A Mixed Comparison of Interventions for Kinesiophobia in Individuals With Musculoskeletal Pain: Systematic Review and Network Meta-Analysis

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Objective: This systematic review aims to make a mixed comparison of interventions for kinesiophobia and individuals with musculoskeletal pain.

Methods: A comprehensive search strategy was conducted in the database of PubMed, MEDLINE, and Web of Science with the inclusion criteria: (1) randomized controlled design; (2) patients with musculoskeletal pain as participants; (3) treatments protocols of kinesiophobia as interventions or comparisons; (4) the score of Tampa Scale Kinesiophobia (TSK) as outcome measures. A network meta-analysis was used to synthesize the data after checking the model consistency. The risk of bias was assessed by the Cochrane Collaboration Risk of Bias Assessment Tool.

Results: Thirty-one studies were included in this review after a comprehensive search strategy with a low risk of bias and good consistency. According to the results of the network meta-analysis, a multi-modal treatment protocol had the highest probability to become the best choice in dealing with kinesiophobia caused by musculoskeletal pain, whereas psychological treatment protocols also showed a potentially positive effect on musculoskeletal pain-induced kinesiophobia.

Conclusion: Multi-modal protocols could be recommended as the preferred option when dealing with kinesiophobia caused by musculoskeletal pain. However, it is still worth mentioning that there are also potentially positive therapeutic effects of psychological interventions. Since the concept of kinesiophobia is based on the fear-avoidance model, the psychological mechanism should be paid enough attention to during treatment.

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Keywords: kinesiophobia, musculoskeletal pain, network meta-analysis, systematic review, non-surgical

INTRODUCTION

Kinesiophobia, which was firstly proposed by Miller in 1990 based on an aspect of the fear-avoidance model, was a conceptual definition that could describe a fear of pain and an excessive, irrational, and debilitating fear to carry out a physical movement due to a feeling of vulnerability to a painful injury or re-injury.
(Kori et al., 2011; Vincent et al., 2013; Czuppon et al., 2014; Smith et al., 2014; Monticone et al., 2015; Urquhart et al., 2015; Zdziarski et al., 2015; Ferrándiz et al., 2016; Dvir et al., 2018; Weissenfels et al., 2019; Gholami et al., 2020; Östenberg et al., 2022; Xiang et al., 2022). The developing mechanism of kinesiophobia is multiple and complex, among which the failure and accidents in an individual’s movements and the following physical and social activity are the most common. Individuals who are highly fear-avoidant believe that pain is a sign of bodily harm and that any activities causing pain are dangerous and should be avoided (Helmhout et al., 2010; Da Luz et al., 2014). Pain, which might be induced by musculoskeletal disorders, surgeries, and other traumas, such as burns and scalds, is the most common feature in the progression of kinesiophobia (Galan-Martín et al., 2020; Riecke et al., 2020).

Kinesiophobia induced by musculoskeletal pain is most common and correlates with factors from biological, cognitive, and occupational perspectives (Luque-Suarez et al., 2019). Moreover, kinesiophobia might also occur and develop during the treatment and rehabilitation progression of musculoskeletal disorders, surgeries, and other traumas, which call for extra and special intervention (Archer et al., 2017).

The Tampa Scale for Kinesiophobia (TSK) and the Kinesiophobia Causes Scale (KCS) are two common tools being used in the assessment of kinesiophobia. The KCS, which is a questionnaire consisting of 20 close-ended questions with a range of scores from 0 to 100, is usually used to diagnose and determine the causes of motor passivity. Higher scores indicate a greater fear of movement. According to previous studies and evidence-based clinical practice, the TSK is mostly recommended in the assessment of kinesiophobia. For example, a systematic review published in 2004 mentioned that the overall score of TSK showed a significant positive correlation with the severity of the physical disability, and changes in TSK scores could be used as a comparative indicator of treatment effectiveness (Heuts et al., 2004). The original version of TSK is a 17-item questionnaire with the ratings available for each item: (1) disagree; (2) partially disagree; (3) partially agree; (4) strongly agree. The score of each item varies from 1 to 4 or 0 to 3. The score of each item would be summed after the participant finishes the assessment and the overall score ranges from 17 to 68 or from 0 to 51 (Roelofs et al., 2004; Damsgard et al., 2007; Lundberg et al., 2009; Mintken et al., 2010). There are also some shortened versions of TSK with high reliabilities and validities, such as TSK-13 and TSK-11, which have been widely used in the assessment of kinesiophobia caused by pain from other disorders and diseases, such as temporomandibular disorders (TSK-TMD) and chronic low back pain (TSK-CLBP) (Woby et al., 2005; Hapidou et al., 2012; Tchachuk and Harris, 2012; Larsson et al., 2014; Neblett et al., 2016). Moreover, TSK has also been translated into many different languages and has been identified with high test-retest reliability and internal consistency.

The choice of intervention treatment protocol options is an essential part of the treatment for musculoskeletal disorders. Studies of intervention treatment protocols for some musculoskeletal disorders have also found that certain treatments have a positive effect on kinesiophobia caused by pain from these musculoskeletal disorders (Vihstadt et al., 2014; Javdaneh et al., 2020; Tagliaferri et al., 2020). However, since most of the treatment protocols for musculoskeletal disorders are mainly focused on the injured tissues, aiming to restore the physiological functional integrity of damaged tissues, the TSK scores were usually reported as a secondary outcome, and there was a limited number of studies that focus on the treatments for kinesiophobia (Lara-Palomino et al., 2013; Monticone et al., 2017; Sarig Babat et al., 2018). A systematic review and meta-analysis published in 2020, which only included randomized controlled trials that used the TSK-17 as outcome measures, identified the effect of multi-modal protocols that combined physical and psychological therapies for kinesiophobia caused by musculoskeletal disorders compared with uni-modal therapy of only physcological therapy or psychological therapy, demonstrating that, despite a large heterogeneity within studies, multi-modal protocols might be more effective in reducing kinesiophobia than the unimodal of only physical or psychological therapy (Xu et al., 2020). Therefore, a further review of studies in which more versions of TSK were used as outcome measures should be made to create more comprehensive, high-quality, and low-bias clinical evidence.

At present, there are numerous intervention treatment protocols for musculoskeletal disorders (Flores et al., 2017; Lenoir et al., 2019; Andersen et al., 2020). Therefore, it is not feasible to make an adjusted indirect comparison of interventions or the comparison of a mixed treatment that included every protocol. However, since some protocols just differ in operational details but are based on the same psychophysical principle and could be reclassified together, in this review, each treatment protocol in the studies included would be reclassified according to its operational characteristics and principles, and then put in the network meta-analysis.

According to previous studies, intervention treatment protocols for musculoskeletal disorders could be reclassified into passive modalities (PM), active physical exercise (APE), supervised training (ST), psychological intervention (PI), external-used devices (ED), treatment as usual (TAU), placebo treatment (Placebo), non-intervention (Blank), and multi-modal protocols (MP). In this review, the term PM is defined as therapist-led passive modalities such as acupuncture, manual massage, medication, and therapy using special equipment (laser, ultrasonic wave, magnet, thermal, etc.) (Heymans et al., 2006; Smeets et al., 2009; Ferrándiz et al., 2016; Saracoglu et al., 2020); the term APE refers to interventions in which participants perform physical training in an unsupervised environment or self-training according to a relevant program (resistance training or mobility training), relaxing, or proprioceptive training (Helmhout et al., 2004; Koumantakis et al., 2005; Gustavsson and von Koch, 2006; Pool et al., 2010; Nassif et al., 2011; Monticone et al., 2014; Miyamoto et al., 2016; Hotta et al., 2020); ST refers to physical training by the patient under the supervision of physiotherapists and caregivers (Hott et al., 2020; Meirelles et al., 2020). The term PI refers to treatments conducted by a professional psychologist or psychologist such as cognitive-behavioral therapy (CBT), meditation, and psychological interview (Lopez-Lopez et al., 2015; Monticone et al., 2016, 2018; Zdziarski-Horodyski et al., 2020; Sato et al., 2021), the term ED means the treatment protocol in which the participants would...
be asked to wear non-invasive therapy devices such as Kinesio tape, orthoses, or sportswear for a long-term (Castro-Sánchez et al., 2012), and the term MP refers to treatment protocols which include two or more protocols mentioned above, for example, physical exercise using VR devices or laser devices. It is important to note that two or more treatments of the same type are not part of a multi-modal protocols program, such as the use of Pilates combined with stretching body exercises in a sports modality (Meijer et al., 2006; Smith et al., 2019; Bahat et al., 2020; Gulsen et al., 2020; Tejera et al., 2020; Javdaneh et al., 2021).

Moreover, the category “Blank” in the reclassification of this review refers to keeping normal life or only receiving patient education with basic health advice (Nassif et al., 2011), whereas the category “TAU” refers to treatment as usual or usual care from nursing staff, and the category “Placebo” refers to sham therapy protocols such as sham manipulation and sham sustained natural apophyseal glides.

The objective of this systematic review is to make a mixed comparison of intervention treatment protocols on kinesiophobia for individuals with musculoskeletal pain by reclassifying treatment protocols from different perspectives according to the change in TSK scores and then to explore the most potential protocols.

METHODS

Protocol and Registration

This systematic review was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines (Moher et al., 2009). The eligibility and exclusion criteria and the search strategy were made and agreed upon by two authors (Jialu Huang and Yining Xu) with a priori to minimize bias. The PROSPERO Registration Number of this review is CRD42021286450.

Eligibility Criteria (PICOS)

The eligibility criteria for inclusion were: (1) randomized controlled trials; (2) patients with musculoskeletal pain as participants; (3) intervention treatment protocols; (4) TAU, Placebo, or Blank protocols as comparisons; (5) the score of TSK as outcome measures.

Exclusion Criteria

Studies were excluded if: (1) participants were patients with pain induced by non-musculoskeletal disorders, such as burns, traumatism, or surgeries; (2) intervention protocols contained surgical or invasive treatment such as surgeries and injections; (3) published abstract without full text or lack of data; (4) outcome measures did not correspond with those in the eligibility criteria; (5) not a randomized controlled trial, such as a cross-sectional study, case report, cohort study, and cross-over trial in a single group.

Search Strategy

A comprehensive reproducible search strategy had been performed on the databases of PubMed, MEDLINE, and Web of Science from January 1990 to December 2021. Reference lists were also searched in all screened studies for identifying gray literature, which refers to the study that had not been openly published. If the data were insufficient, the authors were contacted and requested for missing data. The search terms used in each database were as follows: (1) in PubMed and Embase, the search term was “(kinesiophobia) AND [(randomized) OR (randomized)] [Title/Abstract]”; (2) in Web of Science, the search term was “(AB kinesiophobia) AND (AB randomized OR randomized).”

Risk of Bias Assessment

The risk of bias was assessed by two independent authors (Rongrong Xuan and Julien Baker) according to The Cochrane Collaboration Risk of Bias Assessment Tool (Armijo-Olivo et al., 2012). Every disagreement was discussed, and an independent arbitrator (Yaodong Gu) was invited when there was an agreement that could not be met.

Data Extraction and Synthesis

All searched studies were imported into EndNote 20 (Thomson Reuters, Carlsbad, CA, USA) for further screening. Data were extracted by two independent authors (Jialu Huang and Yining Xu). Any discrepancies would be solved by an independent arbitrator (Yaodong Gu).

Detailed information of included studies was summarized and information such as participants’ characteristics (age, gender, and type of musculoskeletal disorder) and details of intervention protocols with their reclassification were collected and put into an extraction sheet of summary of included studies. The data of each trial, which involved the version of TSK it used, sample size (N), mean value (Mean) with its standard deviation (SD) of each group in baseline, and every recording point would be extracted in an independent sheet for the data pre-processing.

Data Pre-processing

Data pre-processing and analysis were conducted by two independent authors (Jialu Huang and Yining Xu). Microsoft Office Excel (Version 16.0, Microsoft Corporation, Redmond, WA, USA) was used to pre-process the original data by transferring all the outcomes into a uniform unit according to the clinical criteria. The Aggregate Data Drug Information System (ADDIS, Version 1.16.8, Produced by Drugis.org) was used to pool data into the network meta-analysis.

Network Meta-Analysis

Since different versions of TSK have different total scores, the effect size of the network meta-analysis were presented in mean differences (MD) of the percentage of TSK score change. A network geometry was provided to display all kinds of interventions and key information such as the type of intervention represented by each node, direct comparisons between each pair of interventions represented by the edges, and the arms of each comparison which are represented by the number on every edge.

The random-effects standard deviations were calculated under both consistency and inconsistency models and compared with each other to identify if there was inconsistency within
interventions. If there were closed loops in the intervention structure, the inconsistency of the evidence must be assessed. Moreover, while the results are easier to interpret, it requires a separate model to be run for each node to be split. The node-splitting analysis is an alternative method to assess inconsistency in network meta-analysis which assessed whether direct and indirect evidence on a specific node (the split node) agrees (Rouse et al., 2017).

The consistency model was used if there was neither closed-loop nor split node in the intervention structure, the random-effects standard deviations in the consistency and inconsistency models were identical, or the identified discrepancy could be determined by examining the calculating a respective Bayesian p-value in the node-splitting analysis was statistically insignificant ($p > 0.05$). Otherwise, the inconsistency model would be applied (Rouse et al., 2017).

When the consistency model was applied, the results were shown in the rank probability plot. The sum of all rank probabilities is 1, both within a rank over treatments and within a treatment over ranks. Besides, a league table was provided after the model of data analysis had been determined, reporting results that represented the mean difference in the column-defining treatment compared with the row-defining treatment. If the calculation was based on the inconsistency model, only a league table was provided after the model of data analysis had been determined (Catala-Lopez et al., 2014).

**RESULTS**

**Search Strategy and Information Extraction**

Thirty-one studies were included in the final analysis (Beltran-Alacreu et al., 2015; Hidalgo et al., 2015; Pires et al., 2015; Sarig Bahat et al., 2015; Castro-Sánchez et al., 2016; Pillasstrini et al., 2016; Cruz-Díaz et al., 2017; Martínez-Cervera et al., 2017; Yilmaz Yelvar et al., 2017; Birinci et al., 2019; Gholami et al., 2020). The identification process is shown by a flow diagram in Figure 1 (Moher et al., 2009). The information of all included studies is presented in Table 1. All original data are provided in the Supplementary File.
Risk of Bias
The risk of bias for the 31 included studies was assessed in this review and the results are shown in Figure 2. Adequate results were obtained for the randomization and concealment methods of the participants mentioned in the studies. Eight studies adequately described participants and staff as blind, and a total of 21 studies described assessors as blind. The risk of attrition bias was low (low in all studies), the risk of selection bias was low (low in all studies), and the risk of reporting bias was low (low in all studies).

Network Meta-Analysis
Network Geometries
The network geometries showed all categories of treatment protocols, providing information such as the type of treatment represented by each node, the direct comparisons between each pair of interventions represented by the lines, and the arms of each trial represented by the number on the edges. The network geometries of the interventions are presented in Figure 3.

Comparisons of Random Effects Standard Deviations
The results of the random effects standard deviation calculations in both the consistency model and inconsistency model of each outcome measure are provided in Table 2. According to the results, the random effects standard deviations of the consistency model were identical. Therefore, the analysis under the consistency model had a good validity.

Results of Network Meta-Analysis
Table 3 shows the league tables of the network geometries, and the ranking of measures and probabilities is provided in Table 4 and Figure 4. Since a lower score of TSK is regarded as better, the treatment protocol in Rank 1 has the highest probability to be the last treatment choice, whereas that in Rank 9 has the lowest probability to be the first treatment choice.

According to the result, MP had the highest potential probability to be the best choice in treating kinesiophobia caused by musculoskeletal pain (0.32 in Rank 9 and 0.25 in Rank 8) with a statistically significant advantage in the comparison with APE (P < 0.05), whereas ED might have the highest potential probability to be the second-best treatment choice with a probability of 0.25 in Rank 9 and 0.18 in Rank 8. The psychological intervention probability is the third-best treatment choice with a probability of 0.19 in Rank 9 and 0.10 in Rank 8. Corresponding with the results of the included studies, TAU and Blank, which were usually set as interventions in the control group, have a high potential probability in Ranks 1 and 2. Nevertheless, APE has the highest potential probability in Ranks 1 and 2.

DISCUSSION
The objective of this systematic review and network meta-analysis is to make a mixed comparison of intervention treatment protocols for kinesiophobia caused by musculoskeletal pain. After comparing 9 different categories of treatment protocols, the primary findings are as follows. First, multi-modal protocols have the highest potential probability to be the best choice in treating kinesiophobia caused by musculoskeletal pain and have a statistically significant advantage in the comparison with active physical exercise and supervised training. Second, wearing an external-used device have the highest potential probability to be the second-best treatment choice. Third, keeping active in physical exercise might not be a wise choice when the patient has been diagnosed with kinesiophobia induced by musculoskeletal pain.

Multi-modal treatment protocols seem to have the highest potential probability to be the best treatment choice. This result could be supported by high-level clinical evidence. Apart from the systematic and meta-analysis mentioned in the introduction section of this review (Xu et al., 2020), many randomized controlled trials concluded a similar result to support the clinical practice of multi-disciplinary interventions for kinesiophobia caused by musculoskeletal pain. For example, a pragmatic randomized controlled trial conducted in 2020 claimed that a multi-modal treatment protocol combined with nature activity therapy and usual care could be an effective co-adjutant multicomponent treatment for improving fibromyalgia-related symptoms (Serrat et al., 2020), and another randomized controlled trial conducted in 2013 demonstrated that a long-term multidisciplinary treatment program was superior to the exercise program in reducing disability, fear-avoidance beliefs and pain, as well as enhancing the quality of life of patients with chronic low back pain. The effects were clinically tangible and lasted for at least 1 year after the program ended (Monticone et al., 2013). Moreover, from the non-clinical perspective, a review conducted in 2006, which determined the effectiveness and cost-effectiveness of return-to-work outpatient multidisciplinary treatment programs for sick-listed workers with non-specific upper extremity musculoskeletal complaints, found that multidisciplinary treatment affects individuals positively, but shows no significant difference in cost-effectiveness on the societal level as compared to usual care (Meijer et al., 2006).

The multi-modal treatment protocols included in the review referred to approaches from two or more of the following perspectives, which were physiological, and psychological perspectives. The results of the network meta-analysis showed that the effect of multi-modal treatment protocols was better than that of treatment protocols from only a physiological perspective. This result is correspondent with some previous studies. For example, in a review published in 2014, the therapist performed spinal stabilization exercises based on cognitive behavioral therapy for the patient, and the results showed that spinal stabilization exercises based on cognitive behavioral therapy could bring more advantages to the patient when they were performing non-spinal motor tasks such as walking (Monticone et al., 2014). Another review conducted in 2018 demonstrated that patients with chronic low back pain who were given a pain education session by a psychologist after supervised training by a physiotherapist could feel less pain than those who only had supervised training (Pardo et al., 2018). The results of the network meta-analysis also showed that all multi-modal treatment protocols of the included studies contained...
| References                          | Participants                                      | Interventions                                                                 | Outcome (TSK Version) |
|-----------------------------------|---------------------------------------------------|-------------------------------------------------------------------------------|----------------------|
| Gustavsson and von Koch (2006)    | Long-lasting neck pain 39.14 28/29                | Applied Relaxation The program contained 7 1.5-h sessions, over a period of 7 weeks. The sessions consisted of applied relaxation training, 4 body awareness exercises, and information about pain and stress management. | MP TSK-17            |
| Nassif et al. (2011)              | Chronic lower back pain 45.23 32/75               | Treatment as usual 11 individual sessions spread over 20 weeks. Supervised active physical exercise program 60 min of physiotherapy and physical exercise 3 times a week for 2 months with full supervision by an in-house physiotherapist and physical educator. | TAU TSK-13           |
| Castro-Sánchez et al. (2012)      | Chronic non-specific low back pain 48.50 40/59     | No treatment No direct intervention. Kinesio tape Standardized Kinesio Tape application in sitting position. 4 blue-I placed at 25% tension overlapping in a star shape over the point of maximum lumbar pain participants wore the tape, 1 week. | Blank TSK-17 ED TSK-17 |
| Lara-Palomino et al. (2013)       | Chronic non-specific low back pain 48.50 41/61     | Electro-massage Electro-massage, over the lumbar and dorsal–lumbar region, 30 min at stimulation intensity of 30-50 mA, 2/week, 20 sessions. Manual massage Superficial manual massage session on the lower back area, 20 min, 2/week, 20 sessions. Spinal stabilizing exercises in addition to usual-care rehabilitation Spinal stabilizing exercises in addition to usual-care rehabilitation (passive mobilization, stretching, and postural control), 60-min cognitive–behavioral sessions, 1/week, 8 weeks. Usual-care rehabilitation Routine care rehabilitation provided by the physiotherapist includes passive spinal movement, stretching, muscle strengthening and postural control. 60-min motor training sessions twice a week for 8 weeks. | PM TSK-17 PM TSK-13 MP TSK-13 ST |
| Monticone et al. (2014)           | Chronic low back pain 57.80 11/20                 | PNF stretching hold-relax proprioceptive neuromuscular facilitation stretching combined with a structured exercise programme for posttraumatic stiffness of the elbow, 2/week, 6 weeks. Static stretching Static stretching combined with a structured exercise programme for posttraumatic stiffness of the elbow 0.2/week, 6 weeks. | MP TSK-17 MP TSK-13 ST |
| Birinci et al. (2019)             | Posttraumatic stiffness of the elbow 41.34 24/40   | Manual therapy and therapeutic patient education Therapeutic patient education in addition to manual treatment methods (specific passive movement of the cervical facet joints, overall movement of the cervical spine, and high-speed technology in the back area), 8 times in 4 weeks. | MP TSK-11             |
| Beltran-Alacreu et al. (2015)     | Non-specific chronic neck pain 41.40 35/45        |                                                                                              |                      |

(Continued)
| References | Type of pain | Participants | Interventions | Outcome (TSK Version) |
|------------|-------------|--------------|---------------|-----------------------|
| Hidalgo et al. (2015) | Non-specific low back pain | 39.25 | 16/32 | Manual therapy, therapeutic patient education, and a therapeutic exercise, 8 times in 4 weeks. | MP |
| | | | | Therapeutic patient education, therapeutic exercise, in addition to manual treatment methods (specific passive movement of the cervical facet joints, overall movement of the cervical spine, and high-speed technology in the back area). | |
| | | | | Real lumbar Mulligan sustained natural apophyseal glides | PM |
| | | | | Sham lumbar Mulligan sustained natural apophyseal glides | |
| Pires et al. (2015) | Chronic low back pain | 51.00 | 40/62 | Aquatic exercise and pain neurophysiology education | MP |
| | | | | Water exercise programme under the supervision of a therapist, 6-week program consisting of 12 sessions + 2 sessions of pain neurophysiology education. | TSK-13 |
| Sarig Bahat et al. (2015) | Chronic neck pain | 40.90 | 22/32 | Kinematic training | APE |
| | | | | Home neck training method without physiotherapy supervision, 30 min each time, 4–6 times total, 5 weeks. | TSK-17 |
| Priore et al. (2020) | Patellofemoral pain | 22.42 | Unknown | Knee bracing | ED |
| | | | | Participants received instructions to use the knee brace for 2 weeks while performing activities of daily living or sports that had previously resulted in knee pain. | TSK-17 |
| Castro-Sanchez et al. (2016) | Chronic low back pain | 45.00 | 39/62 | Spinal manipulation | PM |
| | | | | Side-lying pelvic girdle manipulation+Side-lying lumbar spine manipulation+Thoracic manipulation. | TSK-17 |
| References                  | Participants                                      | Interventions                                                                 | Outcome (TSK Version) |
|-----------------------------|---------------------------------------------------|-------------------------------------------------------------------------------|-----------------------|
| **Type of pain**             | **Age**   | **Gender (female/all)** | **Treatment**                        | **Abstract of protocol** | **Category** |
| Castro-Sánchez et al. (2016) | Chronic non-specific low back pain               | 51.50 42/64                                                                  | Functional technique  | Patients in this group received a functional technique intervention targeted at the lumbosacral junction. | PM |
| Kurt et al. (2016)           | Patellofemoral pain syndrome                      | 31.27 49/84                                                                  | Craniosacral therapy  | 50-min Physical therapy, 1-week, 10 weeks. | PM |
| Monticone et al. (2016)      | Chronic low back pain                             | 53.50 90/150                                                                 | Classic massage      | 30-min Classic massage, 1-week, 10 weeks. | PM |
| Monticone et al. (2016)      | Chronic low back pain                             | 53.50 90/150                                                                 | Kinesio tape         | 2 days of Kinesio tape. | ED |
| Pillastrini et al. (2016)    | Chronic Non-specific Neck Pain                    | 47.44 71/93                                                                  | Placebo Kinesio tape  | 2 days of placebo Kinesio Tape. | Placebo |
| Cruz-Díaz et al. (2017)      | Chronic Low Back Pain on pain                     | 36.25 63/98                                                                  | 1-h group-based cognitive-behavior therapy and physical training, 2/week, 5 weeks. | Patients engage in active physical activity, 1-h, 2/week, 5 weeks. | MP |
| Martinez-Cervera et al. (2017)| Lateral epicondylalgia                            | 51.94 13/24                                                                  | Manipulative massage and global postural re-education supervised by a physiotherapist, 1-h, 1-2/week, 9 times total. | Manipulative massage under the supervision of a physiotherapist, 30 min, 9 times total. | PM |
| Monticone et al. (2017)      | Chronic neck pain                                | 52.90 121/170                                                                | The multidisciplinary group | 60-min physical training and 60-min psychologist interview/week, 10 weeks, and asked the patient to repeat the exercises at home. | MP |
| Yilmaz Yelvar et al. (2017)  | Non-specific low-back pain                        | 49.55 28/44                                                                  | General physiotherapy | The patient initiates 10 h of exercises including muscle strengthening, regional stretching and spinal mobilization. | APE |

(Continued)
| References                | Participants          | Interventions                                                                 |
|---------------------------|-----------------------|-------------------------------------------------------------------------------|
| Monticone et al. (2018)   | Chronic neck pain     | Virtual walking integrated physiotherapy                                        |
|                           | Age 48.60             | 15 min of intensive training with Hotpack and 15 min of ultrasound deep heating under the supervision of a physiotherapist. 5 sessions/week, 2 weeks in clinic, requested at home, 3 sessions/day. |
|                           | Gender 17/30          | MP                                                                            |
|                           |                       | **Chronic neck pain**                                                         |
|                           |                       | **Type of pain**                                                              |
|                           |                       | **References**                                                                |
|                           |                       | **Interventions**                                                             |
|                           |                       | **Abstract of protocol**                                                      |
|                           |                       | **Category**                                                                  |
|                           |                       | **Type of pain**                                                              |
|                           |                       | **Age**                                                                       |
|                           |                       | **Gender**                                                                    |
|                           |                       | **(female/all)**                                                              |
|                           |                       | **Treatment**                                                                 |
|                           |                       | **Abstract of protocol**                                                      |
|                           |                       | **Category**                                                                  |
|                           |                       | **Type of pain**                                                              |
|                           |                       | **Age**                                                                       |
|                           |                       | **Gender**                                                                    |
|                           |                       | **(female/all)**                                                              |
|                           |                       | **Treatment**                                                                 |
|                           |                       | **Abstract of protocol**                                                      |
|                           |                       | **Category**                                                                  |
|                           |                       | **Type of pain**                                                              |
|                           |                       | **Age**                                                                       |
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|                           |                       | **(female/all)**                                                              |
|                           |                       | **Treatment**                                                                 |
|                           |                       | **Abstract of protocol**                                                      |
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|                           |                       | **Type of pain**                                                              |
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|                           |                       | **(female/all)**                                                              |
|                           |                       | **Treatment**                                                                 |
|                           |                       | **Abstract of protocol**                                                      |
|                           |                       | **Category**                                                                  |
|                           |                       | **Type of pain**                                                              |
|                           |                       | **Age**                                                                       |
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|                           |                       | **(female/all)**                                                              |
|                           |                       | **Treatment**                                                                 |
|                           |                       | **Abstract of protocol**                                                      |
|                           |                       | **Category**                                                                  |
|                           |                       | **Type of pain**                                                              |
|                           |                       | **Age**                                                                       |
|                           |                       | **Gender**                                                                    |
|                           |                       | **(female/all)**                                                              |
|                           |                       | **Treatment**                                                                 |
|                           |                       | **Abstract of protocol**                                                      |
|                           |                       | **Category**                                                                  |
|                           |                       | **Type of pain**                                                              |
|                           |                       | **Age**                                                                       |
|                           |                       | **Gender**                                                                    |
|                           |                       | **(female/all)**                                                              |
|                           |                       | **Treatment**                                                                 |
|                           |                       | **Abstract of protocol**                                                      |
|                           |                       | **Category**                                                                  |
|                           |                       | **Type of pain**                                                              |
|                           |                       | **Age**                                                                       |
|                           |                       | **Gender**                                                                    |
|                           |                       | **(female/all)**                                                              |
|                           |                       | **Treatment**                                                                 |
|                           |                       | **Abstract of protocol**                                                      |
|                           |                       | **Category**                                                                  |
|                           |                       | **Type of pain**                                                              |
|                           |                       | **Age**                                                                       |
|                           |                       | **Gender**                                                                    |
|                           |                       | **(female/all)**                                                              |
|                           |                       | **Treatment**                                                                 |
|                           |                       | **Abstract of protocol**                                                      |
|                           |                       | **Category**                                                                  |
|                           |                       | **Type of pain**                                                              |
|                           |                       | **Age**                                                                       |
|                           |                       | **Gender**                                                                    |
|                           |                       | **(female/all)**                                                              |
|                           |                       | **Treatment**                                                                 |
|                           |                       | **Abstract of protocol**                                                      |
|                           |                       | **Category**                                                                  |
|                           |                       | **Type of pain**                                                              |
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|                           |                       | **Treatment**                                                                 |
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|                           |                       | **Treatment**                                                                 |
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|                           |                       | **(female/all)**                                                              |
|                           |                       | **Treatment**                                                                 |
|                           |                       | **Abstract of protocol**                                                      |
|                           |                       | **Category**                                                                  |
| References                  | Type of pain            | Age   | Gender (female/all) | Treatment                          | Abstract of protocol                                                                 | Category | Outcome (TSK Version) |
|-----------------------------|-------------------------|-------|---------------------|------------------------------------|--------------------------------------------------------------------------------------|----------|-----------------------|
| Gulsen et al. (2020)        | Fibromyalgia            | 41.38 | 16/16               | Combined exercise                  | Patients initiate comprehensive exercise training, including 30 min of aerobic training, 2/week, 8 weeks. | APE      | TSK-17                |
| Hott et al. (2020)          | Patellofemoral pain     | 27.60 | 73/112              | Traditional knee-focused exercise  | Straight-leg raises in the supine position, supine terminal knee extensions, and a mini-squat with the back supported against the wall, 3 sets, 10 repetitions, 3/week, 6 weeks were performed for 6 weeks. | APE      | TSK-13                |
| Meirelles et al. (2020)     | Chronic non-specific    | 48.00 | 28/38               | Active Control                     | Therapeutic exercises under the supervision of a physiotherapist, 2/week, 10 weeks. | ST       | TSK-17                |
| Orthobacal trauma           |                         |       |                     | Active Control +Osteopathic         | Physiotherapist intervention with active control group and orthopedic manipulation techniques with OMTG, 30–45 min, 1/week, 5 weeks. | MP       |                       |
| Manipulation                |                         |       |                     | Integrative care                   | Routine care combined with a social self-support programme guided by orthopedic surgeons and care teams in 1 year. | MP       | TSK-11                |
| Zdziarski-Horodyski et al.  | Orthopedic trauma       | 43.00 | 40/99               | Usual care                         | Regular medication under the supervision of a physiotherapist in 1 year. | PM       |                       |
| Selhorst et al. (2021)      | Patellofemoral pain     | 14.80 | 43/65               | Psychologically Informed Intervention | The experimental group watched a short psychologically informed video (8 min and 30 s) targeting beliefs about pain related fear and pain catastrophizing. | PI       | TSK-11                |
| Gül et al. (2021)            | Chronic low back pain   | 42.30 | 26/31               | Physiotherapy combined with TNE    | A physiotherapy programme of 15 sessions supervised by a physiotherapist and a home exercise programme for their 3 weeks. | MP       | TSK-17                |

TSK, Tampa scale of kinesiophobia; APE, Active Physical Exercise; ST, Supervised training; PI, Psychological Intervention; MP, Multi-modal Protocols; PM, Passive Modalities; ED, External-used Devices; TAU, Treatment as Usual.
treatments from a psychological perspective, indicating that psychological intervention has a potentially positive effect on the kinesiophobia caused by musculoskeletal pain. There is one review included in this study that compares psychological interventions with TAU and finds a significant advantage of psychological intervention over TAU in reducing the severity of kinesiophobia (Selhorst et al., 2021). The results of some previous studies identified the advantage of psychological treatment.
protocols in treating kinesiophobia induced by musculoskeletal pain and demonstrated that psychological treatment could relieve kinesiophobia caused by physical disorders and improve quality of life (Goudie et al., 2018; Innes et al., 2018; Helminen et al., 2020; Serrat et al., 2020; Xu et al., 2022). For example, a review published in 2016, which has also been included in this systematic review, demonstrated that group-based and task-oriented exercises could reduce disability, kinesiophobia, catastrophizing, and enhance the quality of life of individuals with chronic low back pain (Monticone et al., 2016). Moreover, a review by Wicksell’s team, which is a secondary analysis of a randomized controlled trial, resulted in that cognitive behavior therapy could improve the functioning and life satisfaction of people with chronic pain (Wicksell et al., 2010). The potential mechanism of psychological treatments might come from self-efficacy, a review conducted in 2020 shows both pain self-efficacy and negatively charged emotion and expectations toward pain are important factors when dealing with musculoskeletal injured patients (Sinikallio et al., 2014). However, some previous studies concluded different views, a review conducted in 2006 compared the effectiveness of a brief physiotherapy pain management approach using cognitive-behavioral principles with a commonly used method of passive modalities, and identified that the latter approach resulted in higher patient satisfaction overall but the former could be more cost-effective (Moffett et al., 2006). The heterogeneity of the results might be caused by the different expectations of patients when they are selecting treatment protocols. Future studies should compare the effects of different psychological intervention protocols in a particular population to identify the effectiveness of kinesiophobia.

Besides, wearing an externally used device has a high potential probability to be the second-best treatment choice. There are 4 relevant studies included in this review, and 3 studies are randomized controlled trials about the effect of Kinesio tape. For example, a review in 2012 explored the effect of Kinesio tape adhered in the lumbar area, finding that a 1-week treatment of Kinesio tape had a positive effect on relieving pain than the placebo tape (Castro-Sánchez et al., 2012). A review conducted in 2016 evaluated the short-term effects of Kinesio tape on joint position sense, isokinetic measurements, kinesiophobia, symptoms, and functional limitations in patients with patellofemoral pain syndrome, demonstrating that, although short-term Kinesio tape application could not increase hamstring muscle strength, it still could improve joint position sense, pain, kinesiophobia, symptoms, and daily limitations (Kurt et al., 2016). The positive effect of the Kinesio tape application has been identified by several previous studies (Coombes et al., 2016; Karran et al., 2017; Louw et al., 2017; Takacs et al., 2017); however, most of these studies only identified the short-term effect of Kinesio tape. Further studies should identify the long-term effect...
of Kinesio tape and that of other kinds of externally used therapy devices.

What should also be noticed among the results of the network meta-analysis is that, for the treatment of kinesiophobia caused by musculoskeletal pain, active physical exercise might not be recommended with the lowest potential, which seems even lower than placebo, within the 9 treatment protocol categories. The reason might come from two possible aspects. First, active physical exercise might lead to secondary injury and further pain. Second, this result might be caused by the heterogeneity of intervention protocols in these included studies. Therefore, the interpretation of this result should be cautious, and future studies should explore the effect of active physical exercise on kinesiophobia without covariate interference.

Within all 9 categories of treatment protocols, TAU and Blank, which were usually set as interventions in the control group, have a low potential probability to have a positive effect on kinesiophobia caused by musculoskeletal pain. It is because treatment as usual and no-treatment, themselves are not clinical treatment protocols, only being set as interventions in control groups in the included studies. Besides, this result could also indicate that kinesiophobia might not be a self-limiting disease whose symptoms would not resolve themselves over time. It means that if patients with kinesiophobia do not carry out a particular treatment, only usual care would not be effective on their symptoms.

The primary limitation of this systematic review is that there is a limited number of studies that focus on the treatments for kinesiophobia, leading to a lack of arms in some direct intervention comparisons. For example, there is no direct comparison between psychological intervention and externally used devices in the network geometry. Last but not least, the score of TSK is usually reported as a secondary outcome, resulting in publication bias to some extent (Bennell et al., 2020; Öztürk et al., 2021; Serrat et al., 2021).

CONCLUSION

Multi-modal protocols could be recommended as the preferred option when dealing with kinesiophobia caused by musculoskeletal pain. However, it is still worth mentioning that there are also potentially positive therapeutic effects of psychological interventions. Since the concept of kinesiophobia is based on the fear-avoidance model, the psychological mechanism should be paid enough attention to during treatment.
### TABLE 4 | Ranking of measures and probabilities.

| Treatment                        | Rank 1 | Rank 2 | Rank 3 | Rank 4 | Rank 5 | Rank 6 | Rank 7 | Rank 8 | Rank 9 |
|----------------------------------|--------|--------|--------|--------|--------|--------|--------|--------|--------|
| Active physical exercise         | 0.25   | 0.24   | 0.20   | 0.14   | 0.08   | 0.05   | 0.02   | 0.01   | 0.00   |
| Blank                            | 0.03   | 0.07   | 0.12   | 0.16   | 0.18   | 0.18   | 0.13   | 0.10   | 0.04   |
| Multi-modal protocols            | 0.00   | 0.00   | 0.00   | 0.01   | 0.05   | 0.12   | 0.25   | 0.25   | 0.32   |
| Passive modalities               | 0.05   | 0.10   | 0.17   | 0.20   | 0.19   | 0.15   | 0.08   | 0.05   | 0.01   |
| Supervised training              | 0.19   | 0.20   | 0.19   | 0.15   | 0.11   | 0.08   | 0.04   | 0.02   | 0.00   |
| External-used devices            | 0.02   | 0.04   | 0.05   | 0.07   | 0.10   | 0.13   | 0.16   | 0.18   | 0.25   |
| Psychological intervention       | 0.26   | 0.10   | 0.07   | 0.07   | 0.07   | 0.07   | 0.08   | 0.10   | 0.19   |
| Treatment as usual               | 0.08   | 0.15   | 0.09   | 0.09   | 0.09   | 0.09   | 0.11   | 0.16   | 0.13   |
| Placebo                          | 0.11   | 0.09   | 0.10   | 0.11   | 0.14   | 0.14   | 0.13   | 0.13   | 0.05   |

**FIGURE 4 |** Ranking of measures and probabilities (APE, Active Physical Exercise; ST, Supervised training; PI, Psychological Intervention; MP, Multi-modal Protocols; PM, Passive Modalities; ED, External-used Devices; TAU, Treatment as Usual).

### DATA AVAILABILITY STATEMENT

The original contributions presented in the study are included in the article/Supplementary Materials, further inquiries can be directed to the corresponding authors.

### AUTHOR CONTRIBUTIONS

JH conceived the study design, collected and analyzed data, and drafted the manuscript. YX and RX participated in the design of the study, collected, and analyzed data. YG, RX, and JB
conceived the study design, assisted in revising the manuscript, and reviewed the first and final versions of the manuscript. All authors contributed to the article and agreed to the submitted version of the manuscript.

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