hides (1992) ⁵⁹	Hides (1995) ²⁰	Hides (2008) ⁴⁹	Huang ⁶⁶	lkezoe ⁵¹	Lee ⁶³	Masaki (2015) ⁵²	Masaki (2017) ⁷⁴	Nuzzo (2013) ⁶⁰	Nuzzo (2014) ⁶⁷	Pressler ⁶⁸	Rostami ⁷²	Scott ⁶⁵	Stokes ⁵⁰	Sweeney ⁷⁰	Teyhen ⁵⁶	Wallwork ⁵⁷	Watson ⁵⁸	Yoshiko ⁵³	Zhang ⁷³
1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
2	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
3	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1
5	2	2	2	2	0	2	2	2	1	1	2	2	1	2	2	2	2	2	2	2	2	1	2	2	2	2	2
6	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
7	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
10	1	1	1	1	1	1	1	0	0	1	0	0	1	0	1	0	0	0	1	1	1	1	1	0	0	0	1
11	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
12	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0
15	0	0	0	0	NA	0	0	NA	NA	0	0	0	0	NA	0	NA	NA	NA	1	0	NA	1	NA	1	NA	NA	0
16	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
18	1	1	0	0	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1	1
20	1	1	1	1	1	1	1	1	1	1	1	1	0	1	1	1	1	1	1	1	1	1	1	1	1	1	1
21	0	1	0	1	NA	0	1	NA	NA	0	NA	0	1	NA	0	NA	NA	NA	0	0	NA	0	NA	0	NA	NA	0
22	0	1	0	0	NA	0	1	NA	NA	0	NA	0	0	NA	0	NA	NA	NA	0	0	NA	0	NA	0	NA	NA	0
25	1	0	1	0	0	0	1	0	0	1	0	0	0	0	1	0	0	0	1	1	1	1	1	1	1	1	1
27	1	0	1	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0
total	67	78	67	67	53	56	78	67	60	61	63	56	56	67	67	67	67	67	72	72	80	67	80	61	73	73	67
score (%)																											

Table 2. Risk of bias in the included studies (adapted version of the Downs and Black checklist)

761 NA: not applicable

765 Table 3. Results of the included studies

	Patient character	ristics (mean±SD)		Structural			
Author (year)	CLBP group	Control group	Position + US probe	characteristics of the LM + lumbar level	Associated factors	Measure of association (mean±SD)	CLBP vs. control group (mean±SD)
Aboufazeli et al. ⁷¹ (2018)	30 F – 34.6±6.2y BMI: 23.4±3.2kg/m ² VAS ≥ 5 LBP duration > 3 months	30 F – 36.7±6.7y BMI: 23.6±3.3kg/m ²	- prone - 7.5MHz convex probe	 thickness at rest and contraction (CAL+W) L4/5 at most painful side or averaged L-R 			smaller thickness change in CLBP vs. control group (3.21±0.09mm to 4.47±0.40mm vs. 2.88±0.37mm to 3.95±0.40mm; p=0.002)
Berglund et al. ⁵⁴ (2017)	65 CLBP 28 M - 45.6±9.2y BMI: 25.1±3.3kg/m ² VAS: 38.8±22.8 37 F - 40.6±10.1y BMI: 25.3±3.6kg/m ² VAS: 49.6±26.8 LBP duration > 3 months		- prone - 10-12 MHz linear probe	- thickness - L5 bilateral	- sex - side	 larger thickness in M vs. F on large side (2.78±0.43cm vs. 2.54±0.45cm; p=0.03) and on small side (2.52±0.45cm vs. 2.31±0.41cm; p=0.06) significant side difference in M (9.3%) and F (8.8%) (p<0.001) 	NA
Cai et al. ⁵⁵ (2015)	18 CLBP <i>9 M</i> – 29.6±7.3y BMI: 21.5±2.4kg/m ² NPS of last week: 2.3±1.0 <i>9 F</i> – 26.0±2.6y BMI: 22.0±2.1kg/m ² NPS of last week: 2.4±0.9 LBP duration > 3/ < 36 months recreational	18 healthy <i>9 M</i> – 25.6±4.2y BMI: 21.7±2.0kg/m ² <i>9 F</i> – 23.6±2.5y BMI: 21.1±2.1kg/m ²	prone	- thickness at rest and contraction (CAL+W) - L4/5 bilateral	sex	no significant difference in thickness change between M and F (p=0.092)	smaller thickness change in CLBP vs. control group in M only (0.33±0.11cm vs. 0.59±0.19cm; p<0.05)
	runners	runners					

	Patient characteristics (mean±SD)			Structural			
Author			Position +	characteristics	Associated	Measure of association	CLBP vs. control group
(year)	CLBP group	Control group	US probe	of the LM +	factors	(mean±SD)	(mean±SD)
				lumbar level			
Chan et	12 M – 36.6±2.9y	12 M – 25.2±1.1y	- prone/	- CSA and fat	posture	 increase in CSA from prone to 	- smaller CSA in all positions in CLBP vs.
al. ⁶¹ (2012)	BMI: 22.0±0.5kg/m ²	BMI: 21.8±0.8kg/m ²	standing/	area		standing (in control group at L side:	control group (L side: 5.01±0.07cm ² to
	ODI: 22±3%		forward	- L4 bilateral		6.16±0.09cm ² to 7.16±0.10cm ² ;	6.58±0.20cm ² vs. 5.51±0.13cm ² to
	LBP duration: not		stooping			p<0.025), decrease from standing to	7.16±0.10cm ² and R side:
	reported		25°+ 45°			25° stooping (in control group at L	4.81±0.13cm ² to 6.61±0.21cm ² vs.
			- 5-12MHz			side: 7.16±0.10cm ² to 5.51±0.13cm ² ;	5.55±0.13cm ² to 7.06±0.08cm ² ;
			probe			p<0.025), no difference between 25°	p<0.001)
						and 45° stooping (in control group at	- larger fat area in all positions in CLBP
						L side: 5.51±0.13cm ² to	vs. control group (L side: 0.90±0.09cm ²
						5.71±0.36cm²; p=1)	to 1.08±0.23cm ² vs. 0.56±0.10cm ² to
						 no association between posture and 	0.71±0.10cm ² and R side:
						fat area (p=0.978)	0.88±0.13cm ² to 1.13±0.23cm ² vs.
							0.60±0.09cm ² to 0.73±0.11cm ² ;
							p<0.001)
Coldron et		20 F - 19-45y	- prone/	- CSA	posture	- high correlation between prone and	NA
al. ⁶² (2003)		BMI: not reported	left side	- L5 bilateral		side lying (L side: 5.54±1.02cm ² vs.	
			lying			5.39±1.02cm ² ; r=0.90 and R side:	
			- 5MHz			5.48±1.22cm ² vs. 5.44±1.22cm ² ;	
			curvilinear			r=0.91; p<0.001)	
			probe			 no significant difference in CSA 	
						between prone and side lying (L side:	
						p=0.16 and R side: p=0.77)	
Dar et al. ⁶⁴		28 healthy	- prone	 thickness at 	- level	- larger thickness change at L5/S1 for	NA
(2016)		17 M	- 6MHz	rest and	- side	L vs. R side (32.07±6.63% vs.	
		11 F	convex	contraction		26.78±7.95%, p=0.02), only in	
		intervention group:	probe	(contralateral		intervention group (baseline data)	
		32.2±6.4y		leg lift)		- no significant side difference in	
		BMI: 22.4±0.8kg/m ²		- L4/5 + L5/S1		thickness at rest and contraction at	
				bilateral		both levels nor in thickness change at	
		control group:				L4/5 (p>0.05)	
		31 9+2 9v				- no significant difference in	
		$BM1 \cdot 21 + 2 A ka/m^2$				thickness or thickness change	
	l	DIVIT. 24.112.4Kg/11	I	I	1	CHICKHESS OF CHICKHESS CHANGE	l

	Patient character		Structural				
Author (year)	CLBP group	Control group	Position + US probe	characteristics of the LM + lumbar level	Associated factors	Measure of association (mean±SD)	CLBP vs. control group (mean±SD)
						between L4/5 and L5/S1 on same side (p>0.05)	
Djordjevic et al. ⁶⁹ (2015)	36 CLBP <i>18 M</i> <i>18 F</i> 53.2±8.1y BMI: 27.4±4.6kg/m ² ODI: 28.8±11.3% VAS in last 24h: 5.3±2.7 LBP duration: 18.2±3.8 weeks	37 healthy 15 M 22 F 52.6±9.5y BMI: 26.9±5.5kg/m ²	- prone - 3-6MHz curvilinear probe	- thickness in rest and contraction (CAL +resistance) - L4/5 bilateral	side	- significant effect of side at rest and contraction due to significant difference between rest and contraction in both groups on both sides ($F_{3,108}$ = 302.15; p<0.0001) - no significant effect of side or interaction group x side for relative thickness change ($F_{1,142}$ = 0.34; p=0.5608)	 no significant difference for thickness at rest and maximal contraction between CLBP and control group (F_{1,36} = 0.1635; p=0.688) smaller relative thickness change in CLBP vs. control group (0.3±0.2 vs. 0.4±0.2; F_{1,142} = 36.01; p<0.0001)
Hides et al. ⁵⁹ (1992)		48 healthy 21 M 27 F 18-35y BMI in M: 22.3±2.7kg/m ² ; in F: 21.4±2.7kg/m ²	- prone - 5MHz convex probe	- CSA, AP and lateral dimensions - L4 bilateral	- anthrop. factors - side	 no association between CSA and BMI (p>0.1) in M: positive correlations between CSA and weight (r=0.78; p<0.001), CSA and height (r=0.63; p<0.01), CSA and weight x height (r=0.79; p<0.01) in F: positive correlations between CSA and weight (r=0.60; p<0.05), CSA and height (r=0.54; p<0.05), CSA and weight x height (r=0.65; p<0.05) no significant side difference for CSA (p>0.1), shape ratio (p>0.1) AP and lateral dimensions (p>0.1) high correlation between CSA and linear dimensions (in M: r=0.98; p<0.001 and in F: r=0.93; p<0.01) 	NA
Hides et al. ²⁰ (1995)		10 F - 21-31y (mean 25.5y) BMI: not reported	- prone - 7.5MHz linear probe	- CSA - L2 -> S1 bilateral	- level - side	 no significant difference in CSA between L and R at any level (F_{1,275}=0.01; p>0.05) significant difference in CSA between each level (L2: 1.95±0.63cm², L3: 3.18±0.92cm², L4: 	NA

	Patient characte		Structural				
Author (year)	CLBP group	Control group	Position + US probe	characteristics of the LM + lumbar level	Associated factors	Measure of association (mean±SD)	CLBP vs. control group (mean±SD)
						$\begin{array}{l} 4.74{\pm}1.32 cm^2, \text{L5: } 7.14{\pm}0.66 cm^2, \text{S1:} \\ 6.50{\pm}0.81 cm^2; \text{F}_{4.275} = 544.81; \\ \text{p<}0.0001) \end{array}$	
Hides et al. ⁴⁹ (2008)	42 CLBP 21 M 21 F 46.8±13.2y BMI: not reported RMQ: 7.0±5.6 VAS: 4.4±2.7 LBP duration: 62.2±90.6 months	40 healthy 27 M 13 F 28.4±5.7y BMI: not reported	- prone - 5MHz convex probe	- CSA - L2 -> L5 bilateral	- age - sex - level - side	 no association between age and CSA (p>0.05) or asymmetry in CSA (p>0.1) larger CSA at L2->L4 in M vs. F (L2: 2.78±1.13cm² vs. 2.01±1.37cm², L3: 3.85±1.36cm² vs. 3.02±1.40cm², L4: 4.79±1.70cm² vs. 3.80±1.74cm²; p=0.001), not significant at L5 (p=0.22) no association between sex and asymmetry (p>0.1) <i>In control group:</i> increase in CSA to caudal levels 	 - smaller CSA in CLBP vs. control group at L4 (4.07±1.88cm² vs. 5.42±1.88cm²; p=0.001) and L5 (3.78±1.73cm² vs. 6.48±1.72cm²; p=0.001); not at L2 and L3 - more asymmetry in unilateral CLBP vs. bilateral CLBP or control group at L4 (11.8±19.1% vs. 5.1±12.2% vs. 3.4±12.0%; p=0.004) and L5 (17.5±24.2% vs. 10.5±15.5% vs; 1.9±15.2%; p=0.016), not at L2 and L3
Huang et al. ⁶⁶ (2014)	24 CLBP (unilateral) 10 M 14 F 23.8±5.2y H: 168.8±8.6cm W: 62.6±16.4kg VAS: 2.2±1.2 LBP duration > 6 months		- supine - 7.5MHz linear probe	- CSA - L5 bilateral	side	 positive correlation between VAS and ratio of CSA between unaffected and affected sides (r=0.72; p<0.01) ratio un-/affected side: 1.16±0.1 CSA of unaffected side: 8.79±2.1cm² vs. affected side: 7.61±1.96cm² 	NA
lkezoe et al. ⁵¹ (2012)		74 healthy - <i>33 young F</i> – 20.0±0.8y BMI: 22.1±2.3kg/m ² - <i>41 older F</i>	- prone - 5-10MHz probe	- thickness - L4 right	- age - activity level	 no significant difference between independent elderly vs. young F (p>0.05) smaller thickness in dependent elderly vs. young F (22.8±5.44mm vs. 26.7±7.62mm; p<0.01) 	NA

	Patient characteristics (mean±SD)			Structural			
Author (year)	CLBP group	Control group	Position + US probe	characteristics of the LM + lumbar level	Associated factors	Measure of association (mean±SD)	CLBP vs. control group (mean±SD)
		28 independent: 85.7±5.5y BMI: 20.5±3.2kg/m ² 13 dependent: 87.8±6.3y BMI: 16.6±2.1kg/m ²				 smaller thickness in dependent elderly vs. independent elderly F (22.8±5.44mm vs. 23.2±7.49mm; p<0.05) 	
Lee et al. ⁶³ (2006)	16 M - 34-47y (mean 39.9y) BMI: not reported LBP duration > 1y	19 M - 35-47y (mean 41.7y) BMI: not reported	- prone/ standing/ 25°-/45° stooping - 5MHz convex probe	- CSA - L4 + L5 bilateral	posture	In control group: - increase in CSA from prone to standing, decrease from 25° to 45° stooping at L4 - L4 L side: larger CSA in standing vs. 45° stooping (8.92±1.94cm ² vs. 7.44±1.17cm ² ; p=0.032) - L4 R side: larger CSA in standing vs. prone (9.19±1.76cm ² vs. 7.68±1.29cm ² ; p=0.019), standing vs. 25° stooping (9.19±1.76cm ² vs. 7.84±1.66cm ² ; p=0.043) and standing vs. 45° stooping (9.19±1.76cm ² vs. 7.11±1.45cm ² ; p=0.001) (not significant at L5) In CLBP group: - increase in CSA from prone to standing to 25° stooping, decrease in 45° stooping - L4 R side: larger CSA in 25° stooping vs. prone (8.50±1.17cm ² vs. 7.20±0.94cm ² ; p=0.006) and 25° vs. 45° stooping (8.50±1.17cm ² vs. 7.28±1.17cm ² ; p=0.011)	- smaller CSA at L4 in standing in CLBP vs. control group (L side: 7.55±1.45cm ² vs. 8.92±1.94cm ² ; p=0.02 and R side: 8.10±0.97cm ² vs. 9.19±1.76cm ² ; p=0.03) (not significant at L5 or in other positions; p>0.05)
Masaki et al. ⁵² (2015)		36 F – 72.4±8.0y H: 150.2±4.5cm W: 48.8±7.7kg	- prone	- thickness and El - L4 bilateral	age	-no significant association between age and thickness (r=-0.02; p>0.05) or El (r=-0.21; p>0.05)	NA

	Patient characte	eristics (mean±SD)		Structural		sisted Measure of acception	
Author (year)	CLBP group	Control group	Position + US probe	characteristics of the LM + lumbar level	Associated factors	Measure of association (mean±SD)	CLBP vs. control group (mean±SD)
			- 8MHz linear probe				
Masaki et al. ⁷⁴ (2017)	9 CLBP 1 M 8 F 44.7±13.0y H: 157.4±6.6cm W: 52.1±9.4kg ODI: 19.6±7.8% NRS in static situations: 5.0±1.4 NRS in dynamic situations: 5.0±1.7 LBP duration: 98.0±73.1 months	23 healthy <i>8 M</i> <i>15 F</i> 34.7±10.2y H: 164.1±7.5cm W: 56.9±8.9kg	- prone - linear probe	- thickness - L4 bilateral		NA	no significant difference in thickness between CLBP and control group (p>0.05)
Nuzzo et al. ⁶⁰ (2013)		62 M - 36.2±9.4y H: 178.5±8.2cm W: 88.6±15.3kg fire fighters	- prone - 5MHz curvilinear probe	- CSA and thickness - L4 + L5 R	anthrop. factors	positive correlations between weight and L4 CSA (r=0.49; p<0.001), L5 CSA (r=0.43; p<0.001), L4 thickness (r=0.40; p=0.001) and L5 thickness (r=0.45; p<0.001)	NA
Nuzzo et al. ⁶⁷ (2014)		69 healthy 62 M - 36.2±9.4y BMI: 27.7±3.7kg/m ² 7 F - 25,1±3,6y BMI: 24.4±4.0kg/m ² 32% with history of self-reported LBP (not clinically meaningful), no current LBP	- prone - 5MHz curvilinear probe	CSA at L4 + L5 bilateral, thickness at L4 + L5 R	side	 asymmetry of ≥10% in M: 34% at L4, 31% at L5 F: 57% at L4, 14% at L5 mean asymmetry in M: 9.2±8.8% at L4, 9.8±15.1% at L5 F: 13.7±8.6% at L4, 4.8±3.3% at L5 	no significant difference in thickness or CSA between subjects with and without history of self-reported LBP (p>0.05)

	Patient characte		Structural					
Author (year)	CLBP group	Control group	US probe	of the LM + lumbar level	Associated factors	Measure of association (mean±SD)	CLBP vs. control group (mean±SD)	
		fire fighters						
Pressler et al. ⁶⁸ (2006)		30 F - 23±2y BMI 23±2.5kg/m ²	- prone - 5-10MHz linear probe	- CSA - S1 bilateral	side	 L side > R side (4.18±0.55cm² vs. 4.11±0.57cm²; p<0.035) high correlation between CSA at L and R side (r=0.94; p<0.001) asymmetry of 3.5±3.4% 	NA	
Rostami et al. ⁷² (2015)	14 M – 27.2±4.7y BMI: 24.0±4.1kg/m ² VAS: 1.6±2.0 LBP duration > 12 months competitive off- road cyclists	24 M – 27.8±5.3y BMI: 24.9±3.5kg/m ² competitive off- road cyclists	- prone/ on bike in 4 positions - 5MHz curved probe	- CSA atrest and contraction (CAL+ipsi- lateral leg lift) - L4 bilateral		NA	CLBP vs. control group: - smaller CSA at rest in prone at L side (5.67 \pm 0.52cm ² vs. 6.17 \pm 0.59cm ² ; p=0.014) - smaller CSA in contraction in prone at R side (6.47 \pm 0.94cm ² vs. 7.30 \pm 0.87cm ² ; p=0.01) - smaller CSA change during contraction in prone at R side (0.88 \pm 0.45cm ² vs. 1.28 \pm 0.41cm ² ; p=0.009) - smaller CSA in 4 positions on bike at L side (4.77 \pm 0.59cm ² to 4.84 \pm 0.54cm ² vs. 5.31 \pm 0.73cm ² to 5.51 \pm 0.76cm ² ; p<0.05) and R side (4.85 \pm 0.50cm ² to 4.91 \pm 0.55cm ² vs. 5.39 \pm 0.71cm ² to 5.58 \pm 0.71cm ² ; p<0.05)	
Scott et al. ⁶⁵ (2015)	20 CLBP <i>14 M</i> <i>6 F</i> 31.9±7.2y BMI: 24.0±2.2kg/m ² VAS: 5.3±1.9	20 healthy 14 M 6 F 31.3±7.6y BMI: 22.3±3.0kg/m ²	- prone/ sitting - curvi- linear probe	- CSA - L5 bilateral	side	no significant difference L vs. R in prone nor sitting (p>0.05)	no significant difference between CLBP and control group in prone nor sitting (p>0.05)	

Patient characteristics (n		eristics (mean±SD)		Structural			
Author (year)	CLBP group	Control group	Position + US probe	characteristics of the LM + lumbar level	factors	Measure of association (mean±SD)	CLBP vs. control group (mean±SD)
	LBP duration > 3 months						
Stokes et al. ⁵⁰ (2005)		120 healthy <i>52 M</i> – 40.1±13.0y BMI: 25.8±3.2kg/m ² <i>68 F</i> – 34.2±12.8y BMI: 23.0±3.1kg/m ²	- prone - 5MHz convex probe	- CSA, AP and lateral dimensions - L4 + L5 bilateral	- age - sex - antrop. factors - level - side	 no association between CSA and age (p>0.05) no association between symmetry and age (p>0.05) smaller shape ratio at younger age at L5 (p<0.001) larger CSA in M vs. F at L4 (7.87±1.85cm² vs. 5.55±1.28cm²; p<0.001) and L5 (8.91±1.68cm² vs. 6.65±1.00cm²; p<0.001), but not significant when normalized for weight no association between symmetry and sex (p>0.05) smaller shape ratio in F vs. M (0.95±0.17 vs. 1.03±0.17; p=0.025) no association between CSA and BMI (p>0.05) larger CSA at L5 vs. L4 (in M: 8.89±1.69cm² vs. 7.97±1.80cm², in F: 6.64±1.01cm² vs. 5.55±0.99cm²; p<0.001) high correlation between symmetry and L5 (in M: r=0.82 and in F: r=0.80; p<0.001) no association between symmetry and level (p>0.05) 	NA

	Patient characte		Structural				
Author (year)	CLBP group	Control group	Position + US probe	characteristics of the LM + lumbar level	Associated factors	Measure of association (mean±SD)	CLBP vs. control group (mean±SD)
						 smaller shape ratio at L5 vs. L4 in F (0.95±0.17 vs. 1.02±0.17; p<0.001) positive correlations between CSA and AP and lateral dimensions (r>0.6; p<0.0001) 	
Sweeney et al. ⁷⁰ (2014)	10 CLBP (unilateral) 4M 6F 36±12.2y H: 165.7±10.8cm W: not reported RMQ: 5.0±3.1 LBP duration: 28.2±22.0 months	10 healthy 6M 4F 31.8±5.5y H: 170.0±9.2cm W: not reported	- prone/ standing - 5MHz curved probe	- thickness at rest and contraction (CAL) - L4/5 + L5/S1 bilateral	side	no significant difference in thickness at rest or thickness change between painful and non-painful sides in LBP group in prone nor standing (p>0.05)	 no significant difference in thickness at rest between CLBP and control group in prone nor standing (p>0.05) larger thickness change during CAL in standing at L5/S1 in CLBP vs. control group (9.97±10.84% vs. 2.29±3.43%; p=0.05) no significant difference between CLBP and control group during CAL in prone (p>0.05)
Teyhen et al. ⁵⁶ (2012)		340 healthy 244M – 21.8±3.9y BMI: 25.0±2.8kg/m ² 96F – 22.3±5.0y BMI: 24.5±2.9kg/m ² US army soldiers	- prone - 5MHz curvilinear probe	 thickness at rest and contraction (CAL+W) L4/5 bilateral 	- sex - side	 larger thickness in M vs. F at rest (3.11±0.45cm vs. 2.67±0.36cm; p<0.001) and during contraction (3.82±0.48cm vs. 3.26±0.40cm; p<0.001), also when corrected for height and weight (p<0.05) no significant sex difference for %thickness change (p=0.79) -no significant sex difference for asymmetry at rest (p=0.98) or during contraction (p=0.68) 	NA
Wallwork et al. ⁵⁷ (2009)	17 CLBP <i>8M</i> <i>9F</i> 41.9±13.7y H: 174.2±10.3cm W: 76.1±16.7kg VAS ≥ 3	17 healthy <i>8M</i> <i>9F</i> 33.9±11.2y H: 176.6±10.3cm W: 81.2±12.5kg	- prone - 5MHz curvilinear probe	- CSA and thickness at rest and contraction (voluntary swelling) - L2 -> L5 bilateral	- sex - activity level - side	 larger CSA in M vs. F at L2 (difference of 0.15cm²; p<0.05) and L3 (difference of 0.9cm²; p<0.05) no association between sex and thickness change (p>0.05) positive association between activity level and CSA at L3 (F=5.9; 	 smaller CSA in CLBP vs. control group at L5 (3.81±1.2cm² vs. 5.56±1.1cm²; F=29.1; p=0.001) larger CSA in CLBP vs. control group at L2 (2.40±0.9cm² vs. 1.94±0.9cm²; F=5.8; p=0.047)

	Patient character	ristics (mean±SD)		Structural			
Author (year)	CLBP group	Control group	Position + US probe	characteristics of the LM + lumbar level	Associated factors	Measure of association (mean±SD)	CLBP vs. control group (mean±SD)
	LBP duration > 3 months					 p=0.03), L4 (F=11.9; p=0.006) and L5 (F=5.4; p=0.04) no association between activity level and thickness change (p>0.05) significant asymmetry of CSA (mean difference of 0.17cm²) and thickness change (mean difference of 2.7%) at each level (p<0.05) 	 smaller thickness change in CLBP vs. control group at L5 (3.05±7.2% vs. 6.29±6.5%; F=6.6; p=0.02) no significant difference in asymmetry of CSA or asymmetry of thickness change between CLBP and control group (p>0.05)
Watson et al. ⁵⁸ (2008)		25 healthy <i>8M</i> - 31.9±6.5y BMI: 24.8±2.5kg/m ² <i>17F</i> – 32.8±13.6yBMI: 23.9±4.3kg/m ²	- prone - 3.5-5MHz convex probe	- CSA - L5 bilateral	- sex - anthrop. factors - side	- larger CSA in M vs. F (7.58 \pm 1.51cm ² vs. 6.01 \pm 0.70cm ² ; F _{1.23} =12.8; p=0.002), without effect for % body fat (p>0.05) - negative correlation between CSA and body fat (L side: r=-0.41 and R side: r=-0.44; p<0.05) - high correlation between sides (L side: 6.54 \pm 1.32cm ² vs. R side: 6.48 \pm 1.39cm ² ; r=0.92; p<0.001) - mean asymmetry: 4.97% in M and 6.45% in F	NA
Yoshiko et al. ⁵³ (2018)		22 healthy <i>8M</i> - 73±5y BMI: 23±3kg/m ² <i>14F</i> - 82±7y BMI: 22±4kg/m ²	- prone - 8-10MHz linear probe	- thickness and EI - L4/5 R	- age - sex	 positive correlation between age and El (r=0.64; p<0.05) larger thickness in M vs. F (2.99±0.47cm vs. 2.49±0.37cm; p<0.05) lower El in M vs. F (47.45±6.97a.u. vs. 60.65±9.61a.u.; p<0.05) 	NA
Zhang et al. ⁷³ (2018)	24 CLBP – 35.9±7.6y <i>11M</i> <i>13F</i> BMI: 21.8±2.1kg/m ² ODI: 32.8±20.1% VAS: 4.0±1.0	26 healthy – 32.4±7.2y <i>13M</i> <i>13F</i> BMI: 21.0±2.0kg/m ²	- prone - 6-13MHz probe	- CSA and thickness at rest and contraction (head, trunk, arms lifted)		 no significant difference between painful vs. nonpainful sides for CSA (p=0.69), thickness at rest (p=0.82), thickness during contraction (p=0.89) or thickness change (p=0.62) 	 smaller CSA in CLBP vs. control group (2.83±0.74cm² vs. 4.36±0.58cm²; p<0.001) smaller thickness in CLBP vs. control group at rest (1.66±0.21cm vs. 2.10±0.20cm; p<0.001) and during

	Patient characteristics (mean±SD)			Structural			
Author (year)	CLBP group	Control group	Position + US probe	characteristics of the LM + lumbar level	Associated factors	Measure of association (mean±SD)	CLBP vs. control group (mean±SD)
	LBP duration: 6.8±6.1y			- L4 bilateral			contraction (2.17±0.34cm vs. 2.95±0.25cm; p<0.001) - smaller thickness change in CLBP vs. control group (29.69±8.62% vs. 40.43±5.83%; p<0.001)

- 768 AP: anteroposterior, a.u.: arbitrary units, BMI: body mass index, CAL: contralateral arm lift, CAL+W:
- contralateral arm lift with handheld weight, cm: centimeter, CSA: cross-sectional area, CLBP: chronic low back
- pain, EI: echo-intensity, F: female, H: height, kg: kilogram, L: left, LBP: low back pain, LM: lumbar multifidus, M:
- 771 male, m: meter, MHz: megahertz, NA: not applicable, NPS: numeric pain score, ODI: Oswestry Disability Index,
- 772 R: right, RMQ: Roland Morris Questionnaire, US: ultrasound, VAS: Visual Analog Scale, W: weight, y: year

- 1774 If not specifically mentioned, structural characteristics were analyzed at rest.
- 775

776 Figure 1. PRISMA flow chart of study selection process.

- 777 Appendix 1 Checklist for the assessment of the methodological quality: adapted version of the
- 778 **Downs and Black checklist**
- 779 Appendix 2 List of abbreviations
- 780 Appendix 3 Reference list of articles excluded based on full text