Journal of Bodywork & Movement Therapies 25 (2021) 157–164

Contents lists available at ScienceDirect

Journal of Bodywork & Movement Therapies

journal homepage: www.elsevier.com/jbmt

Prevention and Rehabilitation

The effects of cognitive behavioural therapy delivered by physical therapists in knee osteoarthritis pain: A systematic review and meta-analysis of randomized controlled trials

Alexios Pitsillides [a], Dimitrios Stasinopoulos [b], Konstantinos Giannakou [a, *]

[a] Department of Health Sciences, School of Sciences, European University Cyprus, Nicosia, Cyprus
[b] Department of Physiotherapy, Laboratory of Neuromuscular and Cardiovascular Study of Motion, University of West Attica, Athens, Greece

ARTICLE INFO

Article history:
Received 13 April 2020
Received in revised form
14 October 2020
Accepted 4 November 2020

ABSTRACT

Background: Recent evidence suggests that knee osteoarthritis (KOA) chronic pain can result in brain structural and organizational changes. Thus, patients' pain level, emotional status, and perception of their condition might be negatively altered. An approach to reverse such adaptations to chronic pain is cognitive behavioural therapy (CBT). Combining CBT with exercise might enhance therapy outcomes.
Objectives: To identify the effect of combining exercise and CBT when delivered by a physical therapist in KOA pain.
Methods: A systematic search in PubMed, Cochrane, and Medline Complete (EBSCO) databases was conducted from their inception to March 2020, following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines. Study risk of bias and quality were assessed through the Risk-of-bias 2 (ROB2) and PEDro scales.
Results: Six primary studies met eligibility criteria. All studies had a low risk of bias and were divided into two sub-groups, in-person interventions and distance interventions. Both groups of studies showed within group participant improvements. In regards of WOMAC pain subscale, our meta-analysis revealed an overall deduction of −1.42 (95% CI: −1.76, −1.09; $I^2 = 58\%$), −1.62 (95% CI: −1.97, −1.27; $I^2 = 0\%$) in centre-based intervention, and −1.28 (95% CI: −1.75, −0.81; $I^2 = 73\%$) in distance delivered intervention.
Conclusion: Combining exercise and CBT seems to be an effective method to reduce KOA pain, although it is based on a small number of studies. Further studies are needed to reveal any differences when each intervention is applied separately.

1. Introduction

Knee osteoarthritis (KOA) is considered a major cause of disability in the older population (Vos et al., 2012). While this condition is characterized by a variety of symptoms, such as muscle weakness, reduced functionality, and joint instability (Fransen et al., 2015); pain is the major symptom that will lead an individual to seek medical care. Pain represents the brain's response to noxious signals sent by the nociceptive system. When these signals reach above the individual's threshold, the brain will respond with pain (Moseley and Butler 2013). When this alarm stays active for long periods (chronic pain), changes may be observed in the central nervous system (CNS) (Wand et al., 2011; Pelletier et al., 2015). These neuroplastic changes might alter the symptoms by altering the structure and organization of the brain (Pelletier et al., 2015).

This maladaptation can be reversed with interventions such as cognitive or behavioural therapy (Pelletier et al., 2015). Cognitive behavioural therapy (CBT) is an intervention where patients' thoughts, beliefs, and feelings regarding their pathology are addressed. Exercise, together with weight loss, are the most effective conservative approaches to treat KOA (Mills et al., 2018). Such interventions aim to reduce joint mechanical loading through weight reduction or increases in strength (Mills et al., 2018). Whilst the optimal treatment remains unknown, imaging improvements have provided novel insights into the contributions of the CNS to chronic pain in patients with other musculoskeletal disorders (Wand et al., 2011). These findings highlighted the need for

* Corresponding author. Department of Health Sciences, School of Sciences, European University Cyprus, 6 Diogenes Str, Engomi 2404, P.O. Box: 22006, 1516, Nicosia, Cyprus.
E-mail address: K.Giannakou@euc.ac.cy (K. Giannakou).

https://doi.org/10.1016/j.jbmt.2020.11.002
1360-8592/

clinicians to reconsider their approaches to musculoskeletal disorders (Pelletier et al., 2015; Mills et al., 2018). Multidimensional approaches that do not exclusively address KOA as a local pathology have therefore emerged, one of which being the combination of exercise and CBT.

Previously, the effects of CBT in KOA pain have been summarized in a systematic review independently of other interventions (Ismail et al., 2017). In addition, the available interventions that can improve the quality of life or psychological factors of patients with KOA were also evaluated in a previous review study (Briani et al., 2018). We believe that our systematic review will add to the body of evidence as we focused on the combination of both exercise and CBT in KOA pain. We are exploring how this pathology should be not exclusively addressed as a central (CBT) or local (exercise) pathology. In addition, our study is differentiated from the second review study (Briani et al., 2018), as we focus on alternate outcomes of interest and we further investigate the most suitable profession to apply such an intervention, being physical therapists. We consider that it is of high importance to investigate the effectiveness of cognitive interventions combined with exercise. Any positive results might enhance daily practice and thus reduce an individual's symptoms. A better management of KOA population pain might further translate to a reduction of knee surgeries and possible benefits for health systems.

The aim of this systematic review is to reveal the effectiveness of combining exercise and CBT, delivered by physical therapists, in reducing KOA pain. Such an intervention, that consists of therapeutic exercise and psychological interventions shall ultimately be delivered either from a psychologist trained in therapeutic exercise, or from a physical therapist trained in CBT. Given that a KOA patient will most frequently visit a physical therapist when suffering from pain, we decided to limit our search to physical therapists. To the best of our knowledge, this is the first systematic review evaluating the combination of these two interventions, delivered by physical therapist in KOA pain.

2. Methods

This systematic review and meta-analysis was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines (Moher et al., 2009). The protocol of our study was not registered with the International Prospective Register of Systematic Reviews (PROSPERO).

2.1. Search strategy

Two researchers (AP & KG) independently searched PubMed, Cochrane, and Medline Complete (EBSCO) databases to identify randomized clinical trials that examine the effectiveness of exercise combined with CBT in patients with KOA. The literature searches were conducted from inception to March 2020, restricted to English language publications but no date restriction was applied. The search was performed using the Boolean operators AND, OR, parentheses, and quotation marks and adjustments were made as needed to match each database's particularities. The search strategy used the keywords: (knee osteoarthritis OR knee degradation OR knee pathology OR knee pain) AND (cognitive OR metronome OR coping OR behavioural OR somatisation OR pain catastrophizing OR mirror OR self-efficacy) AND (pain OR WOMAC OR VAS OR “Western Ontario AND McMaster Universities Osteoarthritis Index” OR “Numeric pain scale”). Additional information concerning the search strategy is presented in Supplementary Table 1. First, the title and abstract of each article identified through the search were examined, and then the full texts of potentially eligible articles were examined for evaluation. Discrepancies were resolved by mediation and discussion with a third author (DS). Reference list of relevant studies excluded or included was screened to identify additional studies.

2.2. Eligibility criteria and data extraction

Identification of the included studies was done following the PICOS characteristics (Participants, Intervention, Comparison, Outcomes, and Study type) criteria. Participants were only patients with KOA. As for the intervention, studies of CBT and exercise delivered by physical therapists were included; no co-interventions were allowed. For the comparison, studies that had a control/comparison group were eligible for inclusion. The chosen outcome was pain and the only study type eligible was randomized controlled clinical trial. Only studies written in English were considered with no restriction on the time of publication. We did not include review articles, dissertations or theses, published abstracts, book chapters, and points of view/expert opinions. In case of not-reported information, we contacted the corresponding author to request further information data.

Data extraction was performed independently by two authors (AP & KG) and any inconsistencies were resolved with discussion. From each eligible study, the following information was extracted: reference, subject details, intervention, session details, pain outcome measures and time of measures. Then this information was analyzed in order to categorize the included studies in subgroups for further analysis.

2.3. Quality assessment

For the assessment of the methodological quality of the included studies, the Cochrane risk of bias tool (RoB2) was used (Sterne et al., 2019). RoB2 is recommended for assessing the risk of bias in randomized trials. It consists of five domains, each focusing on a different aspect of the trial. Each domain has several signalling questions and an algorithm is then used to judge the methodological quality of the trial, based on answers to these. The categories for each question were classified as low, some concerns, or high risk of bias.

We used a second quality tool to compare the results and examine the studies again when disagreements occurred using the PEDro scale (Morton, 2009). Pedro scale is a 10 points scale where studies with a score over 6/10 are thought to be low methodological bias. Each of the 10 questions can be answered with yes, no or unclear. We used the Best Evidence Synthesis (BES), modified by Tulder et al. (2003) to identify the level of evidence regarding the effectiveness of the techniques studied in our systematic review.

2.4. Data synthesis and statistical analysis

The main outcomes were synthesised qualitatively, based on descriptive statistics and/or the results of statistical analyses reported in the primary studies. All studies included presented pain levels as a continuous variable expressed as mean ± standard deviation (SD) or as mean (confidence interval).

Inverse-variance weighted approach was adopted for continuous data meta-analysis with a Standardized Mean Difference (SMD) and 95% Confidence Interval (CI), to estimate the size of the effect calculated by pooling the SMD of each individual study based on the mean, SD, and sample size. Two-tailed P value < 0.05 was considered statistically significant. We assessed heterogeneity among individual effect estimates and we reported the P value of the $\chi2$-based Cochran Q test. The variation in estimates attributable to heterogeneity is quantified by the measure I^2 metric for inconsistency (Higgins and Thompson 2002). We expected statistical heterogeneity, so we used the random effects model for the meta-analysis. To further explore sources of heterogeneity, we carried out subgroup analyses considering the intervention type (face-to-face or distance delivered). The presence of publication bias was examined by visual inspection of funnel plots and evaluated formally with Egger's regression asymmetry test (Egger et al., 1997; Sterne et al., 2001). All statistical analyses were performed by STATA 14.0 software (STATA Corp, College Station, TX).

3. Results

3.1. Study selection

The databases search yielded 1836 relevant articles. After duplicates and non-RCTs were removed, 1251 articles remained. After a title and abstract screening, 35 studies were eligible for full-text screening. Twenty-one studies were further excluded because the intervention group was not supervised by a physiotherapist. Seven more studies were excluded because the subjects were not patients with only KOA, and 1 study was excluded because the intervention was not a combination of exercise and CBT. Thus, 6 studies were included in this systematic review. Further information concerning the study flow is presented in Fig. 1.

3.2. Study characteristics

A total of 800 patients where included in our systematic review. Participants in all studies included were on average over 45 years old and suffered from KOA. The total number of the patients included in the intervention and control groups was 373 and 427 respectively. The total number of males and females was 121 and 252 respectively in the intervention groups and 158 and 269 in the control groups. We divided the included study results into two categories. The first category included four studies that had a face-to-face setup (Kao et al., 2012; Hunt et al., 2013; Silva et al., 2015; Bennell et al., 2016) while the second one included two studies where a distance intervention was applied (Bennell et al., 2017; Hinman et al., 2019). In regards to pain intensity, the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) scale was used in 5 of the included studies (Kao et al., 2012; Hunt et al., 2013; Bennell et al. 2016, 2017; Hinman et al., 2019). The Short-form 36 (SF-36) questionnaire was used by 2 trials (Kao et al., 2012; Silva et al., 2015), while the Numeric Rating Scale (NRS) was used in 3 (Hunt et al., 2013; Hinman et al., 2019; Bennell et al., 2016) studies. The Arthritis Self-Efficacy Scale (ASES) was used by 2 (Bennell et al., 2017; Hinman et al., 2019) studies and Lequesne index was used in 1 study (Silva et al., 2015). Main characteristics of the studies included are presented in Table 1.

3.3. Pain results

3.3.1. Face-to-face intervention group

Information concerning the pain results of face-to-face intervention is presented in Table 2. Kao et al. presented the total WOMAC score; thus, it was not possible to identify the results of WOMAC pain sub-scale separately. In the same study, SF-36 pain subscale scores were 70.5 ± 18.7, 70.0 ± 16.7, and 70.0 ± 16.7 at baseline, post-intervention, and on follow-up, respectively. There

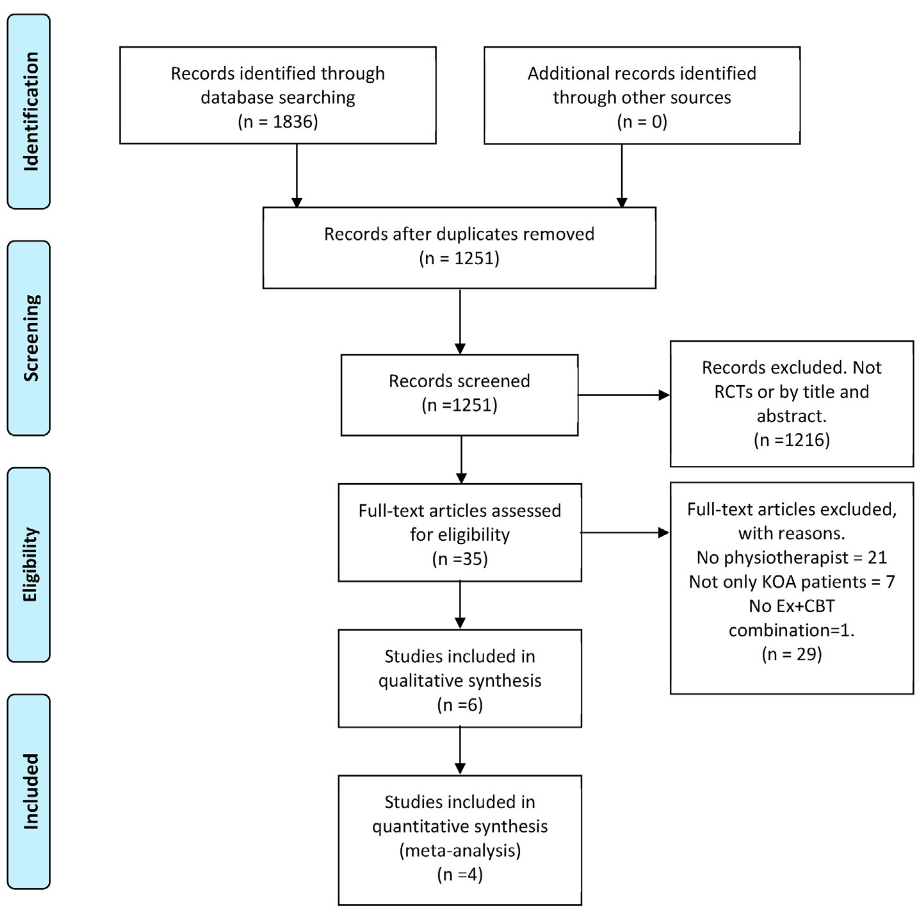

Fig. 1. PRISMA 2009 Flow diagram.

Table 1
Included studies' characteristics.

Reference	Subjects	Intervention	Session details	Pain outcome measures	Time of measures
Kao et al. (2012)	205S IG: n = 114, 67.3 ± 10.1 CG: n = 91, 68.2 ± 11.2	IG: Taipei Osteoarthritis Program CG: routine care	IG: 80 min session once per week. Group of 10 −15. Patient education (20 min), exercise (20 min) and 4 weekly coping sessions (40 min)	SF-36 WOMAC	Baseline, 4 weeks (post) and 8 weeks (follow-up)
Hunt et al. (2013)	20S IG: n = 10, 66.0 ± 4.7 CG: n = 10, 58.9 ± 4.0	IG: exercise and PCST CG: exercise and counselling	IG: 10 weeks, 60 min, one-on-one, lower limb exercises and walking CG: same exercise program but no PCST	NRS WOMAC	Baseline and 11 weeks
Silva et al. (2015)	41S IG: n = 15, 57 ± 6.01 CG: n = 15, 60 ± 7.76	Both groups received self-management education program IG: education and exercise CG: general information	1 session of 90 min self- management education IG: 60 min session, 2 per week for 8 weeks (education 15 min + exercises 45 min)	Lequesne questionnaire SF-36	Baseline and 8 weeks
(K L Bennell et al., 2016)	222S Exercise: n = 75, 62.7 ± 7.9 PCST: n = 74, 63.0 ± 7.9 PCST/Exercise: n = 73, 64.6 ± 8.3	PCST: pain education and training in cognitive and behavioural pain coping skills Exercise: 6 exercises PCST/exercise: both	10 sessions over 12 weeks PCST 45 min Exercise 25 min PCST/exercise 70 min All home-based practice, depended on group	VAS WOMAC	Baseline, 12 weeks and 52 weeks evaluation at clinic 22 weeks, 32 weeks and 42weeks mailed questionnaire
(Kim L. Bennell et al., 2017)	148S IG: n = 74, 60.8 (6.5) CG: n = 74, 61.5 (7.6)	IG: PCST and exercise, internet delivered CG: education Internet delivered	IG: 1st phase: educational material second phase: PCST 35–45 min per session weekly for 8 weeks 3rd phase: 7 skype sessions. Exercise home-based program prescription	Numeric pain scale WOMAC	Online at baseline, 3 months and 9 months
Hinman et al. (2019)	175S IG: n = 87, 62.4 (9.1). CG: n = 88, 62.5 (8.1).	IG: exercise and behavioural change techniques CG: existing service Telephone delivered	IG: 5–10 consultations with a physiotherapist over 6 months Prescribed 5–6 exercises 3 times per week CG: information by an existing service	NRS WOMAC	Baseline, 6 months and 12 months

Abbreviations: WOMAC - Western Ontario and McMaster Universities Osteoarthritis Index; SF-36 – Short-form 36 questionnaire; NRS – Numeric Rating Scale; VAS – Visual Analogue Scale, S – subjects, IG – Intervention group, CG – Control Group. PCST – Pain coping skills training.

were no significant within-group changes group ($p < 0.241$). In the second study (Hunt et al., 2013), the NRS score decreased from 4.2 ± 1.5 to 2.8 ± 1.6 and the WOMAC pain subscale decreased from 6.6 ± 1.0 to 1.7 ± 3.3. In the third study (Silva et al., 2015), the Lequesne pain subscale decreased from 4.93 ± 1.33 to 2.60 ± 1.55. The within-group change was statistically significant ($p < 0.05$). The SF-36 pain subscale score decreased from 44.47 ± 11.78 to 57.60 ± 12.48 ($p < 0.05$) in the same study. The last study included in this subgroup (Bennell et al., 2016) reported a Visual Analogue Scale (VAS) score decrease from 58.4 ± 12.8 to 26.4 ± 18.4 after intervention, 28.2 ± 21.6 at the first follow-up and 31.7 ± 22.6 at the second follow-up. The within-group pain decrease was statistically significant ($p < 0.01$). Concerning WOMAC pain sub-scale, the authors reported a score of 9.0 ± 2.8 at baseline, 4.5 ± 2.9 after the intervention, 5.3 ± 3.3 at the first follow-up, and 5.2 ± 3.3 at the second follow-up.

3.3.2. Distance-delivered intervention group

The pain results of distance-delivered intervention group are presented in Table 3. In the first study of this group (Bennell et al., 2017) the WOMAC pain sub-scale score decreased from 9.0 ± 2.4 to 5.1 ± 2.7 post-intervention and 5.1 ± 2.9 at the first follow-up. The within-group difference from baseline to post-intervention was 3.9 (3.1–4.7) with $p < 0.05$ and 3.7 (2.9–4.5) with $p < 0.05$ from baseline to follow-up. The ASES pain sub-score increased from 6.1 ± 1.8 at baseline to 7.6 ± 2.0 and 7.5 ± 2.0 at post-intervention and follow-up, respectively ($p < 0.05$). In the second study (Hinman et al., 2019), the NRS pain score decreased from 6.0 ± 1.5 at

Table 2
Mean values of centre-based studies, intervention groups (CBT + Exercise).

Study	Pain measure	Baseline [mean (SD)]	Post-intervention [mean (SD)]	Follow-up [mean (SD)]	Second follow-up [mean (SD)]	Baseline to Post-intervention [mean (SD)]	Baseline to follow-up [mean (SD)]	Baseline to second follow-up [mean (SD)]
Kao et al. (2012)	SF-36 pain	70.5 (18.7)	70.0 (16.7)	70.0 (16.7)	–	−0.44 ± 19.2 p < 0.241	−0.44 (19.2) p < 0.241	–
	WOMAC total score	38.5 (31.30	41.7 (32.2)	41.2 (31.2)	–	3.2 ± 34.0	2.7 (33.0)	–
Hunt et al. (2013)	NRS pain	4.2 (1.5)	2.8 (1.6)	–	–	−1.4 (0.6)	–	–
	WOMAC pain	6.6 (1.0)	1.7 (3.3)	–	–	−5.1 (0.5)	–	–
Silva et al. (2015)	Lequesne Index pain	4.93 (1.33)	2.60 (1.55)	–	–	p < 0.05	–	–
	SF-36 pain	44.47 (11.78)	57.60 (12.48)	–	–	p < 0.05	–	–
(K L Bennell et al., 2016)	VAS pain	58.4 (12.8)	26.4 (18.4)	28.2 (21.6)	31.7 (22.6)	31.4 (2.5), p < 0.001	30.6 ± 2.9, p < 0.001	26.3 (2.8), p < 0.001
	WOMAC pain	9.0 (2.8)	4.5 (2.9)	5.3 (3.3)	5.2 (3.3)	4.3 (0.4), p < 0.001	3.7 (0.4), p < 0.001	3.5 (0.5), p < 0.001

Abbreviations: WOMAC - Western Ontario and McMaster Universities Osteoarthritis Index; SF-36 – Short-form 36 questionnaire; NRS – Numeric Rating Scale; VAS – Visual Analogue Scale.

Table 3
Mean values of distance delivered studies, intervention groups (CBT + Exercise).

Study	Pain measure	Baseline [mean (SD)]	Post-intervention [mean (SD)]	Follow-up [mean (SD)]	Second follow-up	Baseline to Post-intervention [mean (SD)]	Baseline to follow-up [mean (SD)]
(Kim L Bennell et al., 2017)	WOMAC pain	9.0 (2.4)[b]	5.1 (2.7)[b]	5.1 (2.9)[b]	–	3.9 (3.1–4.7)[a]	3.7 (2.9–4.5)[a]
	Self-efficacy (ASES) pain	6.1 (1.8)[b]	7.6 (2.0)[b]	7.5 (2.0)[b]	–	−1.5 (−2.0 to −1.0)[a]	−1.3 (−1.8 to −0.8)[a]
Hinman et al. (2019)	NRS pain	6.0 (1.5)[b]	3.5 (2.1)[b]	3.9 (2.4)[b]	–	2.5 (2.0)[b]	2.1 (2.2)[b]
	WOMAC pain	8.6 (2.7)[b]	5.6 (3.0)[b]	5.7 (3.3)[b]	–	3.0 (2.5)[b]	2.9 (2.9)[b]
	Self- efficacy (ASES) pain	5.9 (1.6)[b]	7.3 (1.9)[b]	7.3 (2.0)[b]	–	−1.4 (2.1)[b]	−1.4 (2.0)[b]

Abbreviations: WOMAC - Western Ontario and McMaster Universities Osteoarthritis Index; ASES-Arthritis Self-Efficacy Scale; NRS – Numeric Rating Scale.
[a] Expressed as mean (95% confidence interval).
[b] Expressed as [mean (SD)].

baseline to 3.5 ± 2.1 after intervention and to 3.9 ± 2.4 at follow-up. The WOMAC pain subscale score decreased from 8.6 ± 2.7 at baseline to 5.6 ± 3.0 post-intervention and 5.7 ± 3.3 at follow-up in the same study. Still in the same study, the ASES pain score increased from 5.9 ± 1.6 at baseline to 7.3 ± 1.9 after intervention and to 7.3 ± 2.0 at follow-up.

3.3.3. *Meta-analysis results*

For the purpose of the quantitative meta-analysis, data from four studies that used the WOMAC pain sub-scale for a total of 565 participant were combined. The pooled SMD for the 4 studies based on the random-effects model was −1.42 (95% CI: −1.76, −1.09; $I^2 = 58\%$, P heterogeneity = 0.067). The overall effect size for SMD calculated as Z was 8.37 ($P < 0.0001$) (Fig. 2). The subgroup meta-analysis of centre-based studies for the CBT and exercise combination revealed a statistically important reduction of −1.62 (95% CI: −1.97, −1.27; $I^2 = 0\%$, P heterogeneity = 0.465, $P < 0.0001$) points in WOMAC pain subscale in comparison with control group. Distance delivered intervention subgroup resulted to a statistically important pain decrease with the overall WOMAC pain subscale pain difference was −1.28 (95% CI: −1.75, −0.81; $I^2 = 73\%$, P heterogeneity = 0.054, $P < 0.0001$) (Fig. 2).

3.3.4. *Publication bias*

The publication bias of the studies was determined by visual inspection of funnel plot for asymmetry or outliers and then evaluated formally with Egger's regression asymmetry test. The shape of the funnel plot does not indicate obvious asymmetry (Fig. 3) and Egger's test also provided non-significant results, suggesting no evidence of publication bias in the current meta-analysis

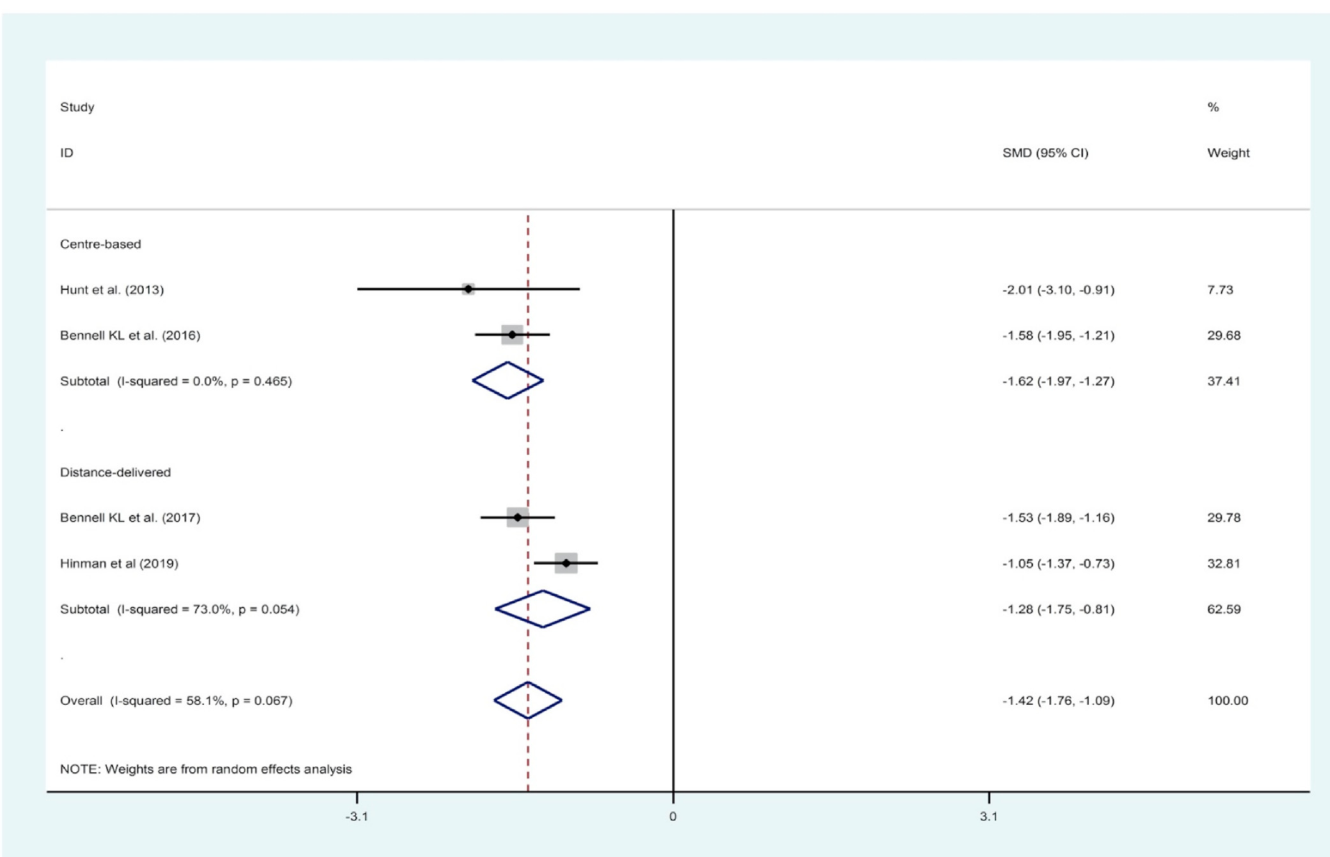

Fig. 2. Forest plot of standardized mean differences in WOMAC pain for the four included in the meta-analysis.

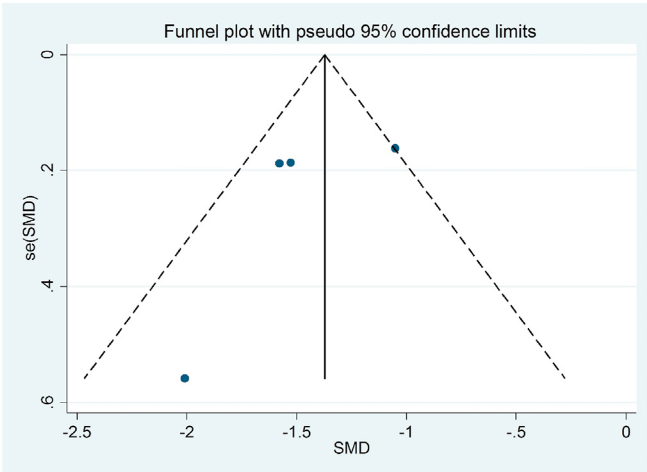

Fig. 3. Funnel plot for publication bias evaluation of the studies included in the meta-analysis.

(P = 0.409).

3.3.5. Methodological quality

As illustrated in Fig. 4, all the included studies had low risk of methodological bias according to the ROB2 tool. This result was further confirmed by the PEDro score. Two of the included studies were evaluated as 6/10 (Kao et al., 2012; Silva et al., 2015), two as 7/10 (Bennell et al. 2016, 2017) and two as 8/10 (Hunt et al., 2013; Hinman et al., 2019) (Table 4).

4. Discussion

In this systematic review we examined the effectiveness of CBT combined with exercise delivered by physical therapists in regards of KOA pain. Our findings suggest that the combination of CBT training and exercise can effectively reduce KOA pain. It is essential for a physical therapist, when managing an individual suffering from KOA, to interrupt his symptoms vicious cycle where pain will decrease activity and inactivity will lead to neural and muscular degeneration. According to our findings adding CBT to exercise might be altering any fault beliefs of a patient that might have been keeping him away from exercising or enhancing his pain.

4.1. Effectiveness of exercise and CBT combination on pain

The first study (Kao et al., 2012) did not report a significant change in pain levels in either pain outcome measure. It is impossible to know if there was a reduction in WOMAC pain subscale since the authors presented only the total score of that scale. In the remaining studies, centre based sub-group analyses (Hunt et al., 2013; Silva et al., 2015; Bennell et al., 2016) revealed improvements in all pain outcome measures. All the measurements (VAS, NRS, WOMAC, SF-36, and Lesquesne) showed improvements.

With regards to the distance-delivered intervention, both included studies (Bennell et al., 2017; Hinman et al., 2019) reported improvements in all of their pain measures. WOMAC and NRS scores decreased and the ASES increased. With 3 high-quality RCTs (Hunt et al., 2013; Silva et al., 2015; Bennell et al., 2016) in favour of this intervention and 1 not reporting effectiveness (Kao et al., 2012), it can be concluded that the combination of CBT and exercise delivered by physical therapists is supported with strong evidence of KOA pain reduction.

In order to identify the differences between combined treatment and with exercise only, studies should include groups where the subjects would only undergo exercise and compare their results to the suggested approach. Only one study (Bennell et al., 2016) had a group with an exercise-only approach. In that study, the vast majority of the measurements were equal and statistically nonsignificant. Thus, it is currently unclear whether CBT combined with exercise is superior to an exercise-only program.

To identify differences between the two interventions, only CBT groups should be included in the studies. Only one such study was done (Bennell et al., 2016) and it was seen that the combination of the two techniques was superior in the first follow-up according to the VAS score and at post-intervention and first follow-up according to the WOMAC pain subscale score. Thus, the results are conflicting and clear recommendations cannot be made. Our results

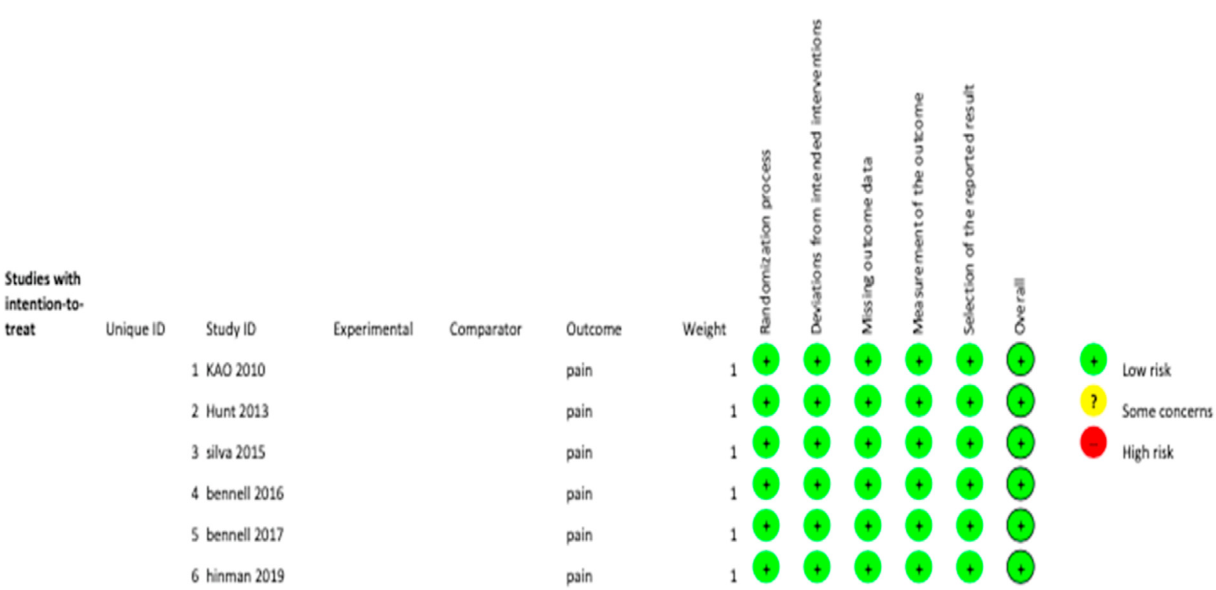

Fig. 4. Methodological quality assessment (RoB2).

Table 4
Pedro scale methodological evaluation.

Study	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	Q9	Q10	Q11	Total
Kao et al. (2012)	Y	Y	N	Y	N	N	N	Y	Y	Y	Y	6/10
Hunt et al. (2013)	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8/10
Silva et al. (2015)	Y	Y	Y	Y	N	N	Y	N	N	Y	Y	6/10
(K L Bennell et al., 2016)	Y	Y	Y	Y	N	N	Y	N	Y	Y	Y	7/10
(Kim L. Bennell et al., 2017)	Y	Y	Y	Y	N	N	N	Y	Y	Y	Y	7/10
Hinman et al. (2019)	Y	Y	Y	Y	N	N	Y	Y	Y	Y	Y	8/10

Note: Eligibility criteria (Q1) item does not contribute to total score. Q1: eligibility criteria were specified, Q2: subjects were randomly allocated to groups (in a crossover study, subjects were randomly allocated an order in which treatments were received), Q3: allocation was concealed, Q4: the groups were similar at baseline regarding the most important prognostic indicators, Q5: there was blinding of all subjects, Q6: there was blinding of all therapists who administered the therapy, Q7: there was blinding of all assessors who measured at least one key outcome, Q8: measures of at least one key outcome were obtained from more than 85% of the subjects initially allocated to groups, Q9: all subjects for whom outcome measures were available received the treatment or control condition as allocated or, where this was not the case, data for at least one key outcome was analyzed by intention to treat, Q10: the results of between-group statistical comparisons are reported for at least one key outcome, Q11: the study provides both point measures and measures of variability for at least one key outcome.

are in agreement with those of a previous systematic review (Ismail et al., 2017). Despite that the authors reported no statistically significant decrease in WOMAC pain subscale of CBT independently, they report significant differences when CBT is combined with other interventions such as exercise.

4.2. Strengths and limitations

There are several strengths to our study. To the best of our knowledge, this is the first systematic review and meta-analysis that evaluates the available evidence from published RCTs on the effectiveness of the combination of these two interventions, delivered by physical therapist in KOA pain. Two reviewers independently and rigorously reviewed and extracted data to minimize the chance of error. In addition, individual studies were assessed for the risk of bias with validated assessment tools.

However, our systematic review presents some limitations. First, only articles written in English were considered, which could have resulted in missed studies. Further, the number of studies comparing the combination of the two interventions with each intervention independently was not sufficient to report any differences between these interventions. Our results cannot be generalized in all health professions since we included only physical therapist delivered intervention studies. Lastly, our search relied only in 3 databases thus it is unknown if any studies have been missed.

Clearly, further high-quality RCTs are needed in order to identify the differences between CBT/exercise with exercise or CBT alone. We opine that CBT interventions can be improved. We suggest that optical and/or acoustic cues are a suitable choice. Such interventions target the central system of an individual during his/her rehabilitation program thus not increasing session time. Additionally, further research is needed in order to identify the most effective CBT method since different approaches have been used by the authors of the included studies.

5. Conclusion

While the combination of exercise and CBT is an effective approach for KOA pain when delivered by physical therapists, the results did not favour the use of this combination against each intervention alone. Furthermore, KOA is a condition that must be addressed not only as a local pathology. Current results are limited but show that by enhancing exercise programs with CBT, additional symptom improvements may take place. Further research is needed to identify the exact impact of such an approach.

5.1. Clinical relevance

- Current available evidence of CBT and exercise for KOA pain shows low risk of bias
- The overall findings show that the combination of both approaches has a positive effect in multiple pain outcome measures

Funding

No funding.

CRediT authorship contribution statement

Alexios Pitsillides: Conceptualization, Writing - review & editing, Formal analysis, Methodology. **Dimitrios Stasinopoulos:** Conceptualization, Writing - review & editing. **Konstantinos Giannakou:** Conceptualization, Writing - review & editing, Formal analysis, Methodology, Supervision, All authors read and approved the final manuscript.

Declaration of competing interest

There was no conflict of interest.

Acknowledgements

The authors declare no conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jbmt.2020.11.002.

References

Bennell, K.L., Ahamed, Y., Jull, G., Bryant, C., Hunt, M.A., Forbes, A.B., Kasza, J., et al., 2016. Physical therapist-delivered pain coping skills training and exercise for knee osteoarthritis: randomized controlled trial. Arthritis Care Res. 68 (5), 590-602. https://doi.org/10.1002/acr.22744.

Bennell, Kim L., Nelligan, Rachel, Dobson, Fiona, Rini, Christine, Keefe, Francis, Kasza, Jessica, French, Simon, et al., 2017. Effectiveness of an internet-delivered exercise and pain-coping skills training intervention for persons with chronic knee pain: a randomized trial. Ann. Intern. Med. 166 (7), 453–462. https://doi.org/10.7326/M16-1714.

Briani, Ronaldo Valdir, Ferreira, Amanda Schenatto, Pazzinatto, Marcella Ferraz, Pappas, Evangelos, De Oliveira Silva, Danilo, Mícolis de Azevedo, Fábio, 2018. What interventions can improve quality of life or psychosocial factors of individuals with knee osteoarthritis? A systematic review with meta-analysis of primary outcomes from randomised controlled trials. Br. J. Sports Med. 52 (16), 1031–1038. https://doi.org/10.1136/bjsports-2017-098099.

Egger, Matthias, George, Davey Smith, Schneider, Martin, Minder, Christoph, 1997.

Bias in meta-analysis detected by a simple, graphical test. Br. Med. J. 315 (7109), 629–634. https://doi.org/10.1136/bmj.316.7129.469.

Fransen, Marlene, McConnell, Sara, Harmer, Alison R., Van Der Esch, Martin, Simic, Milena, Bennell, Kim L., 2015. Exercise for osteoarthritis of the knee: a Cochrane systematic review. Br. J. Sports Med. 49 (24), 1554–1557. https://doi.org/10.1136/bjsports-2015-095424.

Higgins, Julian P.T., Thompson, Simon G., 2002. Quantifying heterogeneity in a meta-analysis. Stat. Med. 21 (11), 1539–1558. https://doi.org/10.1002/sim.1186.

Hinman, R.S., Campbell, P.K., Lawford, B.J., Briggs, A.M., Gale, J., Bills, C., Kasza, J., et al., 2019. Does telephone-delivered exercise advice and support by physiotherapists improve pain and/or function in people with knee osteoarthritis? Telecare randomised controlled trial. Br. J. Sports Med. https://doi.org/10.1136/bjsports-2019-101183.

Hunt, M.A., Keefe, F.J., Bryant, C., Metcalf, B.R., Ahamed, Y., Nicholas, M.K., Bennell, K.L., 2013. A physiotherapist-delivered, combined exercise and pain coping skills training intervention for individuals with knee osteoarthritis: a pilot study. Knee 20 (2), 106-112. https://doi.org/10.1016/j.knee.2012.07.008.

Ismail, Ayah, Moore, Catherine, Alshishani, Natasha, Yaseen, Khalid, Abdullah Alshehri, Mansour, 2017. Cognitive Behavioural Therapy and Pain Coping Skills Training for Osteoarthritis Knee Pain Management: A Systematic Review, pp. 2228–2235.

Kao, Jung, Mu, Wu, Meng Pin, Tsai, Mei Wun, Chang, Wan Wen, Wu, Shu Fang, 2012. The effectiveness of a self-management program on quality of life for knee osteoarthritis (OA) patients. Arch. Gerontol. Geriatr. 54 (2), 317–324. https://doi.org/10.1016/j.archger.2011.05.018.

Mills, K., Hübscher, M., O'Leary, H., Moloney, N., 2018. Current concepts in joint pain in knee osteoarthritis. https://doi.org/10.1007/s00482-018-0275-9.

Moher, D, Liberati, A, Tetzlaff, J, Altman, DG, Prisma Group, 2009 Jul 21. Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. PLoS med 6 (7), e1000097.

Morton, Natalie A De, 2009. The PEDro scale is a valid measure of the methodological quality of clinical trials: a demographic study. Aust. J. Physiother. 55 (2), 129–133. https://doi.org/10.1016/S0004-9514(09)70043-1.

Moseley, G. Lorimer, Butler, David S., 2013. Explain pain supercharged. J. Chiropr. Educ. https://doi.org/10.7899/jce-17-30.

Pelletier, René, Higgins, Johanne, Daniel Bourbonnais, 2015. Is neuroplasticity in the central nervous system the missing link to our understanding of chronic musculoskeletal disorders? BMC Muscoskel. Disord. 1–13. https://doi.org/10.1186/s12891-015-0480-y.

Silva, Flávio S. da, de Melo, Flávio E.S., Marcelo, M., do Amaral, G., Caldas, Vinícius V.A., Pinheiro, Íria Lúcia D., Abreu, Bento J., Wouber, H., Vieira, Brito, 2015. Efficacy of simple integrated group rehabilitation program for patients with knee osteoarthritis: single-blind randomized controlled trial. J. Rehabil. Res. Dev. 52 (3), 309–322. https://doi.org/10.1682/JRRD.2014.08.0199.

Sterne, Jonathan A.C., Egger, Matthias, Smith, George Davey, 2001. Investigating and dealing with publication and other biases in meta-analysis. BMJ 3, 60–62.

Sterne, Jonathan A.C., Savović, Jelena, Page, Matthew J., Elbers, Roy G., Blencowe, Natalie S., Boutron, Isabelle, Cates, Christopher J., et al., 2019. "RoB 2: a revised tool for assessing risk of bias in randomised trials as an essential component of A. BMJ 1–8. https://doi.org/10.1136/bmj.l4898.

Tulder, Maurits Van, Furlan, Andrea, Bombardier, Claire, 2003. Updated Method Guidelines for Systematic Reviews in the Cochrane Collaboration Back Review Group, vol. 28, pp. 1290–1299, 12.

Vos, Theo, Flaxman, Abraham D., Naghavi, Mohsen, Lozano, Rafael, Michaud, Catherine, Ezzati, Majid, Shibuya, Kenji, et al., 2012. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990-2010: a systematic analysis for the global burden of disease study 2010. Lancet 380 (9859), 2163–2196. https://doi.org/10.1016/S0140-6736(12)61729-2.

Wand, Benedict Martin, Parkitny, Luke, Edward O'Connell, Neil, Luomajoki, Hannu, Henry McAuley, James, Thacker, Michael, Lorimer Moseley, G., 2011. "Cortical changes in chronic low back pain: current state of the art and implications for clinical practice. Man. Ther. 16 (1), 15–20. https://doi.org/10.1016/j.math.2010.06.008.