TITLE

Effect of motor control training on trunk muscle morphometry, pain, and disability in people with chronic low back pain: A systematic review and meta-analysis

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ABSTRACT

Objective: The aim of this systematic review and meta-analysis was to evaluate the effects of

motor control training (MCT) on 1) trunk muscle morphometry measured by ultrasound

imaging (USI) and 2) pain and disability in individuals with chronic low back pain.

Methods: PubMed, Web of Science, Scopus, and Cochrane Library databases were searched

from inception until January 2021. Randomized control trials evaluating both muscle

morphometry and pain or disability in individuals with chronic low back pain were included.

Study selection, data extraction, and quality assessment were performed by two reviewers

independently. Modified Downs and Black tool and Grading of Recommendations

Assessment, Development and Evaluation approach were used to assess the risk of bias and

quality of evidence, respectively. A meta-analysis was performed using a random-effects

model with the mean difference (MD) or standardized mean difference (SMD).

Results: Of 3459 studies, 15 studies were selected for inclusion. The results revealed no

differences in the resting thickness of the transversus abdominis (TrA), internal and external

oblique, and lumbar multifidus muscles in studies that compared MCT with other interventions.

The TrA muscles contraction ratio was greater (SMD= 0.93 CI: -0.0 to 1.85) and lower pain

(WMD: -1.07 cm, 95% CI: -1.91 to -0.22 cm, P = 0.01) and disability (SMD= -0.86, 95% CI: -

1.42 to -0. 29, P< 0.01) scores were found in the groups who underwent MCT compared with

other interventions.

Conclusion:

This systematic review and meta-analysis found that motor control exercise training increased

the transverse abdominis contraction ratio (muscle activation) and improved the level of pain

and disability compared to other interventions in people with chronic low back pain. However,

motor control exercise training was not superior to other interventions in increasing the resting

thickness of deep abdominal and lumbar multifidus muscles in intervention times less than 12

weeks.

Keywords: Ultrasonography; Low back pain; Exercise; Rehabilitation

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INTRODUCTION

Low back pain (LBP) is one of the most common musculoskeletal disorders, affecting 49-90% of people during their lifetime[1]. There is no defined origin or pathology in 90% of individuals with LBP [2]. Chronic low back pain (CLBP), defined by a duration of symptoms exceeding three months, leads to disability, substantial treatment costs, work absenteeism, and sick leave [3]. Although multidisciplinary treatments based on the biopsychosocial approach have emphasized addressing the psychosocial aspects of chronic LBP [4], many approaches focus on the biological aspects. One such approach commonly used is the delivery of exercise programs to address impairments in muscle strength, endurance, and morphometry and activation.

Functional or morphometric adaptations of trunk muscles may occur in people with CLBP when compared with pain-free individuals [5, 6]. Features may vary between individuals including compromised muscle structure (eg, atrophy [7] and fatty infiltration [8]), altered activation, automatic/voluntary responses of deep and superficial abdominal muscles and (external oblique (EO), internal oblique (IO) and transversus abdominis (TrA)) [9, 10] lumbar multifidus muscles [5].

Exercise training programs have been designed based on impairments observed in the control and coordination of trunk muscles [11-13]. A recent retrospective analysis of people with CLBP showed that those who presented with poor results on clinical muscle testing of the multifidus muscle at baseline had better outcomes (less pain and disability) in response to exercises targeting that muscle than patients who did not demonstrate such impairments [14]. These results suggest that if muscular changes related to better clinical outcomes could be identified exercise interventions could possibly be designed and applied more effectively.

Changes to key recommendations in clinical practice guidelines for the management of people have emphasized the importance of exercise programs aimed at improving function. One form

of exercise which has been shown to decrease pain and disability levels in people with CLBP is motor control training (MCT) [13]. MCT refers to the motor, sensory and central processes required to control posture and movement. The concept suggests that how a person with LBP loads their spine (by their assumed posture, movements and muscle activation strategies) may contributes to development and persistence of symptoms. MCT involves training of control and endurance of spinal muscles with subsequent progression into functional retraining [15]. Previous reviews have suggested that MCT exercises are superior to minimal intervention and confer benefit when added to another therapy for pain at all-time points and disability at long-term follow-up, but are not more effective than manual therapy or other forms of exercise [13, 16]. A recent systematic review suggested that MCT was associated with greater pain and disability reductions than other short-term interventions [17].

Since LBP is currently the leading cause of disability worldwide, most review studies have focused on the effect of interventions on pain and disability [18]. Nevertheless, understanding muscle structural and functional changes induced by exercise therapy is of great importance for designing exercise programs [19]. To date, only one systematic review has considered the effect of MCT interventions on changes in muscle morphometry and activity associated with changes in pain and disability [20]. Conflicting associations were reported, with the most recent paper included published in 2012. It is, therefore, still unclear whether MCT interventions are associated with changes in both muscle morphometry and changes in pain and disability in people with CLBP. Furthermore, the results of one study [27] contradict findings of other recent studies that have demonstrated changes in muscle morphometry following MCT interventions [21-25]. Therefore, these conflicting findings suggests that a comprehensive critical review is timely.

The purpose of this study was to systematically review published randomized control trials (RCTs) regarding the effects of MCT intervention on the morphometry and function of

abdominal and lumbar trunk muscles measured by ultrasound imaging (USI). The second aim was to assess the changes in pain and disability in the studies that have evaluated muscle morphometry and function following MCT interventions in individuals with CLBP.

METHODS

The current systematic review and meta-analysis was reported according to the guidelines of PRISMA and the protocol was registered at the International Prospective Register of Systematic Reviews (PROSPERO: CRD42019144768).

Data Sources and Search Strategy

The following databases were searched from inception to January 2021: PubMed, Web of Science, Scopus, and Cochrane Library. The references of included studies were searched manually for detecting relevant articles. The search was limited to studies reported in English and those including human adults. Medical subject heading terms, the terms generated in subheadings, and all related search terms were used to design the search strategy. The search strategy consisted of 3 groups of search terms, which were combined 1) LBP, 2) keywords related to MCT interventions, 3) ultrasound Imaging. Literature search strategies are listed in Supplementary 1 (see supplemental file). One reviewer conducted the database searches and removed duplicates using EndNote software. Two reviewers (SSA and SS) independently screened the potential studies by title and abstract to determine their relevance. The same reviewers checked the full text of relevant articles against the eligibility criteria. Disagreements between reviewers were resolved by consultation with a third investigator.

Outcomes

The primary outcome measures were morphometric measures of abdominal and lumbar trunk muscles measured USI, including muscle thickness, cross-sectional area (CSA), length, width, pennation angles and contraction. Studies employing USI were selected as it is inexpensive

(compared with Magnetic Resonance Imaging (MRI)) and readily available in clinical practice. Muscle contraction was measured using the changes in muscle thickness that occurred on contraction and was expressed as a contraction ratio (thickness on contraction/thickness at rest). The contraction ratio is thought to reflect muscle activation. The relationship between changes in muscle thickness and muscle activation at low levels of maximum voluntary isometric contraction has been validated by comparison with electromyography for the abdominal and multifidus muscles [26]. The secondary outcome measures were assessments of pain intensity and disability.

Eligibility Criteria

Studies were eligible if they:

- were RCTs that used MCT in the treatment program of adult individuals (≥18 years of age) with CLBP. MCT interventions were included if the study used terms such as, "Stabilization exercises" or "Core stability" or Pilates exercise.
- 2) assessed the effect of MCT on pain intensity and/or disability
- 3) used USI to measure abdominal and lumbar trunk muscle morphometry and function
- 4) had undergone a peer-review process.

Articles were excluded if they were:

- 1) observational studies (case-control, cross-sectional or cohort)
- 2) evaluated the efficacy of MCT intervention on pain intensity or disability in the absence of assessments of trunk muscles morphometry using USI.

Data Extraction

Two reviewers (SSA and SS) independently extracted the following data: subjects' characteristics, sample size, LBP type and duration and details relating to the intervention (eg, , type, duration, and frequency of treatment sessions and intervention progression). Data from questionnaires assessing pain and disability, the USI methodology employed (eg, , ultrasound

mode, transducer frequency, and testing position or task) and the mean and standard deviation (SD) of the outcomes was also extracted. A consensus meeting between the reviewers determined the accuracy of the data extraction.

Quality Assessment (risk of bias)

The quality of included studies was assessed by two independent reviewers (SS and SSA). The modified Downs and Black was used to assess the risk of bias in both randomized and nonrandomized comparative studies, which consists of 27 items that address the following methodological components: reporting, external validity, internal validity (bias and confounding) and power [27]. Downs and Black checklist was modified to include criteria that were relevant to assess potential bias in the included studies [28].

Quality of Evidence

The certainty in the evidence and strength of each outcome's recommendations was evaluated according to the Grading of Recommendation, Assessment, Development, and Evaluation (GRADE) [29]. Consideration of the study design included five downgrade items: a) limitation of study design (>25% of participants from studies with high risks of bias), b) inconsistency of the results ($I^2 \ge 50\%$), c) indirectness of evidence, d) imprecision of measurement (<300 participants or <5 studies), and e) publication bias. Three upgrade qualities of evidence were included a) large effect size was detected, b) dose-response relationship and c) plausible residual confounding. The quality of evidence was graded into four levels: high, moderate, low, and very low.

Data Synthesis

Outcomes were analyzed using the sample size, post-intervention mean, and standard deviation for both the control and intervention groups in each study. Mean difference (MD) or standardized mean difference (SMD) was calculated with a 95% confidence interval (CI). A random-effects model was employed due to the significant heterogeneity. Effect sizes were

defined as small: SMD = 0.2 to 0.5; moderate: SMD = 0.5 to 0.8; and large: SMD > 0.8. [30] To allow use of the MD to represent the effect size of pain outcomes, all mean values and standard deviations were converted into scales from 0 to 10 points.

Heterogeneity among the included studies was explored quantitatively using the I^2 statistic and qualitatively by comparing study characteristics. An I^2 index of <25% reflected low heterogeneity, <75% indicated moderate heterogeneity, and \geq 75% was deemed to reflect high heterogeneity [31].

In cases where two articles covered results from the same study population, only one article was pooled. When a trial was designed to compare more than two treatments (ie, a comparison trial), we divided the control group into several parts so that the total numbers were added to the group's original size (to avoid counting the control group participants twice) [32]. In the case of high heterogeneity, a sensitivity analysis was performed to determine each study's effect on the pooled effect size, omitting one study each time and evaluating its effect on the overall effect size and 95% CI. Subgroup analysis was performed where possible to determine the possible sources of heterogeneity, including subgroup analyses based on the intervention applied for the control arm "motor control versus other forms of exercise" or "MCT versus no exercise", intervention duration (short-term < 8w, long-term ≥ 8w) and MCT progression (static dynamic stage or progressed to the functional stage) and the quality of the included studies. All subgroup differences were tested for significance and an I^2 statistic. All tests were performed using the statistical software package STATA (Version 14), and a two-sided p-value < 0.05 was considered statistically significant. Potential publication bias was explored using funnel plots. The funnel plots and Egger's linear regression test were used to investigate publication bias. Egger's test assessed the funnel plots' symmetry, and p-value < 0.05 was defined as significant publication bias. When publication bias was suspected, a trim-and-fill

method was used to adjust for publication bias in the meta-analysis to evaluate the effect of this on interpreting the results.

RESULTS

The process of study selection of the systematic review is summarized in Figure 1. A total of 3459 citations were retrieved from the electronic databases. After removing 748 duplicates, 2711 titles and abstracts were reviewed. The full-text versions of 97 studies were assessed, and 15 RCTs were included in this review [12, 21-25, 33-41].

Study Characteristics

The sample sizes of the 15 included studies ranged from 20 to 109 participants, and the average age ranged from 21.8 to 48.6 years. All studies investigated individuals with CLBP. The characteristics of the included studies are presented in (Supplementary 2, see supplemental file).

Intervention

The duration of the MCT programs conducted ranged from 4 to 12 weeks. The frequency of sessions ranged from 1-5 times per week (Supplementary 2, see supplemental file). Seven studies progressed the MCT interventions from static isometric contractions to the functional stage without resistance [23-25, 33-36]. Thirteen studies incorporated a control exercise intervention [12, 21, 23-25, 33-39, 41], mostly including general exercise [24, 34-36, 39, 41] or McKenzie method [21, 23, 25]. Three out of these 13 studies had two control groups. Two studies compared MCT with a high load sling exercise and a general exercise [35, 36], and another study compared MCT with an equipment-based exercise and no treatment [37]. Two remaining studies compared MCT with "no exercise" and "no treatment" groups [22, 40].

Abdominal and lumbar muscle morphometry and function

Muscle thickness was the most commonly used measurement parameter in all studies. Eight studies investigated the effects of MCT on muscle thickness during rest of TrA [21, 22, 24, 33, 34, 38, 39], IO [22, 24, 33], EO [22, 24, 33], rectus abdominis (RA) [24] and multifidus muscles [12, 21, 34, 38, 39]. Six articles analyzed treatment-related changes in the "contraction ratio" of the TrA, IO, and EO muscles [23, 25, 35, 37, 40, 41]. Only one study also evaluated abdominal muscle timing using USI [36]. One study assessed the alteration in the CSA of the lumbar multifidus muscle following MCT treatment [39]. The included studies did not assess other aspects of muscle morphometry that could be measured using USI, such as muscle length, width, and pennation angles.

Pain

Fourteen studies assessed pain intensity using a visual analog scale (VAS) [12, 21-25, 34, 37-41], or a numeric pain rating scale (NPRS) [35, 36]. The entry-level of pain was generally moderate (VAS:4.5 to 7.4 cm) [41], except in one study that included individuals with high pain intensity at baseline (Supplementary 2, see supplemental file) [34].

Disability

Ten studies assessed disability using the Roland-Morris Disability Questionnaire (RMDQ), [22, 37, 40, 41] the Oswestry Disability Index (ODI) [24, 33, 36], the Patient-Specific Functional Scale (PSFS) [23, 25], and the Functional Rating Index (FRI) [21]. The level of disability reported by the study participants at entry was generally moderate based on the defined scores for instruments [41-43]. However, one study included participants with a low disability level [40], and another study included individuals with reported high disability levels at baseline (Supplementary 2, see supplemental file) [24].

Risk of bias assessment

Regarding the quality of the included studies, seven studies (46.67%) attained a rating of "high" quality [12, 22, 23, 25, 37, 40, 41] and the remaining eight articles (53.33%) received a

"medium" quality rating (Table 1) [21, 24, 33-36, 38, 39]. Figure 2 represents the common areas of bias in the included studies.

Quality of evidence

The quality of the evidence could be analyzed for five outcome measures (resting thickness of the TrA and multifidus muscles, contraction ratio for the TrA muscle, pain, and disability) using the GRADE approach (Table 2) [29]. The average quality ranged from "low" to "moderate", three outcomes demonstrated "moderate" levels of quality (resting thickness TrA, pain and disability), two demonstrated the "low-level" quality of evidence (resting thickness multifidus muscles and contraction ratio for thickness change of TrA).

META-ANALYSIS

Resting thickness of the abdominal and multifidus muscles

The overall SMD was -0.06 (95% CI -0.20 to 0.07) with low heterogeneity (I^2 :10.8%), which revealed no difference in the effect of MCT compared to other interventions for the thickness of abdominal and multifidus muscles at resting position. Subgroup analysis based on muscle groups was performed (Figure 3A). Seven trials were pooled to examine the effects of MCT on the resting thickness of the TrA muscle [21, 22, 24, 33, 34, 38, 39]. The pooled SMD was 0.09 (95% CI: -0.13 to -0.32) (P= .81) with moderate heterogeneity (I^2 : 10%) obtained; three trials assessed the resting thickness of both the IO and EO muscles [22, 24, 33]. Effect sizes for the IO muscle: SMD= -0.14, (95% CI: -0.47 to 0.19, I^2 0%) and EO: SMD= -0.14, (95% CI: -0.47 to 0.18, I^2 0%). The effect size of the five trials on the resting thickness of the multifidus muscle was -0.14, 95% CI: -0.46 to 0.17, I^2 51.9%), with moderate heterogeneity [12, 21, 34, 38, 39]. The sensitivity analysis suggested that the combined SMDs were stable after any of the studies were excluded from the meta-analysis. Subgroup analysis showed that there were no changes in the heterogeneity or subgroup effect size for all outcomes. The publication bias assessment using the funnel plot was asymmetrical (no dots on the upper part,

representing large studies) (Supplementary 3, see supplemental file). The Egger's test was not statistically significant and suggested no publication bias for muscle thickness (coefficient = -1.30; P= 0.3).

Contraction ratio of the TrA muscle

Five studies assessed the effect of MCT on the contraction ratios of the TrA muscle [23, 35, 37, 40, 41]. The results of pooled effect sizes (SMD= 0.93 CI: - 0.0 to 1.85) demonstrated a moderate effect of MCT with high heterogeneity I^2 : 89.9% (Figure 3B). Further subgroup analysis based on the type of control group participants considerably reduced heterogeneity to 0% in the subgroup that compared MCT with "no exercise", with strong effect size (SMD= 1.17 CI:0.73 to 1.16). Sensitivity analysis showed that removing Ehsani et al.'s [41] trial changed the overall estimated effect size (SMD= 0.43, 95% CI: -0.17 to 1.02; P= 0.16). This was the only study that measured the contraction ratio of TrA muscle in the standing position. The funnel plot examination (Supplementary 3, see supplemental file) and the Egger (P= 0.03) showed potential publication bias. After the trim-and-fill analysis, two studies were added, and the pooled effect size changed from 0.89 to 0.23.

Pain

The meta-analysis of the 12 trials [12, 21-25, 34, 37-41], which compared changes in pain intensity associated with the intervention, indicated a significant difference in pain reduction between the MCT and control interventions (other exercise or no intervention) (WMD: -1.07 cm, 95% CI: -1.91 to -0.22 cm, P=0.01) with high heterogeneity I^2 : 93 % (Figure 4). Subgroup analysis based on study quality, type of control group (exercise or no exercise), duration and progression of intervention did not change the heterogeneity. However, a significant high effect of MCT intervention on reducing pain was obtained only in the subgroup that progressed the exercise to functional level (WMD: -1.47 cm, 95% CI: -2.47 to -0.47cm, P<0.01), and subgroup analysis based on the quality revealed reduced pain only in the high-quality studies

(WMD: -1.53 cm, 95% CI: -2.58 to -0.47cm, P< 0.01). Sensitivity analysis showed that none of the trial's estimated values were outside the 95% CI. The summary results did not significantly differ when we omitted studies one at a time. Therefore, the results remained stable and robust. An asymmetric funnel plot and significant Eggers test revealed publication bias (P<0.01). However, further analysis with the trim-and-fill test showed that this publication bias did not impact the estimates.

Disability

Nine RCT studies assessed the effect of MCT on disability, where the overall effect size of the studies which compared MCT with other exercises or no exercise revealed a significant moderate effect size (SMD= -0.86, 95% CI: -1.42 to -0. 29, P< 0.01) with high heterogeneity 82.7% (Figure 5). Subgroup analysis based on the duration of intervention moderately changed heterogeneity in the group applying a longer duration of treatment (I^2 : 61%) (\geq 8), with a significant moderate effect size (SMD= -0.61, 95% CI: -1.09 to -0. 13, P= 0.012). The funnel plot was asymmetrical in Supplementary 3 (see supplemental file); however, the non-significant Egger's test did not suggest publication bias (P= 0.14). A further trim-and-fill test confirmed the absence of publication bias.

DISCUSSION

This meta-analysis primarily aimed to systematically summarize RCTs evaluating the effect of MCT on morphometry and function of the abdominal and lumbar trunk muscles measured by USI in individuals with CLBP. The second aim was to assess whether the included studies showed reductions in pain and disability in individuals with CLBP following MCT based interventions.

Most of the included studies used muscle resting thickness as an outcome measure for assessing the effects of MCT interventions. This outcome measure was possibly the most commonly used

because linear measurements using USI are faster and easier to conduct than measuring CSAs (of the lumbar multifidus) and can be used to assess muscle contraction of the abdominal wall and multifidus muscles (at low percentages of maximal voluntary contraction) [26]. However, a disadvantage is that linear measurements do not reflect the quality, CSA or volumes of muscles such as the multifidus, which may be more relevant. For example, muscle CSA has been shown to be correlated with strength in peripheral muscles [44], and fatty infiltration measured with MRI has been shown to change with exercise interventions in parallel with decreasing pain and disability [45].

The current meta-analysis did not find that MCT increased the resting thickness of the multifidus, TrA, IO, and EO muscles more than control interventions with low to moderate quality of evidence (Figures 3-4). However, the length of the intervention periods reported in the included studies was relatively short, with the vast majority of programs lasting 8 weeks or less. Although a single training session can trigger protein synthesis, changes in morphometry are usually evident beyond 8 weeks of training [46]. It is also possible that the benefits of an intervention in individuals with long-lasting pain may take longer to be achieved, as they may present with increased deconditioning and changes in muscle consistency, such as fatty infiltration [47]. It is hypothesized that MCT aims to restore the morphometry and function of key trunk muscles by progressing from isometric contractions of deep trunk muscles to loaded functional activities [15]. However, most of the implemented protocols in the included RCTs did not progress to higher load exercises in the applied MCT interventions, and increased load (eg, , resistance training) is required to induce muscle hypertrophy [48]. Another outcome assessed was the contraction ratio, in which a high effect size was obtained for MCT versus control groups without exercise interventions, albeit with low quality of evidence. It seems that various forms of exercise might have had a positive effect on the contraction ratio, and the results were not unique to the MCT approach. Since the contraction ratio could be considered

as a surrogate measure of muscle activity [26], results could indicate that activity of the TrA muscle could be affected by various types of exercise interventions. Only one study evaluated the CSA of the multifidus muscle, and there were not any differences between results for MCT intervention when compared with general exercise [39].

Limitations

Several limitations should be considered when interpreting the results of this systematic review and meta-analysis. Firstly, aspects of muscle morphometry such as pennation angles and muscle fiber length were not included. Although an increase in muscle size is a typical outcome of training, changes may also occur in pennation angles and length of muscle fibers [49]. For example, muscles with long fascial attachments first show changes in pennation angle [50], which could be a limitation of previous studies that measured only muscle thickness, not other features of the abdominal muscles. This could be a limitation of studies that have only measured muscle thickness. Secondly, most studies that we included did not describe the experience of examiners performing the ultrasound imaging, including the reliability of their measurements. Collectively, the results of this systematic review indicated that MCT was effective in reducing disability and pain in patients with CLBP with a moderate level of evidence. This supports the results of previous studies [17, 51] and clinical practice guidelines that have highlighted the importance of exercise therapy for the management of people with CLBP [52]. Although resting thickness did not change considerably, it is unknown whether other exercise effects such as psychological, neural, physiological, or other muscle parameters, which were not measured, might have been associated with decreased pain and disability with MCT intervention.

There was substantial heterogeneity across the trials regarding the type of MCT program implemented in terms of duration, frequency, and progression (eg, , static-dynamic versus progressive functional programs). Subgroup analysis revealed lower pain scores in the MCT

groups (by 1.43/10) that progressed to the functional stage. MCT aims to restore the function of deep trunk muscles by progressing from isometric contractions of deep trunk muscles to exercises in static positions with focusing on spinal position, then progressed to dynamic tasks, and the final stage involves training using functional activities [15]. Most of the protocols implemented in the included RCT studies did not progress as recommended in MCT interventions. The pain scores were significantly decreased concerning MCT (converting all to 0 -10 scale), and equal to the minimal clinically important difference of 1.0 reported for decreases in chronic musculoskeletal pain intensity [53], and less than 2.0, which has been often cited regarding the effects of treatment for LBP [54]. A more recent validation study of using the VAS for people with LBP has reported a broader range for minimally important change of 1.5-2.8 [55].

Interestingly, results showed that subgroup analysis based on the duration of the intervention affected disability outcome, in a way that studies continuing the MCT interventions for eight weeks or more showed lower disability levels compared to other interventions. It is also important to note that studies included in the present review were relatively short-term, with the vast majority of programs lasting 10 weeks or less. MCT programs are underpinned by motor learning principles that target changing the motor control adaptation and integrating spinal muscle coordination by forming a new motor pattern into functional activities. Motor learning would be possible with long-term practice [56]. The present review highlights the importance of progressing the MCT exercises to the functional stage with longer intervention durations.

Limitations

The findings of this systematic review and meta-analysis should be considered in light of some limitations. All studies evaluated muscle thickness, and other muscle geometric parameters such as CSA, fascicle length, and pennation angle were not evaluated in the included studies.

Moreover, a limitation associated with using USI is the lack of information regarding muscle consistency and fatty infiltration available from computerized tomography and MRI. The participants had CLBP with low to moderate pain intensity and disability levels. Therefore, the results of this review cannot be generalized to other LBP populations.

Future studies

Future prospective studies, including larger sample sizes and more sophisticated measures of muscle parameters, adjusting for confounders, may be warranted. Large prospective studies targeting patients who have defined deficits in muscles of interest at baseline may be recommended to understand better the relationship between muscle morphology changes and clinical outcomes.

CONCLUSION

The results of our study indicated that MCT interventions reduced pain and disability in people with chronic LBP. However, corresponding changes in trunk muscle morphometry were not observed. These results support previous research indicating no association between morphological changes in the abdominal and multifidus muscles and clinical outcomes Despite more recent RCTs having been conducted since the last systematic review, which first examined this relationship, the implications of both studies are similar. One possibility is that clinical outcomes for those with CLBP are influenced by multiple factors, such as psychosocial factors, that could confound the relationship between pain and disability and biological factors such as muscle morphology. Other variables described in a recent retrospective study included the type of LBP (eg, , recurrent versus continual), whether there were co-morbidities such as groin pain/hip pathology or evidence of structural spine changes such as scoliosis [14].

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 Table 1. Quality assessment table of the included studies

Author/Date		Reporting Bias				External validity Internal validity/ measurement bias				Internal validity/ Confounding Powe			Power	Score/percent	Quality					
Author/Date	1	2	3	4	5	6	7	8	9	10		12	13	14	15	16	17	18	Score/percent	Quanty
Akbari et al. (2008) [34]	1	1	1	0	2	1	0	0	0	1	1	0	1	0	1	0	0	1	61.1	Moderate
Vasseljen et al. (2010) [35]	1	1	1	0	1	1	0	1	0	0	1	1	1	0	1	1	0	1	66.6	Moderate
Vasseljen et al. (2012) [36]	1	1	1	0	1	1	0	1	0	0	0	1	1	0	1	1	0	1	61.1	Moderate
Hosseinifar et al. (2012) [21]	1	1	1	0	2	1	0	0	0	0	1	0	1	0	1	0	0	0	50	Moderate
Park et al. (2013) [33]	1	0	1	0	2	1	0	0	0	0	0	0	1	1	0	0	0	0	38.8	Moderate
Halliday et al. (2016) [23]	1	1	1	1	1	1	0	1	0	0	1	1	1	1	1	1	0	1	77.7	high
Shamsi et al. (2016) [24]	1	1	1	1	1	1	0	0	0	0	0	0	1	1	1	0	1	0	55.5	Moderate
Berglund et al. (2017) [12]	1	1	1	1	2	1	0	1	0	0	0	1	1	1	1	1	0	0	72.2	high
Cruz-Diaz et al. (2017) [37]	1	1	1	1	2	1	0	0	1	0	1	1	1	0	1	0	0	1	72.2	high
Finta et al. (2018) [38]	1	1	1	1	2	1	1	0	0	0	0	1	1	0	1	0	1	0	66.6	Moderate
Nabavi et al. (2018) [39]	1	0	1	1	1	1	1	1	0	0	1	0	1	0	1	0	1	1	66.6	Moderate
Noormohammadpour et al. (2018) [22]	1	1	1	0	2	1	0	1	1	0	1	1	0	1	1	1	0	1	77.7	high
Halliday et al. (2019) [25]	1	1	1	1	1	1	1	1	0	0	1	1	1	1	1	1	0	1	83.3	high
Ehsani et al. (2019) [41]	1	1	1	1	2	1	0	1	1	1	1	1	1	1	1	0	0	1	88.8	high
Ahmadizadeh et al. (2020) [40]	1	1	1	1	1	1	1	0	0	0	1	0	1	1	1	0	1	1	72.2	high

Legend for table 1 Items of quality assessment checklist.

- 1 Is the hypothesis/aim/objective of the study clearly described?
- Are the main outcomes to be measured clearly described in the Introduction or Methods section?
- 3 Are the characteristics of the patients included in the study clearly described?
 - Are the interventions of interest clearly described? Treatments and placebo (where relevant) that are to be compared should be clearly
- 4 described.
- Are the distributions of principal confounders in each group of subjects to be compared clearly described? (Yes = 2 Partially = 1 No = 0)
- 6 Does the study provide estimates of the random variability in the data for the main outcomes?
- 7 Have the characteristics of patients lost to follow-up been described?
- 8 Were the results reported precisely?
- Were the subjects asked to participate in the study representative of the entire population from which they were recruited?
- Was an attempt made to blind study subjects to the intervention they have received?
- Was an attempt made to blind those measuring the main outcomes of the intervention?
- Were the statistical tests used to assess the main outcomes appropriate?
- Were the main outcome measures used accurate (valid and reliable)?
- Were the patients in different intervention groups (trials and cohort studies) recruited from the same population?
- Were study subjects randomized to intervention groups?
- Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?
- Were losses of patients to follow-up taken into account?
- Did the study have sufficient power to detect a clinically important effect

Table 2. Grading of recommendation, assessment, development, and evaluation (GRADE) of the included studies.

		Down grade	items			Upgrad	de items		No of patient	ts	Effect size	Quality of evidence
Outcome	No of studies	Limitations	Inconsistency	Imprecision	Publication bias		rocnonco	Plausible residual confounding	intervention	Control	(95% CI)	Grade rating
Resting thickness TrA	7	Serious ^a (-1)	No	No	No	No	No	No	187	178	0.09 (-0.13, 0.32)	moderate
Resting thickness LMU	5	Serious ^a (-1)	Serious ^a (-1)	No	No	No	No	No	180	170	-0.14 (-0.46-0.17)	Low
Thickness Change TrA	4	Serious ^a (-1)	NO	Serious ^b (-1)	No	No	No	No	180	149	0.43 (-0.17, 1.02)	Low
Pain	12	Serious ^a (-1)	Serious (-1)	No	No	No	Yes (+1)	No	393	370	-1.07 (-1.91, -0.22)	moderate
Disability	9	Serious ^a (-1)	Serious (-1)	No	No	No	Yes	No	299	282	-0.86 (-1.42, -0.29)	moderate

LMU=lumbar multifidus, TrA=transversus abdominis, Serious (-1), No (0), Yes (+1)

High: Further research is very unlikely to change our confidence in the estimate of effect.

Moderate = Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low = Further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low = Any estimate of effect is very uncertain.

^a high risk of bias indicated by (selection bias and measurement bias and randomization)

^b I²>50%

^C insufficient studies or sample size included in meta-analysis

d Particular training intensity yielded a more prominent effect

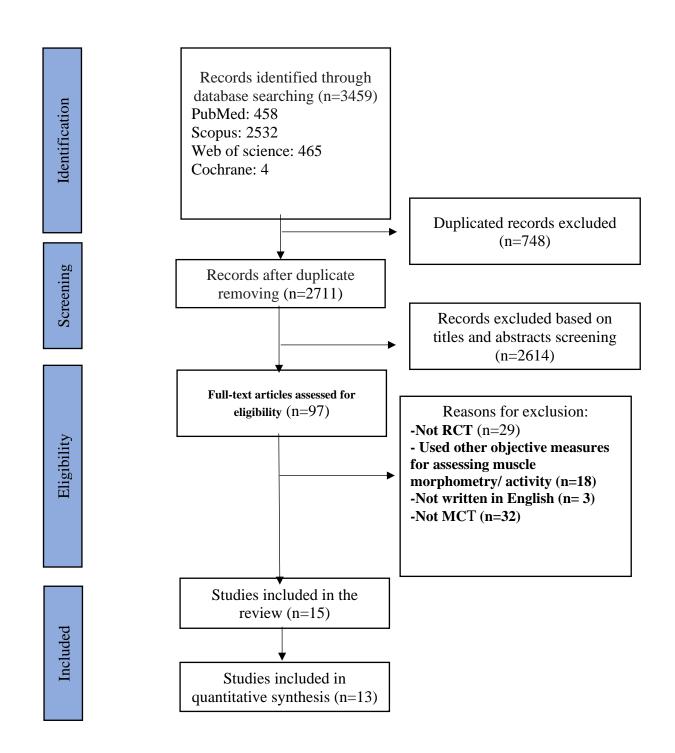


Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) flow diagram mapping the review.

MCT = Motor control training, RCT=randomized control trial

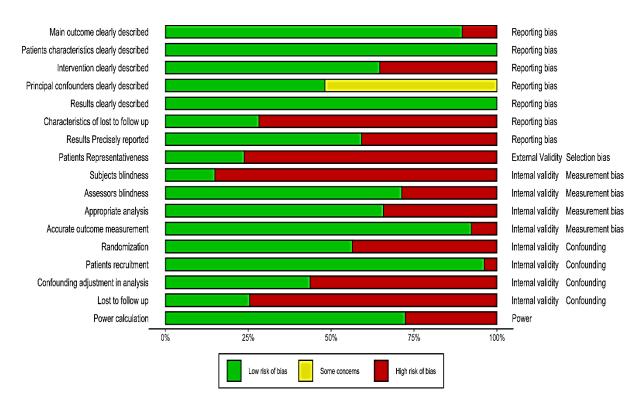


Figure 2. Risk of bias assessment of the included studies.

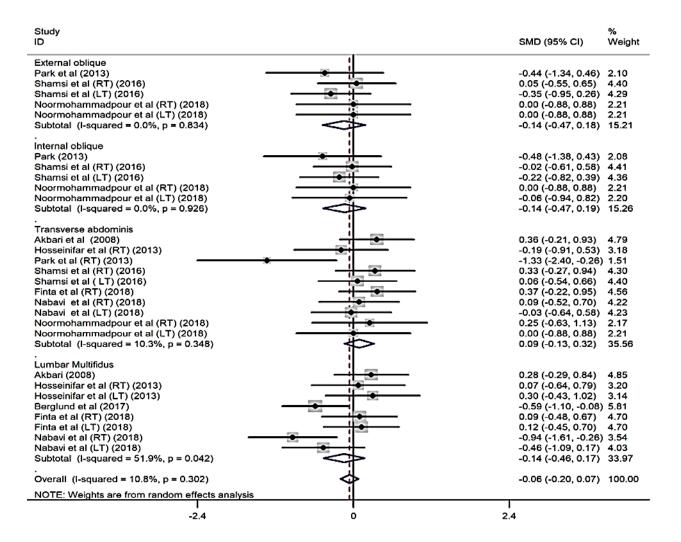


Figure 3 A

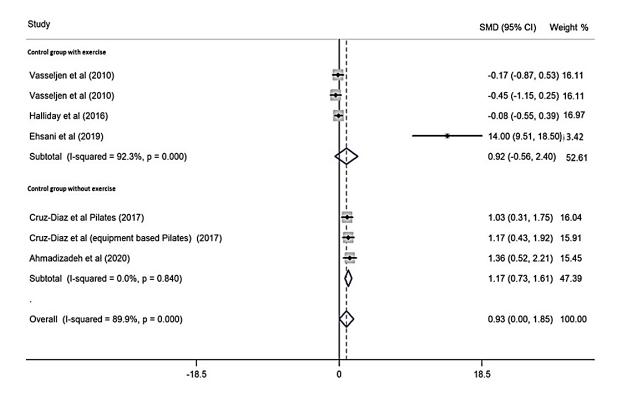


Figure 3 B

Figure 3. Standardized mean difference (95% CI) of the effect of motor control training on: A) thickness of trunk muscles at rest, B) transverse abdominis contraction ratio (muscle thickness change)

RT: right, LT: left

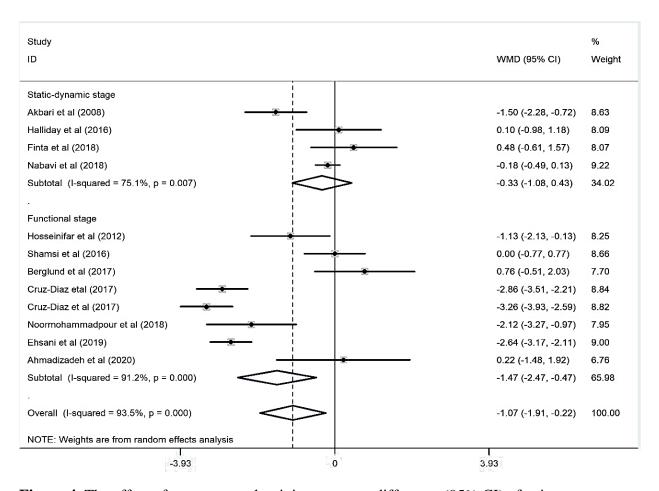


Figure 4. The effect of motor control training on mean difference (95% CI) of pain.

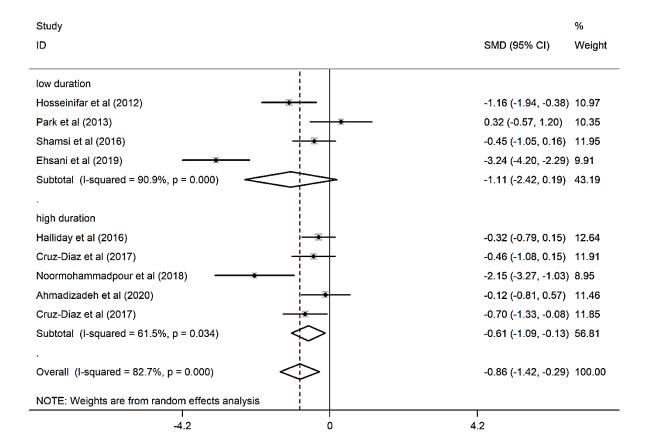


Figure 5. The effect of motor control training on standardized mean difference (95% CI) of disability.

SUPPLEMENTAL FILE

Supplementary 1: Literature search strategies Search strategy for PubMed/ Medline (NLM).

("level of pain" [All Fields] OR "pain intensity" [All Fields] OR "pain level" [All Fields]) AND ("low back pain" [tiab] OR "Low Back Ache" [tiab] OR "Low Back Pain" [tiab] OR "Lower Back Pain" [tiab] OR "Lumbago" [tiab] OR "Mechanical Low Back Pain" [tiab] OR "Postural Low Back Pain" [tiab] OR "Recurrent Low Back Pain" [tiab] OR "back pain" [tiab] OR backache [tiab] OR "Vertebrogenic Pain Syndrome" [tiab]) AND (Exercise [All Fields] OR "Exercise Therapy" [All Fields] OR "Rehabilitation Exercise" [All Fields] OR "Pilates Training" [tiab] OR "Pilates-Based Exercises" [tiab] OR "Exercise Movement Techniques" [All Fields] OR "Aerobic Exercise" [All Fields] OR "Exercise Training" [All Fields] OR "Physical Activity" [All Fields] OR "Physical Fitness" [All Fields] OR "Endurance Training" [All Fields]) AND ("motor activity" [All Fields] OR (Activity [All Fields]) OR "Motor Timing" [All Fields]) OR onset [All Fields] OR latency [All Fields] OR "Ultrasonography" [All Fields] OR "Ultrasonic Imaging" [All Fields]] OR "Ultrasound Imaging" [All Fields]]

Search strategy for Scopus

(ALL ("level of pain") OR ALL ("pain intensity") OR ALL ("pain level")) AND (TITLE-ABS ("low back pain") OR TITLE-ABS ("Low Back Ache") OR TITLE-ABS ("Low Back Ache") OR TITLE-ABS ("Low Back Pain") OR TITLE-ABS ("Lower Back Pain") OR TITLE-ABS ("Low Back Pain") OR TITLE-ABS ("Mechanical Low Back Pain") OR TITLE-ABS ("Postural Low Back Pain") OR TITLE-ABS ("Recurrent Low Back Pain") OR TITLE-ABS ("back pain") OR TITLE-ABS (backache) OR TITLE-ABS ("Vertebrogenic Pain Syndrome")) AND (ALL (Exercise) OR ALL ("Exercise Therapy") OR ALL ("Rehabilitation Exercise") OR TITLE-ABS ("Pilates Training") OR TITLE-ABS ("Pilates-Based Exercises") OR ALL ("Exercise Movement Techniques") OR ALL ("Aerobic Exercise") OR ALL ("Exercise Training") OR ALL ("Physical Activity") OR ALL ("Physical Fitness") OR ALL ("Endurance Training")) AND (ALL ("motor activity") OR (ALL(Activity) OR ALL ("Motor Timing")) OR ALL (onset) OR ALL (latency) OR ALL ("Ultrasonography") OR ALL ("Ultrasonic Imaging") OR ALL ("Ultrasound Imaging"))

Search strategy for Web Of Science (WOS)

(ALL=("level of pain") OR ALL=("pain intensity") OR ALL=("pain level"))

AND (TS=("low back pain") OR TS=("Low Back Ache") OR TS=("Low Backache") OR TS=("Low Backache") OR TS=("Lower Back Pain") OR TS=("Lumbago") OR TS=("Mechanical Low Back Pain") OR TS=("Postural Low Back Pain") OR TS=("Recurrent Low Back Pain") OR TS=("back pain") OR TS=(backache) OR TS=("Vertebrogenic Pain Syndrome")) AND (ALL=(Exercise) OR ALL=("Exercise Therapy") OR

ALL=("Rehabilitation Exercise") OR TS=("Pilates Training") OR TS=("Pilates-Based Exercises") OR ALL=("Exercise Movement Techniques") OR ALL=("Aerobic Exercise") OR ALL=("Exercise Training") OR ALL=("Physical Activity") OR ALL=("Physical Fitness") OR ALL=("Endurance Training")) AND (ALL=("motor activity") OR ALL=(Activity) OR ALL=("Motor Timing") OR ALL=(onset) OR ALL=(latency) OR ALL=("Ultrasonography") OR ALL=("ultrasound") OR ALL=("Ultrasonic Imaging")) OR ALL=("Ultrasound Imaging"))

Study	Study population (n)/ Average age (SD)	Disease duration	Intervention	Pain scale: mean (SD) before intervention	Disability scale: mean (SD) before intervention	Muscle variables/US frequency, mode	Result
Akbari et al. (2008) [34]	Subjects with chronic LBP: Group A (n =25)/39.6 (3.5) years; Group B (n = 24)/40 (3.6) years	Group A: 15.08(1.9) month Group B: 14.9 (3.1) month	double-blind RCT, each group received 8-week (2 times per weeks) exercise Group A: Motor control exercise: isolated, low load contraction of the TrA and LMU muscles in 4 different positions Group B: General exercise: maximum contraction of the abdominal and paravertebral muscles	` /	-	Thickness of TrA and LMU muscles during rest/ 7.5 MHz, B-mode	No significant between group difference.
Vasseljen et al. (2010) [35]	Subjects with chronic nonspecific LBP: Group A (n=36)/40.9(11.5) years, Group B (n=36)/43.4(10.2) years, Group C (n=37)/36(10.3)	Group A: 6(range 2- 19) years Group B: 9(range 2- 15) years Group C: 6(range 3.5-11.5) years	Single-blind RCT, each group received one exercise session per week over 8 weeks Group A: Ultrasound guided core stability exercise: ADIM exercises under real-time B-mode ultrasound guidance, co contraction of deep trunk muscles and pelvic floor muscles, home exercises Group B: sling exercise: high load specific exercise for the lumbo-pelvic area with emphasis on maintaining neutral position of spine Group C: General exercise: general trunk muscles strengthening exercises	Group B:3.6(1.7)	-	Contraction thickness ratio of TrA, IO and EO muscle during ADIM/ 10 MHz, B- mode	Significantly lower IO contraction thickness ratio and reduced TrA lateral slide in the US guided group compared to other interventions.

Study	Study population (n)/ Average age(SD)	Disease duration	Intervention	Pain scale: mean (SD) before intervention	Disability scale: mean (SD) before intervention	Muscle variables/US frequency, mode	Result
Vasseljen et al. (2012) [36]	Subjects with chronic nonspecific LBP: Group A (n=33)/41.5(11.9) years, Group B (n=34)/42.7(10) years, Group C (n=35)/36.3(10.4)	Group A:6 (range 0.4- 38) years Group B:7 (range 0.5- 26) years Group C:6 (range 0.3- 27) years	Single-blind RCT, each group received one exercise session per week over 8 weeks Group A: core stability exercise: ADIM exercises, co-contraction of deep trunk and pelvic floor muscles, home exercises Group B: sling exercise: elastic bands were attached to the pelvis to help the patient maintaining the lumbar spine stable in neutral position throughout a range of leg/ arm positions and movements, elastic band support was gradually reduced for exercise progression Group C: general exercise: general trunk and extremity muscles strengthening and stretching exercises	NPRS: Group A: 3.4 (1.3) Group B:3.5(1.8) Group C: 3.1(1.6)	ODI: Group A: 20.0 (7.2) Group B: 19.9 (9.0) Group C: 19.6 (8.3)	Change in onset (before to after the intervention) of TrA, IO, EO muscle during rapid shoulder flexion/10MHz, M-mode	No significant between group difference.
Hosseinifar et al. (2013) [21]	Subjects with chronic nonspecific LBP: Group A (n=15)/40.1(10.8) years, Group B (n=15)/36.6 (8.2) years	>3 months	Single-blind RCT, each group received 6 weeks (18 sessions, 3 times per week) exercise Group A: stabilization exercise: 6 steps with emphasis on isolated and co-contraction training of deep trunk and pelvic floor muscles Group B: McKenzie exercise: four extension type and two flexion type exercise	VAS: Group A: 4.33 (1.58) Group B: 4.40 (1.95)	FRI: Group A: 39.13 (15.53) Group B: 46.16 (17.87)	Thicknesses of TrA muscle during rest, ADIM and ASLR, Thicknesses of LMU muscle during rest and elevation of the contralateral arm / 12MHz, B-mode	Significant greater increasing thickness of the TrA and LMU muscles in MCT group and lower disability score. No significant between group in pain.

Study	Study population (n)/ Average age(SD)	Disease duration	Intervention	Pain scale: mean (SD) before intervention	Disability scale: mean (SD) before intervention	Muscle variables/US frequency, mode	Result
Park et al. (2013) [33]	Subjects with chronic nonspecific LBP: Group A (n=10)/ 45.72(15.43) years Group B (n=10)/ 41.35(6.13) years	>6 months	RCT, each group received 4 weeks (3 times per week) exercise Group A: ADIM Group B: core training: side bridge with abdominal bracing	-	ODI: Group A: 23.55(3.94) Group B: 20.25(4.55)	TrA, IO, EO muscles thickness during rest/ 10MHz, B-mode	No significant difference between groups for muscles thickness and disability.
Halliday et al. (2016) [23] and (2019) [25]	Subjects with nonspecific LBP Group A (n=35)/ 48.8(12.1) years, Group B (n=35)/ 48.3(14.2) years	Group A: 26.6 (22.3) weeks Group B: 37.7 (28.8) weeks	Single-blind RCT, each group received 12 exercise sessions over 8 weeks Group A: McKenzie exercise: repeated or sustained end-range loading strategies in loaded or unloaded postures, according to the patient's directional preference Group B: motor control exercise: isolated and co-contraction training of deep trunk and pelvic floor muscles during static and dynamic tasks with simultaneous breathing control	VAS: Group A: 4.50 (2.2) Group B: 5.40 (2.00)	PSFS: Group A: 12.32 (4.35) Group B: 11.31 (4.46)	Contraction ratio TrA, IO, EO muscles thickness during rest and low-load isometric knee flexion and extension/5MHz, B-mode	No significant difference between groups for muscles thickness, pain and disability
Shamsi et al. (2016)[24]	Subjects with nonspecific LBP Group A (n=22)/ 39.2(11.7) years, Group B (n=21)/ 48.0 (10.2) years	≥3 months	Quasi-RCT, each group received 16 exercise sessions over 3weeks Group A: core stability exercise: low levels of isometric contraction of abdominal muscles in minimally loading positions. Co-contraction training of local muscles Group B: general exercise: Abdominal and paravertebral muscles contraction	Group A: 5.13(0.98)	ODI: Group A: 50.5(12.1) Group B: 50.1(11.3)	Thicknesses of TrA, IO, EO and RA muscles during rest /15MHz, B-mode	A significant increase in RA muscle thickness was seen in general exercise group. No significant difference between groups for other outcomes.

Study	Study population (n)/ Average age (SD)	Disease duration	Intervention	Pain scale: mean (SD) before intervention	Disability scale: mean (SD) before intervention	Muscle variables/US frequency, mode	Result
Berglund et al. (2017) [12]	Subjects with nonspecific LBP Group A (n=32)/ 43.3(10.3) years Group B (n=33)/42.3(9.8) years	≥3 months	Single-blind RCT, each group received 12 exercise sessions over 2 months Group A: high-load lifting exercise: maintaining the lumbar neutral position while lifting and lowering the barbell from the floor Group B: low-load motor control exercises: maintaining the lumbar neutral position while performing movements with arms or legs	VAS: Group A: 4.13(2.38) Group B: 4.84(2.70)	1	LMU muscle thickness during rest /10-12 MHz, B-mode	No significant difference between groups regarding LMU muscle thickness and pain intensity.
Cruz- Diaz et al. (2017) [37]	Subjects with chronic LBP Group A (n=34)/ 36.94(12.46) Years Group B (n=34)/ 35.5 (11.98) years Group C (n=30)/ 36.32(10.67)	≥3 months	Single-blind RCT, groups A and B received two exercise session per week over 12 weeks Group A: Pilates mat Group B: Equipment based Pilates Group C: control group: no treatment	VAS: Group A: 4.64(1.22) GroupB:4.95(1.12) Group C: 4.84(1.04)	RMDQ: Group A: 11.38(5.02) Group B: 11.23(5.13) Group C: 10.50(4.89)	Contraction ratio of TrA muscle thickness during ADIM compared with the resting condition / 5MHz, B-mode	Both Pilates methods were effective in reducing the pain and disability scores and increasing the thickness of the TrA muscle compared to the control group.
Finta et al. (2018) [38]	Subjects with chronic nonspecific LBP Group A (n=21)/ 21.33(4.73) Years Group B (n=26)/ 22.31(5.15) Years	≥3 months	RCT, each group received two exercise session per week over 8 weeks Group A: Complex training training including dynamic and static balance and trunk muscles strengthening) Group B: complex training program and diaphragm training	VAS: Group A: 5.75 (1.68) Group B: 5.70 (1.74)	-	TrA, LMU and diaphragm muscles thickness during rest and sitting/5-10 MHz (TrA, diaphragm) 2-6 MHz (LMU), B-mode	Significant higher LMU thickness in the diaphragm training group.

Study	Study population (n)/ Average age(SD)	Disease duration	Intervention	Pain scale: mean (SD) before intervention	Disability scale: mean (SD) before intervention	Muscle variables/US frequency, mode	Result
Nabavi et al. (2018) [39]	Subjects with chronic nonspecific LBP Group A (n=20)/40.75(8.23) years Group B (n=21)/34.05(10.75) years	≥3 months	Single-blind RCT, each group received three exercise session per week over 4 weeks Group A: Stabilization exercise: stabilization exercise and routine physiotherapy (warm up and electrotherapy) Group B: routine exercise: routine physiotherapy	VAS: Group A: 3.30 (range 2.15- 4.27) Group B: 3.48 (range 2.18-4.12)	-	TrA, LMU muscles thickness and LMU CSA during rest/ 7.5 MHz (TrA) 3.5 MHz (LMU), B-mode	NO significant difference between studies.
Noormohammadpour et al. (2018) [22]	Subjects with chronic nonspecific LBP Group A (n=10)/43.3(7.5) years Group B (n=10)/41.3(6.4) years	Group A: 18.2 (6.4) months Group B: 16.4 (5.9) months	Single-blind RCT, group A received 8 weeks supervised home exercise Group A: Multi-step core stability exercise: ADIM and maintaining the lumbar paravertebral muscles during static and dynamic positions Group B: control group: no treatment	VAS: Group A: 3.84 (2.17) Group B: 3.62 (2.72)	RMDQ: Group A: 7.8(3.4) Group B: 9.5(4.9)	Thicknesses of TrA, IO, EO muscles during rest and ADIM/ 6–13 MHz, B- mode	A significant increase in all three abdominal muscles thickness, and significant reduced pain and disability in MCT group.
Ehsani et al. (2019) [41]	Subjects with chronic nonspecific LBP Group A (n=20)/36.40 (7.02) Years Group B (n=20)/35.50 (6.12) Years	≥3 months	Triple-Blinded RCT, each group received 10 session routine electrotherapy and 6-week (3 times per weeks) exercise Group A: Supervised stabilization exercise: exercise for deep trunk muscles in the different positions and static to dynamic conditions Group B: general exercise: exercise without emphasis on the deep trunk muscles contraction	VAS: Group A: 4.68 (0.82) Group B: 4.80 (0.92)	RMDQ: Group A: 11.65 (2.43) Group B: 12.25 (2.16)	Contraction ratio of TrA, IO, EO muscles during a related standing task compared with the resting condition, 7.5 MHz, B-mode	TrA muscle contraction ratio was significantly increased and disability score was reduced in the MCT group. Significant difference between groups regarding pain intensity and disability level.

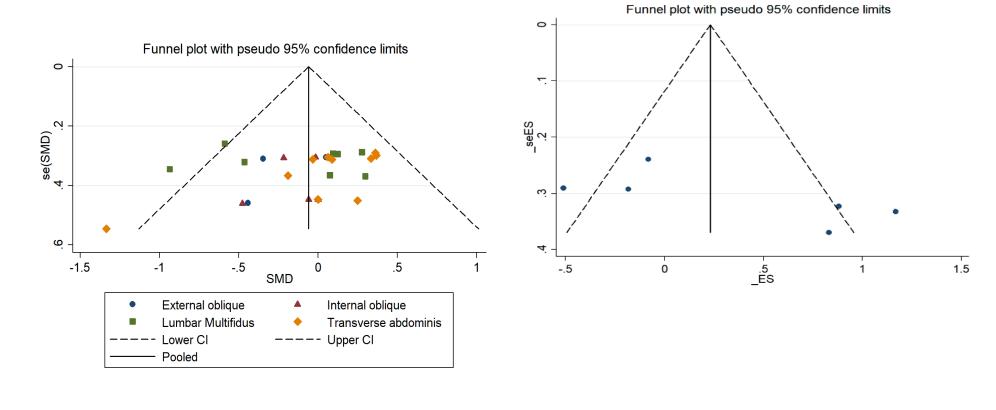
Supplementary 2. Details of included studies.

Study	Study population (n)/ Average age(SD)	Disease duration	Intervention	Pain scale: mean (SD) before intervention	Disability scale: mean (SD) before intervention	Muscle variables/US frequency, mode	Result
Ahmadizadeh et al. (2020) [40]	Subjects with chronic nonspecific LBP Group A (n=16)/ 31.12 (8.29) Years Group B (n=16)/ 34.19 (8.36) Years	≥3 months	Single-blind RCT, both groups received self-care training and group A received 8-week (3 times per weeks) exercise Group A: Stabilization exercise: 10 exercises for deep trunk muscles strengthening and restoring stability of the lumbar spine and lumbar-pelvic region Group B: control group: no treatment	VAS: Group A: 6.42 (2.50) Group B: 5.11 (1.95)	RMDQ: Group A: 5.81(4) Group B: 4.38 (2.3)	Contraction ratio of TrA, IO muscle during rest and abdominal hollowing/ 5.7 MHz, B-mode	TrA, IO thickness, significantly increased in the MCT group. No significant difference between groups regarding pain intensity and disability level.

ADIM= abdominal drawing-in maneuver, ASLR= active straight leg raising, B-mode = brightness mode, CSA= cross sectional area, EO = external oblique, FRI= functional rating index, IO = internal oblique, LBP=low back pain, LMU=lumbar multifidus, M-mode= motion mode, NR: not reported, NPRS= numerical pain rating scale, ODI= Oswestry disability index, PSFS=patient-specific functional scale, RCT= randomized clinical trial, RA=rectus abdominis, RMDQ= Rolland-Morris disability questionnaire, TrA=transversus abdominis, US=ultrasound, VAS= visual analogue scale

Supplementary 3

A)



Funnel plot, A) Muscle thickness, B) transverse abdominis contraction ratio,

B)

