

Meta-analysis and systematic review of acupotomy combined with puncture and moxibustion in the treatment of knee osteoarthritis

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Background: This study aimed to systematically evaluate the therapeutic effects of acupotomy combined with acupuncture and moxibustion on knee osteoarthritis (KOA), which was expected to provide a reference for clinical treatment of KOA using traditional Chinese medicine (TCM).

Methods: The databases PubMed, Embase, Medline, Ovid, and Springer were searched to retrieve randomized controlled trials (RCTs) on KOA treatment by acupotomy combined with acupuncture and moxibustion. The search time was set as from the date the database was established to 31 December 2020. The Cochrane Handbook for Systematic Reviews of Intervention 5.0.2 was used to conduct bias risk assessment on the included literature, and Review Manager 5.3 software was used for meta-analysis.

Results: A total of 10 RCTs were included in this study, including 1,073 participants. Meta-analysis results showed that compared with the control group, the clinical treatment efficiency of the experimental group was higher [mean difference (MD) =5.72; 95% confidence interval (CI): 3.39 to 9.64; Z=6.54; P<0.00001], and the postoperative visual analogue scale (VAS) scores were reduced (MD =-1.72; 95% CI: -2.41 to -1.03; Z=4.86; P<0.00001).

Discussion: Acupotomy combined with acupuncture and moxibustion treatment for KOA can increase clinical treatment efficiency, and relieve postoperative pain, suggesting that the combination of acupotomy, acupuncture, and moxibustion has better therapeutic effects on KOA and can be promoted clinically.

Keywords: Acupotomy; acupuncture and moxibustion; knee osteoarthritis (KOA); meta-analysis

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Introduction

Knee osteoarthritis (KOA) is the most common area of osteoarthritis (OA), and is mainly characterized by the progressive degeneration and destruction of cartilage, articular cartilage repair, osteophyte formation, subchondral bone remodeling, and so on (1). The elderly are predominantly affected by KOA, and it is more common

in women than men. Patients with KOA usually have symptoms such as knee pain, swelling, and joint snapping. If not treated in time, it will affect the knee joint function and the patient's quality of life (2). At present, the treatment methods for KOA include drug therapy, non-drug therapy, additional therapy, and surgical treatment. Non-surgical therapy is routinely applied. Drug therapy can be delivered

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via injection of anti-inflammatory analgesics or sodium hyaluronate into the joint cavity, but it is difficult to achieve the expected therapeutic effect (3).

Acupotomy and acupuncture and moxibustion are commonly used methods of traditional Chinese medicine (TCM) for the treatment of KOA. Acupuncture and moxibustion includes simple acupuncture, moxibustion, warm needle moxibustion, electric acupuncture, fire needle, and acupuncture point injection. Among them, moxibustion is an important TCM treatment. The moxa is prepared by drying the leaves and kneading to remove impurities, and then moxa is made into moxa sticks. The moxa is ignited to generate heat to stimulate specific acupoints, and to reinforce essence to adjust the function disorder. Clinical studies have shown that the combined application of acupotomy, acupuncture, and moxibustion can effectively relieve cartilage tissue pain, reduce pressure in the patient's knee joint, and restore the movement function of the knee joint (4). Though there is increasing research on the treatment of KOA with acupotomy and acupuncture and moxibustion, the systematic efficacy and quality evaluation of research is lacking. As a result, it is difficult to objectively reflect the therapeutic effects of acupotomy and acupuncture and moxibustion on KOA. Based on the reasons above, we adopted meta-analysis to systematically evaluate randomized controlled trials (RCTs) of acupotomy combined with acupuncture and moxibustion for the treatment of KOA.

We present the following article in accordance with the PRISMA reporting checklist (available at https://dx.doi.org/10.21037/apm-21-1083).

Methods

Literature retrieve

A total of 5 English databases (PubMed, Embase, Ovid, Medline, and Springer) were used to retrieve literature on the treatment of KOA by acupotomy combined with acupuncture and moxibustion. The retrieval time was set as from the establishment of each database to 31 December 2020. The search was performed using a combination of subject terms and free words, including "Knee Osteoarthritis", "KOA", "acupotomy", "acupuncture and moxibustion", "needle knife", and "acupotomology". The search terms were connected with "AND" or "OR". The retrieval was carried out by 2 researchers independently.

The inclusion and exclusion criteria

The inclusion criteria were as follows: (I) participants were patients who had been clinically diagnosed with KOA, unrestricted by gender and source; (II) RCT research published in English databases; (III) for literature of acupotomy treatment for KOA, the experimental group accepted acupotomy therapy, and the control group accepted other therapies. For literature of acupotomy combined with acupuncture and moxibustion for KOA, the experimental group accepted the combined treatment, and the control group accepted other treatment methods; (IV) There were clear inclusion criteria, diagnostic criteria, and therapeutic effects evaluation criteria for participants; (V) evaluation indexes included clinical treatment efficiency and visual analogue scale (VAS) score.

The exclusion criteria were as follows: (I) retrospective analyses, case reports, cohort studies, and other non-RCTs; (II) non-English literature or unpublished literature; (III) participants were ROA patients or patients with ROA combined with other diseases; (IV) literature with animals as research subjects; (V) literature published in duplicate; (VI) literature with incomplete research data so that it was impossible to calculate the corresponding index.

Literature screening

The software Endnote X6 (Clarivate Analytics, Philadelphia, PA, USA) was used to build a database and remove repetitive literature. The remaining literature were then screened by 2 senior experts. Literature that was not related to this research was excluded first through reading the title and abstract. Literature that did not meet the requirements was excluded further by reading the full text. The quality evaluation was performed next. If there were inconsistencies between the 2 experts, a consensus conclusion was obtained either through discussion, or a third expert was invited to arbitrate.

Data extraction

The 2 experts used a unified Excel table to extract data independently. We then performed 3 preliminary experiments before data extraction. If there were inconsistencies among experts, a consensus conclusion was reached through discussion, or a third expert was invited to arbitrate. The data extracted included: (I) research title; (II) first author and year of publication; (III) name of the

publication; (IV) The publication time of the research; (V) basic information of research participants: average age, gender, treatment plan, and drug dosage; (VI) grouping method and statistical method of the experimental group and the control group; (VII) source, sample size, and outcome indexes of the cases.

Literature quality evaluation

A risk assessment of bias was conducted at the same time by 2 researchers. If there were inconsistencies, the results were determined through discussion, or a third expert was invited for arbitration. The quality evaluation of this study referred to the standards in the Cochrane Handbook for Systematic Reviews of Intervention 5.0.2 (https://training.cochrane.org/handbook/archive/v5.0.2/), and the evaluation content included whether the random method was described properly; whether allocation concealment was adopted; whether the blind method was used for subjects; whether the blind method was used for the outcome assessor; whether the research data was complete; whether there was a selective report; and whether there were other biases.

Statistics

The software STATA 11.0 (StataCorp LLC., College Station, TX, USA) was used to analyze the included literature, and Review Manager 5.3 (RevMan, Copenhagen, The Nordic Cochrane Center, The Cochrane Collaboration, 2014) was used for meta-analysis and to draw the forest plot. The publication bias of the literature was analyzed by funnel chart. For binary variables such as clinical treatment efficiency, the odds ratio (OR) was used as the effect size, with the 95% confidence interval (95% CI) calculated. For continuous variables such as VAS score, Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) score, and interleukin-6β (IL-6β) level, if the detection indexes had the same unit, the weighted mean difference (MD) was used as the effect size, and if the units were different, the standardized MD (SMD) was used as the effect size. The I² test was used to evaluate the heterogeneity of the included literature. If I²>50%, it meant that there was large heterogeneity between the studies. The random effects model (REM) was used for meta-analysis. If I²<50%, it meant that the homogeneity between the studies was relatively good, and the fixed effects model (FEM) was used for meta-analysis of the combined effect size. The

combined effect size test was performed using U test and 95% CI, and the result of U test was expressed by P value. A P value <0.05 was the threshold for significance.

Results

Meta-analysis of acupotomy treatment for KOA

Basic information of included literature

A total of 936 related references were obtained in the preliminary retrieve, among which 383 were retrieved from PubMed, 231 from Embase, 166 from Ovid, 94 from Medline, and 62 from Springer. After the preliminary search, the titles of the references were input into the Endnote X6 software, and 188 duplicates were eliminated. We then invited 2 researchers to read the title and the abstract section of the literature. A total of 336 references remained according to the inclusion and exclusion criteria. Finally, 323 articles were further eliminated after having their full texts read carefully and cross-examined, with a total of 13 references (5-17) identified. The publication time was from 2007 to 2020, including 1,073 cases, with 536 in the experimental group and 537 in the control group. The baseline data such as age and disease course of the 2 groups were comparable (Figure 1, Table 1).

The bias risk assessment of included literature

The Cochrane tool was used to evaluate the bias risk of the 13 references included in this study, and then the bias risk map was drawn using Review Manager 5.3 software, as shown in *Figures 2* and 3. The risk of bias assessment included 7 items: (I) whether a random sequence was used; (II) whether allocation concealment was used; (III) whether the blind method was used for the subjects; (IV) whether the blind method was used for the outcome assessor; (V) whether the research data was complete; (VI) whether it was a selective report; (VII) whether there were other biases.

The effective rate of acupotomy for KOA

A total of 11 references with a total of 970 KOA patients included analyzed the effective rate of clinical treatment of patients, of which 480 were in the experimental group, with 429 effective cases, and 490 were in the control group, with 402 effective cases. The heterogeneity test results (I²=78%, P<0.00001) indicated that there was a certain degree of heterogeneity among the studies. Hence, the REM was used for analysis, and the analysis results are shown in

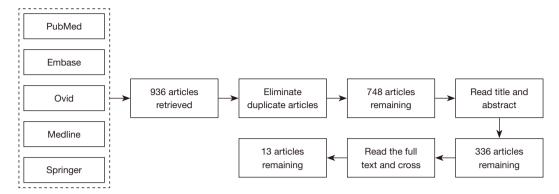


Figure 1 Literature retrieve process of acupotomy treatment for KOA. KOA, knee osteoarthritis.

Table 1 Basic characteristics of the included literature

First author	Year of publication	Group	Sample size	Gender	Intervention
Zhang Y	2007	Experimental	24	♂1; ♀23	Needle knife
		Control	24	<i>₫</i> 5; ♀19	Electroacupuncture
Li Z	2011	Experimental	50	_	Needle knife
		Control	50		Electroacupuncture
Chen M	2011	Experimental	60	∂18; ♀42	Needle knife
		Control	60	∂¹19; ♀41	Electroacupuncture
Shen W	2015	Experimental	60	∂23; ♀37	Needle knife + NSAIDS
		Control	60	∂26; ♀34	NSAIDS
Sun K	2016	Experimental	36	∂9; ♀2 7	Needle knife
		Control	37	∂12; ♀25	Acupuncture
Wang XB	2016	Experimental	36	∂9; ♀2 7	Needle knife
		Control	37	∂12; ⊋2 5	Acupuncture
Zhong ZP	2017	Experimental	60	∂23; ♀37	Needle knife + NSAIDS
		Control	60	∂26; ⊊34	NSAIDS
Wang XC	2017	Experimental	50	∂17;	Small needle knife
		Control	50	∂19; ⊊31	Acupuncture
Zhu DY	2017	Experimental	20	∂7; ♀13	Small needle knife
		Control	20	♂6; ♀14	Sodium hyaluronate
Xiu ZB	2018	Experimental	40	∂18; ⊋22	Needle knife + manual therapy
		Control	40	∂17; ⊊23	Acupuncture + manual therapy
Hong HQ	2019	Experimental	31	∂7;	Needle knife
		Control	30	∂13; ⊊17	Acupuncture
Sun XJ	2019	Experimental	30	∂9; ⊋21	Small needle knife
		Control	30	∂8; ♀22	Sodium hyaluronate
Wang Y	2020	Experimental	39	∂17;	Needle knife
		Control	39	∂16;	Acupuncture

 $NSAIDS, \, non-steroidal \, anti-inflammatory \, drugs.$

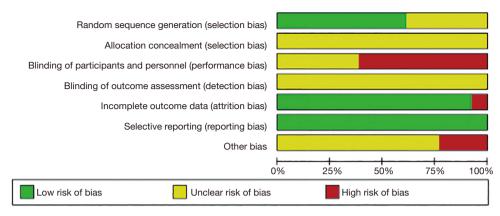


Figure 2 Meta-analysis bias risk assessment bar graph of acupotomy treatment of KOA. KOA, knee osteoarthritis.

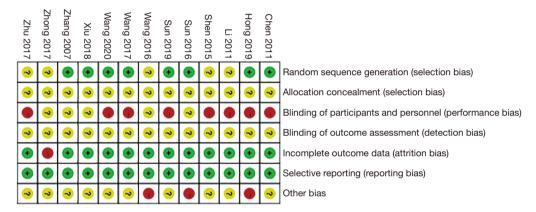


Figure 3 Meta-analysis bias risk assessment graph of acupotomy treatment of KOA, KOA, knee osteoarthritis.

	Experimental		rimental Control			Odds Ratio	Odds Ratio			
Study or Subgroup	Events	Total	Events	Total	Weight	M-H, Random, 95% C		M-H, Rand	om, 95% CI	
Chen 2011	58	60	54	60	9.5%	3.22 [0.62, 16.66]		+	•	
Hong 2019	29	31	22	30	9.5%	5.27 [1.02, 27.33]		1	•	
Li 2011	47	50	41	60	10.5%	7.26 [2.00, 26.31]			_	
Shen 2015	54	60	50	60	11.0%	1.80 [0.61, 5.32]		+	-	
Sun 2016	34	36	34	37	8.9%	1.50 [0.24, 9.55]				
Sun 2019	29	30	20	30	8.1%	14.50 [1.72, 122.40]			_	_
Wang 2017	50	50	45	50	6.2%	12.21 [0.66, 226.97]		+	•	_
Wang 2020	38	39	31	39	8.1%	9.81 [1.16, 82.71]			_	-
Xiu 2018	38	40	32	40	9.5%	4.75 [0.94, 23.98]		İ	•	
Zhang 2007	23	24	22	24	7.2%	2.09 [0.18, 24.73]			•	
Zhong 2017	29	60	51	60	11.5%	0.17 [0.07, 0.39]				
Total (95% CI)		480		490	100.0%	3.09 [1.11, 8.56]			•	
Total events	429		402							
Heterogeneity: Tau ² =	2.15; Chi2 :	78%	0.001		+	4000				
Test for overall effect:	Z = 2.17 (P	= 0.03)					0.001	0.1 1 [experimental]	10 [control]	1000

Figure 4 Forest plot of clinical treatment effective rate of acupotomy for KOA. KOA, knee osteoarthritis; HR, hazard ratio; CI, confidence interval.

Figure 4. The combined effect size of the meta-analysis was (MD =3.09; 95% CI: 1.11 to 8.56; Z=2.17; P=0.03), and the diamond in the forest diagram was located on the right

side of the vertical line, which suggested that the clinical effective rate of acupotomy treatment was higher than that of the control group.

	Experimental			Control			Mean Difference		Mean D	ifference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Rand	om, 95% CI
Chen 2011	1.27	0.74	60	3.64	0.78	60	17.0%	-2.37 [-2.64, -2.10]	•	
Hong 2019	2.94	0.98	31	4.42	0.77	30	16.7%	-1.48 [-1.92, -1.04]	•	
Sun 2016	2.03	1.7	36	3.76	2.15	37	15.2%	-1.73 [-2.62, -0.84]	-	
Sun 2019	3.41	0.62	30	5.48	0.43	30	17.0%	-2.07 [-2.34, -1.80]	•	
Wang 2020	0.98	0.15	39	1.03	0.23	39	17.2%	-0.05 [-0.14, 0.04]		†
Xiu 2018	2.51	0.73	40	3.52	0.74	40	16.9%	-1.01 [-1.33, -0.69]	•	'
Total (95% CI)			236			236	100.0%	-1.44 [-2.47, -0.42]	•	
Heterogeneity: Tau ² =	1.59; Ch	-10 -5	0 5 10							
Test for overall effect:	Z = 2.76	[experimental]								

Figure 5 Forest plot of VAS score after acupotomy treatment of KOA. VAS, visual analogue scale; KOA, knee osteoarthritis; CI, confidence interval; SD, standard deviation.

	Experimental			Control				Mean Difference		Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV. Random, 95% C		IV, Random, 95% CI		
Hong 2019	19.28	8.93	31	22.67	7.72	30	22.0%	-3.39 [-7.57, 0.79]				
Shen 2015	48.57	37.19	60	54.96	26.12	60	7.8%	-6.39 [-17.89, 5.11]				
Sun 2016	22.14	14.54	60	34.89	15.28	60	18.8%	-12.75 [-18.09, -7.41]				
Wang 2016	34.5	15.82	36	37.38	14.85	37	14.6%	-2.88 [-9.92, 4.16]				
Zhang 2007	12.13	9.66	24	15.21	9.65	24	18.4%	-3.08 [-8.54, 2.38]				
Zhu 2017	18.59	7.3	20	19.35	10.13	20	18.4%	-0.76 [-6.23, 4.71]		+		
Total (95% CI)			231			231	100.0%	-4.76 [-8.50, -1.03]		•		
Heterogeneity: Tau ² = 11.91; Chi ² = 11.78, df = 5 (P=0.04); I ² = 58%										-25 0 25	50	
Test for overall effect:	Z = 2.50	(P=0.0	-50	[experimental] [control]	50							

Figure 6 WOMAC score forest plot after acupotomy treatment of KOA. WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; KOA, knee osteoarthritis; CI, confidence interval; SD, standard deviation.

VAS score after acupotomy treatment of KOA

In this study, a total of 6 references analyzed the postoperative VAS scores of participants, with a total of 472 KOA patients included, including 236 cases in the experimental group and 236 cases in the control group. The heterogeneity test results (I²=99%, P<0.00001) indicated that there was a certain degree of heterogeneity among the studies. Hence, the REM was used for analysis, and the analysis results are shown in *Figure* 5. The combined effect size was (MD =-1.44; 95% CI: -2.47 to -0.42; Z=2.76; P=0.006), and the diamond in the forest diagram was on the left side of the vertical line, which indicated that the postoperative VAS score of the acupotomy treatment was lower than that of the control group, that is, the patients experienced less postoperative pain.

WOMAC score after acupotomy treatment of KOA

A total of 6 references analyzed the WOMAC scores of participants in this study, with a total of 462 KOA patients included, including 231 cases in the experimental group and 231 cases in the control group. The heterogeneity test results (I²=58%, P=0.04) suggested that there was a certain degree of heterogeneity among the studies. Hence, the REM was used for analysis, and the analysis

results are shown in *Figure 6*. The combined effect size of meta-analysis was (MD =-4.76; 95% CI: -8.50 to -1.03; Z=2.50; P=0.01), and the diamond in the forest diagram was located on the left side of the vertical line, which indicated that the postoperative WOMAC score of the acupotomy treatment was lower than that of the control group.

IL-1β levels after acupotomy treatment of KOA

In this study, 3 references evaluated postoperative IL-1 β levels in participants, with a total of 219 KOA patients included, including 110 in the experimental group and 109 in the control group. The heterogeneity test results (I²=74%, P=0.02) suggested that there was a certain degree of heterogeneity among the studies. Hence, the REM was used for analysis, and the analysis results are shown in *Figure* 7. The combined effect size of meta-analysis was (MD =–5.80; 95% CI: –7.16 to –4.44; Z=8.38; P<0.00001), and the diamond in the forest diagram was located on the left side of the vertical line, which indicated the level of IL-1 β after acupotomy treatment was lower.

Analysis of the publication bias of acupotomy for KOA

The software Review Manager 5.3 was used to analyze

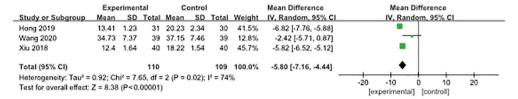


Figure 7 Forest plot of IL-1β level after acupotomy treatment of KOA. IL-1β, interleukin-1β; KOA, knee osteoarthritis; SD, standard deviation; CI, confidence interval.

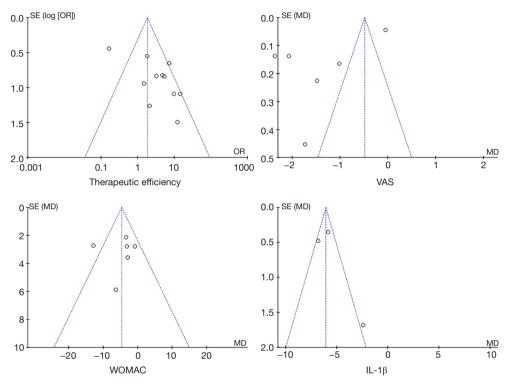


Figure 8 Funnel chart of various outcome evaluation indexes for KOA treated by acupotomy. KOA, knee osteoarthritis; VAS, visual analogue scale; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; IL-1, interleukin-1.

the outcome indexes of acupotomy treatment KOA, with a funnel chart drawn, as shown in Figure 8. In the funnel chart of clinical treatment efficiency and WOMAC score, the scattered points representing the literature were basically distributed within the credible interval, and the scattered points were relatively concentrated, which suggested that the publication bias of the literature was low. However, some of the scattered points in the funnel chart of participants' VAS scores and IL-1 β levels fell outside the credible interval, and the points were scattered, which suggested that there was a certain publication bias in the literature.

Meta-analysis of acupotomy combined with acupuncture and moxibustion in the treatment of KOA

Basic information of included literature

A preliminary search of 5 English databases resulted in a total of 811 related references, of which 238 were retrieved from PubMed, 189 from Embase, 145 from Ovid, 121 from Medline, and 118 from Springer. After the preliminary search, the titles of the references were input into Endnote X6, and 623 references were obtained after duplicates had been eliminated. We then invited 2 researchers to read the title and abstract section of the literature, and 260 references remained according to the inclusion and

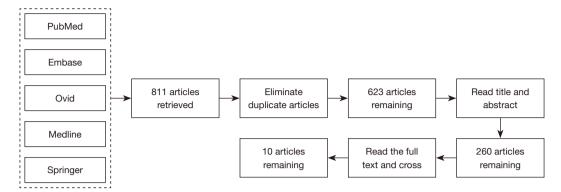


Figure 9 Literature retrieval process of acupotomy combined with acupuncture and moxibustion treatment of KOA. KOA, knee osteoarthritis.

exclusion criteria. Finally, 250 references were further eliminated after their full texts were carefully read, with a total of 10 references (18-27) included in this study. The publication time was from 2011 to 2020, with 983 research cases involved, including 500 in the experimental group and 483 in the control group. The baseline data such as age and disease course of the 2 groups were comparable (*Figure 9*, *Table 2*).

The bias risk assessment of included literature

The Cochrane bias risk assessment tool was used to evaluate the bias risk of the 10 references included in this study, and the software RevMan 5.3 was used to draw the bias risk chart. The results are shown in Figures 10 and 11. (I) Whether a random sequence was used: all of the 10 included references adopted the random grouping method. Among them, Cheng et al. pointed put the specific random method they used, suggesting low risk, and Wang et al. did not mention specifically which random method was used, suggesting unclear risk. (II) Whether allocation concealment was used: 10 references did not mention whether allocation concealment was applied to participants, suggesting unclear risk. (III) Whether the blind method was used for the subjects: Cheng et al. mentioned in their study that patients had signed an informed consent form, suggesting high risk, and Wang et al. did not mention whether the subjects were blinded, suggesting unclear risk. (IV) Whether the blind method was used for the outcome assessor: 10 references did not mention whether the outcome assessor was blinded, suggesting unclear risk. (V) Whether the research data was complete: the outcome data of 10 references was complete, indicating low risk. (VI) Whether it was a selective report: all of 10 references were

not selective reports, indicating low risk. (VII) Whether there were other biases: in the study of Wang et al., there were different numbers of subjects in experimental group and control group, suggesting high risk, and it was undetermined whether there were other biases in the study of Cheng et al., suggesting unclear risk.

The clinical treatment efficiency of acupotomy combined with acupuncture and moxibustion treatment of KOA

In this study, 9 references analyzed the effective rate of clinical treatment of patients, with a total of 921 KOA patients included, of which 470 cases were in the experimental group, with 451 effective cases, and 451 cases were in the control group, with 366 effective cases. The heterogeneity test results (I²=0%, P=0.95) suggested that the heterogeneity between the studies was small. Hence, the fixed-effects model was used for analysis, and the analysis results are shown in *Figure 12*. The combined effect size of meta-analysis was (MD =5.72; 95% CI: 3.39 to 9.64]; Z=6.54; P<0.00001), and the diamond in the forest diagram was located on the right side of the vertical line, which suggested that the effective rate of acupotomy combined with acupuncture and moxibustion for KOA patients was higher than that of the control group.

The postoperative VAS score of acupotomy combined with acupuncture and moxibustion treatment for KOA

In this study, 6 references analyzed the postoperative VAS scores of participants, with a total of 713 KOA patients included, including 358 cases in the experimental group and 355 cases in the control group. The heterogeneity test results (I^2 =99%, P<0.00001) indicated that there

Table 2 Basic characteristics of the included literature

First author	Year of publication	Group	Sample size	Gender	Intervention
Wang WH	2010	Experimental	44	∂12; ♀32	Needle knife + acupuncture
		Control	30	∂7; ♀23	Acupuncture
Gong ZX	2011	Experimental	76	∂34; ♀42	Small needle knife + acupuncture
		Control	73	ੰ33 ; ♀40	Sodium hyaluronate
Cheng Y	2013	Experimental	30	_	Small needle knife + bloodletting
		Control	30		Electroacupuncture
Li Q	2014	Experimental	32	-	Small needle knife + warm acupuncture
		Control	32		Tuina
Li Z	2014	Experimental	38	∂16; ♀22	Needle knife + moxibustion
		Control	38	∂20; ♀18	Moxibustion
Zhu CJ	2015	Experimental	100	♂45; ♀55	Small needle knife + acupuncture
		Control	100	∂47; ⊊53	Sodium hyaluronate
Li F	2016	Experimental	30	∂10; ⊋2 0	Needle knife + pseudo-ginseng-cake moxibustion
		Control	30	<i>₫</i> 12; ♀18	Diclofenac sodium sustained release tablets + glucosamine sulfate
Wu D	2017	Experimental	52	∂20; ⊋3 2	Needle knife + warm acupuncture
		Control	52	∂21; ⊋3 1	Warm acupuncture
Zhan X	2019	Experimental	57	∂ 23; ♀34	Needle knife + acupuncture
		Control	57	∂22; ⊋ 35	Sodium hyaluronate
Sun J	2020	Experimental	41	♂20; ♀21	Micro needle knife + warm acupuncture
		Control	41	♂21; ♀20	Warm acupuncture

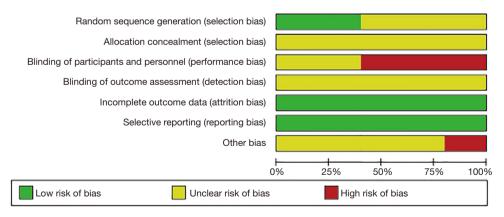


Figure 10 The meta-analysis bias risk assessment bar chart of acupotomy combined with acupuncture and moxibustion for KOA. KOA, knee osteoarthritis.

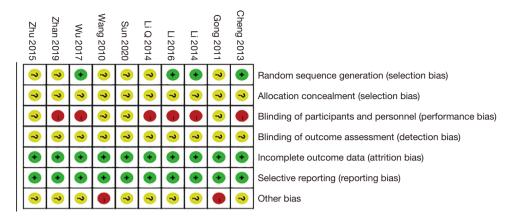


Figure 11 Meta-analysis risk bias assessment graph in the treatment of KOA by acupotomy combined with acupuncture and moxibustion. KOA, knee osteoarthritis.

	Experimental		Control			Odds Ratio	Odds Ratio
Study or Subgroup	Events	Total	Events	Total	Weight	M-H. Fixed, 95% C	M-H, Fixed, 95% CI
Cheng 2013	29	30	28	30	6.4%	2.07 [0.18, 24.15]	-
Gong 2011	75	76	63	73	5.8%	11.90 [1.48, 95.55]	
Lì 2016	37	38	28	36	5.2%	10.57 [1.25, 89.50]	
Li Q 2014	30	32	25	32	10.8%	4.20 [0.80, 22.06]	
Sun 2020	37	41	30	41	20.2%	3.39 [0.98, 11.74]	-
Wang 2010	41	44	23	30	12.9%	4.16 [0.98, 17.66]	-
Wu 2017	51	52	45	52	6.0%	7.93 [0.94, 66.98]	•
Zhan 2019	55	57	45	57	10.9%	7.33 [1.56, 34.48]	
Zhu 2015	96	100	79	100	21.8%	6.38 [2.10, 19.36]	-
Total (95% CI)		470		451	100.0%	5.72 [3.39, 9.64]	•
Total events	451		366				
Heterogeneity: Chi ² = 2	2.68, df = 8	(P = 0.1)	95); I ² = 0		1001		
Test for overall effect:	Z = 6.54 (P	0.001 0.1 1 10 1000 [experimental] [control]					

Figure 12 Forest plot of clinical treatment effective rate of acupotomy combined with acupuncture and moxibustion for KOA. KOA, knee osteoarthritis; CI, confidence interval.

	Experimental			Control			Mean Difference			Mean Difference		
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI		IV, Random, 95%	CI	
Gong 2011	2.11	0.57	76	4.67	0.45	73	16.9%	-2.56 [-2.72, -2.40]		•		
Li Q 2014	1.25	0.88	32	2.33	1.12	32	15.7%	-1.08 [-1.57, -0.59]		*		
Sun 2020	2.82	0.36	41	3.47	0.74	41	16.7%	-0.65 [-0.90, -0.40]		•		
Wu 2017	2.8	0.3	52	3.7	0.5	52	16.9%	-0.90 [-1.06, -0.74]		•		
Zhan 2019	2.08	0.26	57	4.8	0.28	57	17.0%	-2.72 [-2.82, -2.62]		•		
Zhu 2015	2.17	0.56	100	4.51	0.32	100	16.9%	-2.34 [-2.47, -2.21]		•		
Total (95% CI)			358			355	100.0%	-1.72 [-2.41, -1.03]		•		
Heterogeneity: Tau ² = 0.73; Chi ² = 551.87, df = 5 (P < 0.00001); I ² = 99%										-5 0	5 10	
Test for overall effect: Z = 4.86 (P<0.00001)										[experimental] [control	-	

Figure 13 The postoperative VAS score forest plot of acupotomy combined with acupuncture and moxibustion treatment for KOA. VAS, visual analogue scale; KOA, knee osteoarthritis; CI, confidence interval; SD, standard deviation.

was a certain degree of heterogeneity among the studies. Hence, the REM was used for analysis, and the analysis results are shown in *Figure 13*. The combined effect size of meta-analysis was (MD =-1.72; 95% CI: -2.41 to -1.03; Z=4.86; P<0.00001), and the diamond in the forest plot

was on the left of the vertical line, which indicated that the postoperative VAS score of KOA patients treated with acupotomy combined with acupuncture and moxibustion was lower than that of the control group, that is, the patients experienced less postoperative pain.

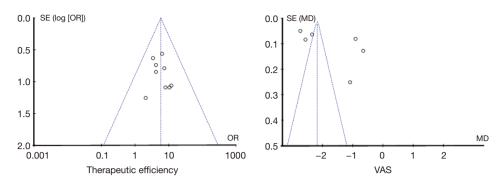


Figure 14 Funnel chart of various outcome evaluation indexes of acupotomy combined with acupuncture and moxibustion treatment for KOA. KOA, knee osteoarthritis; VAS, visual analogue scale.

The publication bias analysis on acupotomy combined with acupuncture and moxibustion treatment for KOA

The software RevMan 5.3 was used to analyze the publication bias of the outcome indexes of the acupotomy combined with acupuncture and moxibustion treatment of KOA, with a funnel chart drawn, as shown in *Figure 14*. The scatter points representing the literature were all distributed within the credible interval in the funnel chart of the effective clinical treatment, and the scatter points were concentrated, which suggested that the publication bias of the literature was low. However, most of the scattered points fell outside the credible interval in the funnel chart of the participants' VAS scores, and the distribution was relatively scattered, which suggested that the literature had a certain degree of publication bias.

Discussion

A common type of chronic osteoarthritis, KOA is clinically manifested as knee pain, swelling, and movement disorders. It mostly occurs in the elderly with high incidence. It is held in TCM that the clinical manifestations of KOA belong to the categories of "arthralgia", "bone malaise", and "back and leg pain". It is believed that due to wind-chill dampheat, the meridian is blocked, leading to poor circulation of qi and blood and dystrophy of the joint (28). Clinical TCM treatment methods focus on warming and activating the meridians and promoting blood circulation to dissipate blood stasis. Acupotomy for KOA can not only dredge the meridians, but also separate adhesion tissue, restoring the mechanical balance of knee joints (29). Acupuncture and moxibustion can promote the flow of Oi, blood, and body fluid around the knee joint, and relieve the pain of the patient. The combined treatment of acupotomy and

acupuncture and moxibustion can restore the stability of the knee joint and reduce the probability of inflammation, which is of great significance to the treatment of KOA (30).

To realize more accurate systematic evaluation of the therapeutic effects of acupotomy combined with acupuncture and moxibustion on KOA, we conducted a meta-analysis on the therapeutic effects of acupotomy on KOA first, with a total of 13 references included and 1,073 research cases involved. The meta-analysis showed KOA patients treated by acupotomy demonstrated higher clinical treatment efficiency, less postoperative pain, and a reduced IL-1 β level. The meta-analysis of the combined treatment for KOA included a total of 10 references, with 983 cases involved. The results showed that KOA patients of the combined treatment exhibited higher clinical treatment efficiency than that of the control group, and lower postoperative VAS scores, suggesting that the combined treatment of KOA can effectively relieve postoperative pain.

Conclusions

In the study, a systematic analysis was performed to evaluate the clinical therapeutic effects of acupotomy combined with acupuncture and moxibustion in the treatment of KOA. The outcomes showed that acupotomy combined with acupuncture and moxibustion for KOA can increase treatment efficiency and relieve postoperative pain. However, some limitations of the study should be noted. The number of the included references was small. Only 2 indexes were used for comparison, namely, clinical treatment efficiency and VAS score, and only the therapeutic effects at the end of treatment were analyzed, which is not enough to evaluate the long-term therapeutic effects of acupotomy combined with acupuncture and moxibustion. In the follow-

up, RCTs of an expanded sample size and higher quality are needed to strengthen the findings of this study, so as to accurately evaluate the clinical therapeutic effects of acupotomy combined with acupuncture and moxibustion in the treatment of KOA.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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