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#### Research article

# Efficacy of non-pharmacological treatments for knee osteoarthritis: A systematic review and network meta-analysis

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#### ABSTRACT

*Purpose*: This study aims to conduct a network meta-analysis to compare the clinical efficacy of seven distinct non-pharmacological therapies for knee osteoarthritis. We hope that our research findings can provide reference for clinical practitioners in formulating treatment plans.

*Methods*: Through a computer-based search, we systematically retrieved randomized controlled trials (RCTs) on non-pharmacological therapies for knee osteoarthritis from eight databases, including CNKI, Wanfang, VIP, PubMed, Web of Science, Embase, Scopus, and The Cochrane Library. Following screening, data extraction, and methodological quality assessment, relevant data were included and analyzed using R 4.2.3 software.

Results: A comprehensive analysis of 24 RCTs involving 2582 patients encompassed seven diverse non-pharmacological therapies. The efficacy rankings, based on Visual Analog Scale (VAS) scores, were as follows: shock wave therapy > needle-knife > laser therapy > acupuncture > ultrasound > exercise > transcutaneous electrical nerve stimulation. Similarly, based on Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) total scores, the efficacy rankings were as follows: shock wave therapy > needle-knife > laser therapy > acupuncture > ultrasound > transcutaneous electrical nerve stimulation > exercise. Among the three WOMAC subscales, the efficacy rankings for non-pharmacological therapies were as follows: For stiffness: laser therapy > exercise > shock wave therapy > acupuncture > needle-knife > ultrasound > transcutaneous electrical nerve stimulation; For daily activities: shock wave therapy > laser therapy > needle-knife > acupuncture > ultrasound > transcutaneous electrical nerve stimulation > exercise; For pain: shock wave therapy > needle-knife > laser therapy > acupuncture > exercise > transcutaneous electrical nerve stimulation > ultrasound.

Conclusion: Based on the currently limited research, we can prioritize the use of shockwave therapy to treat patients with knee osteoarthritis. However, it is essential to emphasize that further rigorous and well-designed randomized controlled trials are necessary to validate the conclusions drawn from this study.

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# 1. Introduction

Knee Osteoarthritis (KOA) is a chronic degenerative disease characterized by pathological changes in the bones, cartilage, synovium, ligaments, muscles, and surrounding adipose tissues of the knee joint. These changes lead to symptoms such as pain, stiffness, and limited functional mobility. In advanced stages, muscle atrophy may also occur, significantly reducing patients' quality of life [1]. The prevalence of KOA is increasing due to the growing aging population and rising rates of obesity, affecting a larger number of individuals [2]. Currently, there is no available treatment that can reverse the disease's progression. Therefore, the primary goals of treatment are pain relief and functional recovery.

The treatment strategies for KOA encompass both surgical and non-surgical approaches, with a focus on non-pharmacological interventions [3]. Non-pharmacological treatments serve as the first-line therapy for early-stage KOA, offering advantages such as efficacy, cost-effectiveness, and low risk [4–6]. The 2019 treatment guidelines from the American College of Rheumatology strongly recommend the use of Tai Chi exercise for managing KOA [7]. Appropriate non-pharmacological interventions in the early stages of KOA play a crucial role in delaying symptoms and improving patients' quality of life. We followed the PICOS principle to retrieve literature and selected seven intervention measures commonly used in clinical practice and with high research frequency for treating KOA. These therapies include needle-knife, acupuncture, ultrasound, shock wave therapy, laser therapy, transcutaneous electrical nerve stimulation and exercise. In order to clarify the comparative ranking of the efficacy of various therapies, achieve better treatment outcomes, and address the current lack of comparative analysis despite the diversity of treatment options, which hinders clinical practitioners from obtaining optimal guidance for non-pharmacological therapies. We conducted a network meta-analysis to rank the efficacy of these seven non-pharmacological therapies, aiming to provide evidence-based medicine for non-pharmacological treatment of KOA.

#### 2. Materials and methods

This systematic review and network meta-analysis is conducted based on the PRISMA 2020 guidelines [8]. This study has been registered on the PROSPERO website (CRD42023475151).

# 2.1. Literature search strategy

Eight databases, namely CNKI, Wanfang, VIP, PubMed, Web of Science, Embase, Scopus, and The Cochrane Library, were comprehensively searched from the inception of each database until October 2023. The search encompassed both Chinese and English languages, utilizing a combination of subject terms and free terms. The search terms included knee osteoarthritis, needle knife, acupuncture, laser therapy, ultrasound therapy, shock wave, transcutaneous electrical nerve stimulation, exercise therapy, etc.

#### 2.2. Inclusion criteria

(1) Patients diagnosed with KOA based on both domestic and international diagnostic criteria were eligible for inclusion [9–14]. (2) Intervention measures: The treatment group received various non-pharmacological therapies such as needle-knife, acupuncture, ultrasound, shock wave, laser, and other similar interventions. The control group received Western medicine, intra-articular hyaluronic acid injection, placebo, or comparisons between different non-pharmacological treatments. (3) Outcome measures: Pain assessment was evaluated using the Visual Analog Scale (VAS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).

# 2.3. Exclusion criteria

(1) Duplicate publications were excluded, and only the most recent publication was included. (2) Review articles, animal experiments, and meta-analyses were excluded as they did not meet the criteria of being RCTs. (3) Studies with inconsistent outcome measures were excluded from the analysis. (4) Studies with flawed experimental designs and incomplete data were also excluded from the study.

#### 2.4. Literature screening and data extraction

EndnoteX9.1 was utilized for literature management. After removing duplicate articles, literature screening and data extraction were independently performed by two researchers. In case of any disputes or uncertainties during the process of literature screening and data extraction, the two researchers would first engage in mutual discussion. If a resolution could not be reached, a third independent researcher would be consulted to facilitate a discussion and make a decision. The extracted data included author names, publication year, intervention measures, sample size, age, gender distribution, and outcome indicators.

#### 2.5. Assessment of study quality

Two independent researchers utilized the revised Cochrane risk-of-bias tool for randomized trials (RoB 2) to assess the quality of the included RCTs [15]. The overall bias risk for each study was categorized into three levels: "low risk of bias", "some concerns" and

"high risk of bias".

#### 2.6. Statistical methods

The random-effect network meta-analysis (NMA) was conducted using R 4.2.3 with the 'netmeta' and 'gemtc' packages. Frequentist NMA was selected as primary analysis, and Bayesian NMA was chose as sensitivity analysis. A network plot represents the relationships between various interventions, where larger circles indicate larger sample sizes, thicker lines indicate more comparisons between interventions, and closer connections. If a closed loop appears in the network plot, an inconsistency test is conducted. To assess inconsistency within the network, we employed both global and local approaches: A) Global Approach: We used the total Q statistic, which can be decomposed into within-design heterogeneity (variation between studies of the same design) and between-design inconsistency (variation between studies of different designs). We applied the design-by-treatment interaction model to test for inconsistency across the entire network. B) Local Approach: We used the node-splitting method to compare direct and indirect

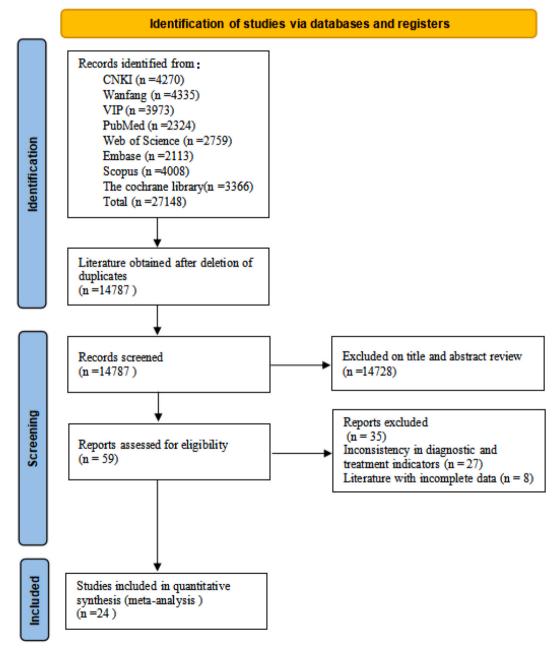


Fig. 1. Flowchart of literature screening.

evidence for each pairwise comparison. This method helps identify specific comparisons that exhibit inconsistency. Moreover, the global  $I^2$  value and the local  $I^2$  value for each pairwise comparison were assessed for heterogeneity. Effect sizes and 95 % confidence intervals can be obtained by drawing a forest plot. Additionally, the effectiveness of different non-pharmacological treatments can be ranked using the Surface under the Cumulative Ranking Curve (SUCRA). Based on risk of bias assessment, the studies identified as a relatively higher risk were removed for another sensitivity analysis. Ranks of treatments based on SUCRA score from primary and sensitivity analysis were compared to assess the robustness of our findings.

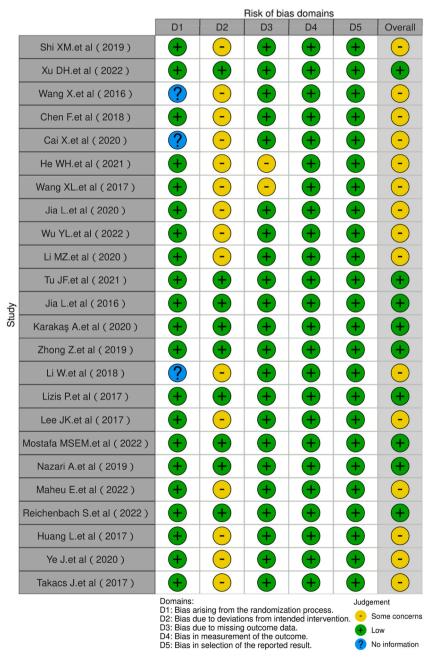


Fig. 2. Risk of bias assessment plot (RoB-2).

Table 1
Basic characteristics of the included studies.

Study	N	treatment group			control group			Outcomes
		t	Age	n(male/ female)	t	Age	n(male/ female)	
Shi XM.et al.(2019) [15]	120	Needle knife	$58.22 \pm \\8.13$	66(21/45)	Intra-articular injection	58.6 ± 7.88	54(18/36)	12
Xu DH.et al.(2022) [16]	88	Needle knife	$56\pm 6$	44(14/30)	placebo	$58\pm4$	44(14/30)	1
Wang X.et al.(2016) [17]	230	Needle knife	$\begin{array}{c} 51.4 \pm \\ 1.7 \end{array}$	115(43/ 72)	acupuncture	$52.4 \pm 2$	115(40/ 75)	1
Chen F.et al.(2018) [18]	140	acupuncture	$57.94 \pm \\3.5$	70(36/34)	Western medicine	$58.19 \pm \\3.1$	70(38/32)	1
Cai X.et al.(2020) [19]	150	acupuncture	$57.3 \pm 4.5$	75(41/34)	Western medicine	$56.7 \pm 4.7$	75(43/32)	2
He WH.et al.(2021) [20]	72	acupuncture	$53\pm 6$	36(7/29)	Western medicine	$51\pm 6$	36(9/27)	12
Wang XL.et al.(2017) [21]	46	acupuncture	$61\pm 6$	25(8/17)	placebo	$58\pm7$	21(2/19)	1)
Jia L.et al.(2020) [22]	97	Ultrasonic Therapy	$62.24 \pm 9.83$	49(12/37)	Western medicine	$60.94 \pm 11.75$	48(14/34)	12
Wu YL.et al.(2022) [23]	92	shock wave	$53.87 \pm \\5.93$	46(14/32)	Intra-articular injection	$54.06 \pm \\6.13$	46(17/29)	12
Li MZ.et al.(2020) [24]	36	shock wave	57.4 ± 9.1	18(1/17)	placebo	$58.4 \pm 13$	18(2/16)	12
Ги JF.et al.(2021) [25]	291	acupuncture	$62.8 \pm \\7.6$	145(34/ 111)	placebo	$62.7 \pm 6.6$	146(40/ 106)	2
Jia L.et al.(2016) [26]	106	Ultrasonic Therapy	$\begin{array}{c} \textbf{63.42} \pm \\ \textbf{9.73} \end{array}$	53(14/39)	placebo	$61.34 \pm \\10.25$	53(16/37)	12
Karakaş A.et al.(2020) [27]	75	Ultrasonic Therapy	$59.1 \pm \\7.45$	39(8/31)	placebo	$60.75\ \pm$ $7.46$	36(4/32)	12
Zhong Z.et al.(2019) [28]	63	shock wave	$62.5 \pm \\8.2$	32(11/21)	placebo	$63.2 \pm 7.7$	31(12/19)	12
Li W.et al.(2018) [29]	105	shock wave	$60.1 \pm \\10.1$	60(38/22)	Laser Therapy	$58.7 \pm \\11.2$	45(27/18)	1)
Lizis P.et al.(2017) [30]	40	shock wave	$63.5 \pm 8$	20(13/7)	exercise therapy	$65 \pm 8.4$	20(9/11)	1
Lee JK.et al.(2017) [31]	61	shock wave	67.7 ± 5.5	31(25/6)	Intra-articular injection	$69.1 \pm 6.2$	30(26/4)	12
Mostafa MSEM.et al. (2022) [32]	40	Laser Therapy	$\begin{array}{c} 40.12 \pm \\ 9.45 \end{array}$	20	shock wave	$46.62 \pm \\8.68$	20	12
Nazari A.et al.(2019) [33]	60	Laser Therapy	$61.5 \pm \\3.9$	30(13/17)	exercise therapy	$62.24 \pm \\3.87$	30(14/16)	12
Maheu E.et al.(2022) [34]	110	transcutaneous electrical nerve stimulation	$66.9 \pm \\8.1$	55(18/37)	Western medicine	$66 \pm 7.8$	55(21/34)	1)
Reichenbach S.et al. (2022) [35]	220	transcutaneous electrical nerve stimulation	$64.8 \pm 9.9$	108(56/ 52)	placebo	$66.3 \pm \\10.3$	112(52/ 60)	12
Huang L.et al.(2017) [36]	250	exercise therapy	$68.07 \pm \\ 9.16$	128(27/ 101)	Western medicine	$67.42\ \pm$ $7.29$	122(24/ 98)	12
Ye J.et al.(2020) [37]	50	exercise therapy	$64.48 \pm \\7.81$	25(12/13)	placebo	$63.08 \pm \\3.65$	25(8/17)	2
Takacs J.et al.(2017) [38]	40	exercise therapy	$66.1 \pm \\ 8.7$	20(1/19)	placebo	$67.1 \pm 5.4$	20(7/13)	1

N: total sample size of the trials; t: intervention measures; n: number of cases in each trials group; @ WOMAC, the Western Ontario and McMaster Universities Osteoarthritis Index; @ VAS, Visual Analog Scale.

# 3. Results

#### 3.1. Literature search and screening

A total of 27,148 articles related to non-pharmacological treatments for KOA were retrieved from 8 databases. After a thorough screening process, 24 RCTs were included [16–39], involving 2582 participants. The detailed process of literature screening is illustrated in Fig. 1.

#### 3.2. Study quality assessment

If the bias risk assessment result in all fields is "low risk of bias", then the overall bias risk assessment result is "low risk of bias"; If there is a domain bias risk assessment result that is "some concerns" and there is no "high risk of bias" domain, then the overall bias risk assessment result is "some concerns"; As long as there is a domain with a bias risk assessment result of "high risk of bias", the overall bias risk assessment result is "high risk of bias" [15]. The overall quality of the included studies is moderate, and no high-risk studies were found. The risk of bias assessment is shown in Fig. 2.

#### 3.3. Basic characteristics of the literature

The included literature was published between 2016 and 2022 [16–39], involving a total of 2582 patients who were diagnosed with KOA. The trials encompassed 7 non-pharmacological interventions for KOA. The basic characteristics of the included literature are summarized in Table 1.

# 3.4. Efficacy analysis

To evaluate the effectiveness of non-pharmacological therapies in relieving pain and improving functional activities in patients with KOA, we conducted a network meta-analysis including 24 eligible trials (involving commonly used 7 non-pharmacological treatment methods). In this study, VAS and WOMAC were selected as outcome measures. Regarding WOMAC scores, we analyzed the overall score as well as the subscales for joint stiffness, joint function, and pain. The corresponding codes for the intervention measures are presented in Table 2.

We evaluated the effectiveness of these 7 non-pharmacological therapies in relieving pain in KOA patients using VAS scores as outcome measures (Fig. 3). The interventions included acupuncture with 66 participants, exercise therapy with 183 participants, transcutaneous nerve stimulation with 108 participants, acupuncture therapy with 256 participants, ultrasound therapy with 92 participants, shock wave therapy with 116 participants, and laser therapy with 97 participants. The SUCRA data showed the efficacy ranking of the 7 non-pharmacological therapies based on VAS scores as follows: shock wave therapy > needle-knife > laser therapy > acupuncture > ultrasound > exercise > transcutaneous electrical nerve stimulation.

We not only conducted a statistical analysis on the total WOMAC scores of the eligible studies (Fig. 4), but also investigated the three subscales of WOMAC separately, aiming to gain further insights into the non-pharmacological therapies' impact on improving function and symptoms in patients with KOA. In the statistical analysis of the total WOMAC scores, acupuncture had 44 participants, exercise therapy had 223 participants, transcutaneous nerve stimulation had 163 participants, acupuncture therapy had 25 participants, ultrasound therapy had 88 participants, shock wave therapy had 195 participants, and laser therapy had 95 participants. The SUCRA data showed the efficacy ranking of the 7 non-pharmacological therapies in treating KOA based on total WOMAC scores as follows: shock wave therapy > needle-knife > laser therapy > acupuncture > ultrasound > transcutaneous electrical nerve stimulation > exercise.

In the statistical analysis of the WOMAC subscale, WOMAC stiffness score, among the eligible studies (Fig. 5), acupuncture had 225 participants, exercise therapy had 75 participants, transcutaneous nerve stimulation had 163 participants, acupuncture therapy had 391 participants, ultrasound therapy had 39 participants, shock wave therapy had 112 participants, and laser therapy had 75 participants. The SUCRA data showed the efficacy ranking of the 7 non-pharmacological therapies in treating KOA based on WOMAC

**Table 2**Codes for corresponding intervention measures.

number	code	Intervention measures		
1	Α	needle knife		
2	В	exercise therapy		
3	С	transcutaneous electrical nerve stimulation		
4	D	acupuncture		
5	E	Ultrasonic Therapy		
6	F	shock wave		
7	G	Laser Therapy		
8	H	intra-articular injection		
9	I	medicine		
10	J	placebo		

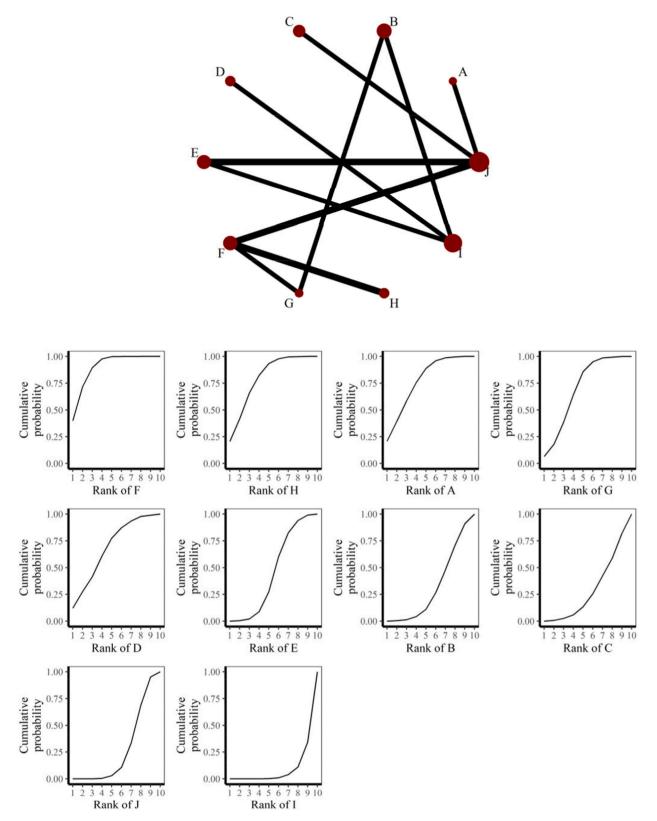
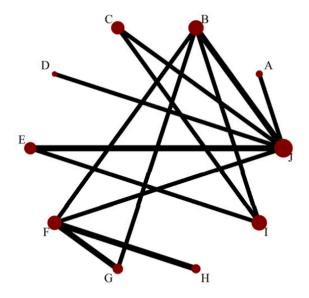


Fig. 3. VAS score efficacy assessment chart.



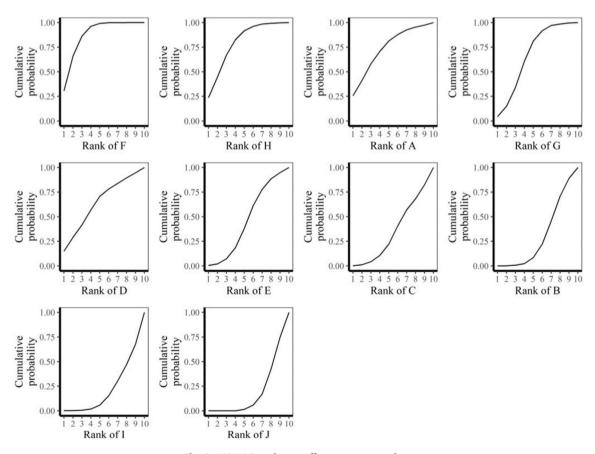
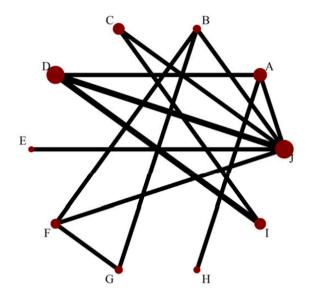
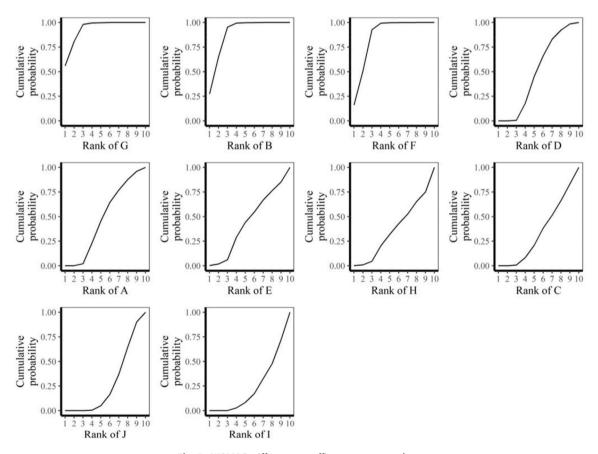
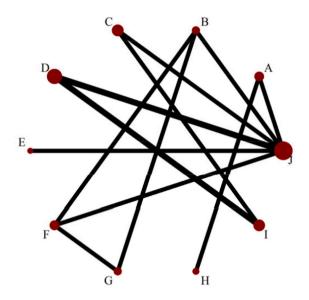


Fig. 4. WOMAC total score efficacy assessment chart.





 $\textbf{Fig. 5.} \ \ \textbf{WOMAC} \ \ \textbf{stiffness} \ \ \textbf{score} \ \ \textbf{efficacy} \ \ \textbf{assessment} \ \ \textbf{chart}.$ 



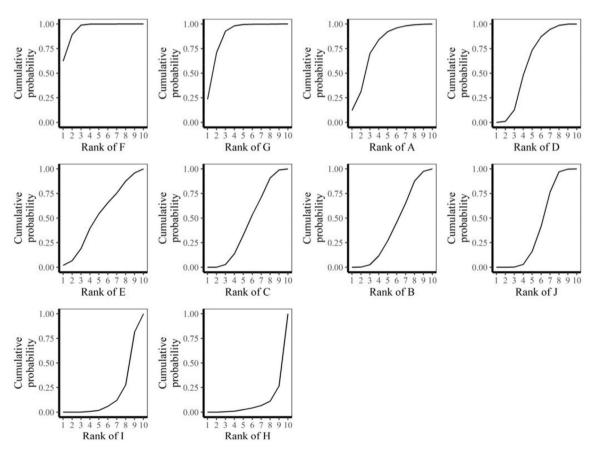
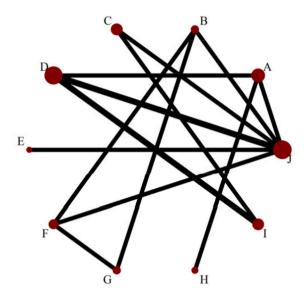


Fig. 6. WOMAC daily activity score efficacy assessment chart.



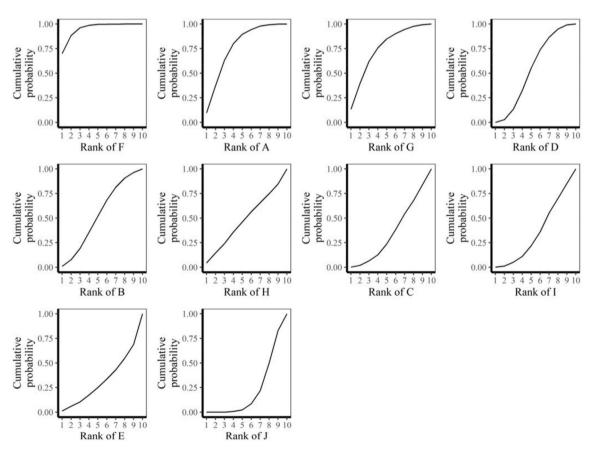


Fig. 7. WOMAC pain score efficacy assessment chart.

 $stiffness\ score\ as\ follows: laser\ the rapy > exercise > shock\ wave\ the rapy > acupuncture > needle-knife > ultrasound > transcutaneous\ electrical\ nerve\ stimulation.$ 

In the statistical analysis of the WOMAC subscale, WOMAC daily activity score, among the eligible studies (Fig. 6), acupuncture had 225 participants, exercise therapy had 75 participants, transcutaneous nerve stimulation had 163 participants, acupuncture therapy had 391 participants, ultrasound therapy had 39 participants, shock wave therapy had 112 participants, and laser therapy had 75 participants. The SUCRA data showed the efficacy ranking of the 7 non-pharmacological therapies in treating KOA based on WOMAC daily activity score as follows: shock wave therapy > laser therapy > needle-knife > acupuncture > ultrasound > transcutaneous electrical nerve stimulation > exercise.

In the statistical analysis of the WOMAC subscale, specifically WOMAC pain score, among the eligible studies (Fig. 7), acupuncture

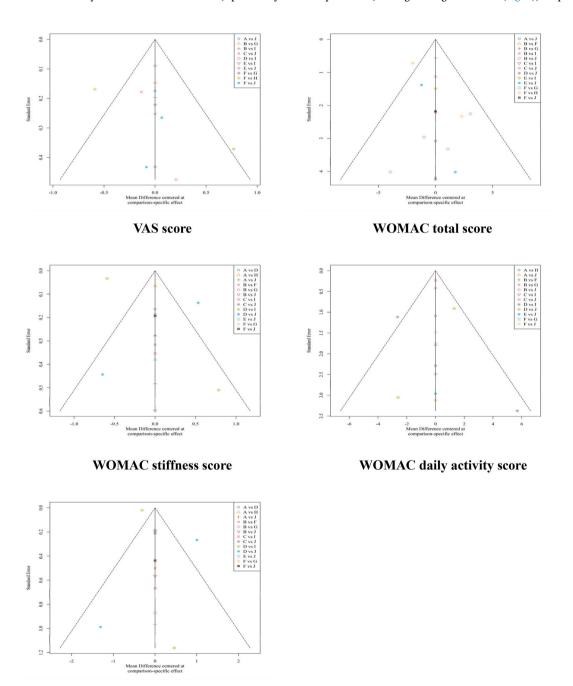


Fig. 8. Network meta-funnel plot.

**WOMAC** pain score

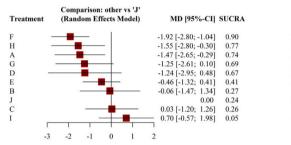
had 225 participants, exercise therapy had 75 participants, transcutaneous nerve stimulation had 163 participants, acupuncture therapy had 391 participants, ultrasound therapy had 39 participants, shock wave therapy had 112 participants, and laser therapy had 75 participants. The SUCRA data showed the efficacy ranking of the non-pharmacological therapies in treating KOA based on the WOMAC pain score as follows: shock wave therapy > needle-knife > laser therapy > acupuncture > exercise > transcutaneous electrical nerve stimulation > ultrasound.

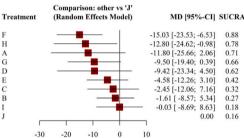
# 3.5. Inconsistency testing and sensitivity analysis

Closed loops were observed in the evidence network diagrams we created, prompting us to conduct an inconsistency test, with the results detailed in Appendix 1. The results of the heterogeneity test are shown in Appendix 2. Sensitivity analysis (Appendix 3) was conducted to assess the robustness of our study results. A funnel plot was created to assess for publication bias (Fig. 8).

#### 3.6. Network meta-analysis forest plot analysis

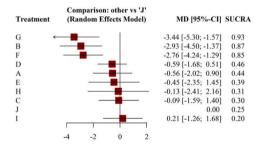
We used R 4.2.3 software to plot forest plots. In total, we included 13 literature studies, generating a total of 45 paired comparisons, among which 13 were statistically significant (Fig. 9) when using the VAS as the outcome measure. Oral medication showed statistical significance compared to acupuncture, needle-knife, ultrasound, shock wave therapy, laser therapy and intra-articular injections. Placebo demonstrated statistical significance compared to needle-knife, shock wave therapy and intra-articular injections. Shock wave therapy showed statistical significance compared to exercise therapy, transcutaneous electrical nerve stimulation and ultrasound.

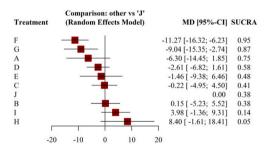




**VAS** score

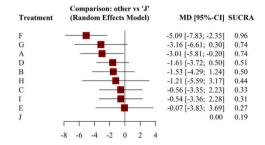
**WOMAC** total score





# **WOMAC** stiffness score

WOMAC daily activity score



# **WOMAC** pain score

Fig. 9. Network meta-analysis forest plot.

Laser therapy showed statistical significance compared to exercise therapy.

We included a total of 17 literature studies using WOMAC total score as the outcome measure, generating 45 paired comparisons, among which 4 were statistically significant (Fig. 9). Placebo demonstrated statistical significance compared to intra-articular injections and shock wave therapy. Oral medication showed statistical significance compared to shock wave therapy showed statistical significance compared to shock wave therapy.

We included a total of 15 studies using WOMAC stiffness subscale as the outcome measure, generating 45 paired comparisons, among which 11 were statistically significant (Fig. 9). Placebo showed statistical significance compared to exercise therapy, shock wave therapy, and laser therapy. Oral medication showed statistical significance compared to exercise therapy, shock wave therapy, and laser therapy. Exercise therapy showed statistical significance compared to transcutaneous electrical nerve stimulation and acupuncture. Laser therapy showed statistical significance compared to transcutaneous electrical nerve stimulation and acupuncture. Shock wave therapy showed statistical significance compared to transcutaneous electrical nerve stimulation.

We included a total of 15 studies using WOMAC daily activities subscale as the outcome measure, generating 45 paired comparisons, among which 22 were statistically significant (Fig. 9). Intra-articular injections demonstrated statistical significance compared to needle-knife, acupuncture, shock wave therapy, and laser therapy. Oral medication showed statistical significance compared to needle-knife, acupuncture, shock wave therapy, and laser therapy. Placebo demonstrated statistical significance compared to needle-knife, shock wave therapy, laser therapy, and intra-articular injections. Needle-knife showed statistical significance compared to exercise therapy, transcutaneous electrical nerve stimulation and acupuncture. Shock wave therapy showed statistical significance compared to exercise therapy, transcutaneous electrical nerve stimulation, acupuncture, and ultrasound. Laser therapy showed statistical significance compared to exercise therapy, transcutaneous electrical nerve stimulation and acupuncture.

We included a total of 15 studies using WOMAC pain subscale as the outcome measure, generating 45 paired comparisons, among which 7 were statistically significant (Fig. 9). Placebo demonstrated statistical significance compared to needle-knife and shock wave therapy. Shock wave therapy showed statistical significance compared to oral medication, exercise therapy, transcutaneous electrical nerve stimulation, acupuncture and ultrasound.

#### 4. Discussion

KOA is primarily characterized by symptoms of knee pain, stiffness, and limited functional activity. However, most treatment measures carry potential risks, especially surgical interventions, which are traumatic and often accompanied by dreaded complications. Non-pharmacological therapies, on the other hand, offer the advantages of simplicity, convenience, effectiveness, and affordability, making them widely applied in the treatment of KOA. In this study, we reviewed previous research and selected seven commonly used non-pharmacological treatments for KOA, based on their high research frequency and clinical prevalence. We then employed network meta-analysis to analyze the effectiveness of these seven therapies. The systematic evaluation revealed that shock wave therapy was the most effective in improving VAS scores, as well as self-reported functional improvements measured by the WOMAC total score, daily activities subscale, and pain subscale. Furthermore, shock wave therapy not only has the advantages of low cost and high safety but is also easily accessible for widespread implementation of this intervention measure. Laser therapy, on the other hand, showed the most effective self-reported improvement in the WOMAC stiffness subscale.

Wang et al. conducted a network meta-analysis to evaluate non-pharmacological treatments for KOA. The analysis results showed that shock wave therapy is superior to other non-pharmacological therapies in improving short-term VAS scores and inflammatory cytokines.

[40]. Additionally, studies have reported a close association between inflammatory cytokines and the occurrence of pain symptoms [41]. Due to the significant improvement in VAS scores associated with shock wave therapy, the notable effectiveness of shock wave therapy in improving WOMAC total scores, as well as the subscales for daily activities and pain, may be a direct result of pain relief, consequently facilitating greater ease in functional activities for patients. Shock wave therapy increases the activity of chondrocytes and has a protective effect on articular cartilage, regardless of whether KOA is in the early or late stage [42,43]. Research has found that shock wave therapy can promote the recovery of degenerative meniscus, reduce cartilage degradation in KOA, while also improving subchondral bone remodeling [44-46]. Hsu et al. found that shock wave therapy can enhance the expression of protein-disulfide isomerase-associated 3, an important factor in the 1α,25-Dihydroxyvitamin D3 signaling pathway associated with calcium homeostasis and gene transcription, thus promoting bone formation [47]. Additionally, An et al. reported that shock wave therapy can promote the production of cartilage-specific extracellular matrix by stimulating the proliferation of meniscal cells and upregulating cartilage-repairing factors [48]. Our analysis results also revealed that laser therapy is most effective in improving the WOMAC stiffness subscale. Martins et al. found that laser intervention helps enhance antioxidant enzymatic activity and protects cartilage tissue from oxidative damage [49]. Li et al. found that laser therapy can enhance lower limb muscle strength in patients, effectively improving knee joint stability [50]. For patients with severe knee joint stiffness, we may consider using shock wave therapy combined with laser therapy for treatment. However, the specific mechanisms of shock wave and laser therapy in treating KOA are not yet fully understood, necessitating further research to better assess their potential value in KOA treatment. Additionally, we found that shock wave therapy, needle-knife, laser therapy and acupuncture consistently ranked among the top four in terms of improving VAS scores and WOMAC total score. Zhou et al. found that acupuncture can alleviate knee joint pain in patients by modulating pain perception through the descending pain modulation system [51]. Lin et al. found that needle-knife therapy can effectively improve clinical symptoms in patients by inhibiting the expression of inflammatory cytokines [52]. Therefore, in clinical practice, it is recommended to prioritize the use of these non-pharmacological therapies or combine them to treat patients with KOA.

Our study also found differences in the efficacy rankings of non-pharmacological treatments across the WOMAC pain, stiffness, and

function subscales. These differences may arise from several factors that warrant consideration. Physiological variations in how patients respond to different non-pharmacological treatments, with some prioritizing pain reduction over stiffness alleviation or functional improvement, could influence subscale outcomes. Additionally, the inherent measurement characteristics of the WOMAC scale, which assesses pain, stiffness, and functional limitations distinctly, might contribute to these discrepancies. Psychological factors such as individual pain perception and interpretations of stiffness and functional abilities could also impact reporting across subscales. Finally, the diversity within our study sample, encompassing variations in demographic profiles and disease severity, may further elucidate these differences.

This study has certain limitations: (1) Our study only included RCTs and excluded non-RCTs, which may limit the analysis of treatment comparisons and the diversity of patient populations. (2) The limited availability of studies for specific comparisons may impact the robustness and reliability of our findings. (3) Studies with high risk of bias may introduce uncertainties and limitations in the interpretation of results, thereby influencing the overall strength and reliability of our conclusions. To mitigate these limitations, we employed rigorous inclusion criteria and sensitivity analyses to assess the impact of bias on our results. (4) Some potential trials may have been missed due to incomplete search terms. Further data can be collected to support subgroup and meta-regression analyses to better understand potential effect modifiers. Moreover, the findings of this study still require further validation through the inclusion of more rigorously designed, multicenter, high-quality, large-sample studies to consolidate and strengthen the results of this study.

#### 5. Conclusion

The results of this study indicate that compared to other interventions, shock wave therapy can effectively alleviate pain and daily functional activities in patients with KOA. However, for improving stiffness in KOA patients, laser therapy may be the most effective. We can develop personalized treatment plans for patients in clinical practice based on their conditions, aiming to provide the best therapeutic outcomes for them.

# CRediT authorship contribution statement

ShiHang Cao: Writing – original draft, Supervision, Software, Data curation. Qiang Zan: Supervision, Data curation. Baohui Wang: Methodology, Data curation. Xiaochen Fan: Software, Data curation. Ziying Chen: Validation, Supervision, Software. Fengxiang Yan: Writing – review & editing, Software, Data curation.

#### Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

#### **Abbreviations**

VAS Visual Analog Scale

WOMAC Western Ontario and McMaster Universities Osteoarthritis Index

RCTs andomized controlled trials

KOA Knee Osteoarthritis

SUCRA Surface under the Cumulative Ranking Curve

# Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e36682.

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