Effect and safety of acupotomy in treatment of knee osteoarthritis: a systematic review and Meta-analysis

Fang Ting, Li Qi, Zhou Fanyuan, Liu Fushui, Liu Zhongyong, Zhao Meimei, Chen Mei, You Jianyu, Jin Yuli, Xie Jinmei

Fang Ting, Liu Fushui, Department of Acupotomy Chiropractors, The Affiliated Hospital of Jiangxi University of Traditional Chinese Medicine, Nanchang 330006, China
Li Qi, Jiangxi Normal University, Nanchang 330022, China
Zhou Fanyuan, Zhao Meimei, Chen Mei, You Jianyu, Jin Yuli, Xie Jinmei, College of Clinical Medicine, Jiangxi University of Traditional Chinese Medicine, Nanchang 330004, China
Liu Zhongyong, Department of Cardiovascular Medicine, The Affiliated Hospital of Jiangxi University of Traditional Chinese Medicine, Nanchang 330006, China

Supported by: China National Natural Science Foundation of China: Study of Acupotomy on Autophagy and Apoptosis of Cervical Muscles in Cervical Spondylosis Mediated by PI3K/Akt/mTOR Signaling Pathway (No. 81560792)

Correspondence to: Liu Fushui, Department of Acupotomy Chiropractors, The Affiliated Hospital of Jiangxi University of Traditional Chinese Medicine, Nanchang 330006, China. lftcm@163.com; Liu Zhongyong, Department of Cardiovascular Medicine, The Affiliated Hospital of Jiangxi University of Traditional Chinese Medicine, Nanchang 330006, China. lzyongmail@163.com

Telephone: +86-13340118325; +86-15270889717
Accepted: September 12, 2019

Abstract

OBJECTIVE: To evaluate the clinical efficacy and safety of acupotomy in treatment of knee osteoarthritis (OA).

METHODS: Extensive literature searches were carried out in PubMed, EMBASE, Cochrane Library (Issue 5, 2017), Chinese Biomedical Literature Database, China National Knowledge Infrastructure Database, China Science and Technology Journal Database and Wanfang Database. All databases were retrieved from their inception until May 31, 2017. Randomized controlled trials incorporating acupotomy versus intra-articular sodium hyaluronate for knee osteoarthritis were included. According to Cochrane Reviews’ Handbook (5.2), two reviewers screened each article and extracted data independently and were blinded to the findings of each reviewer. Meta-analysis was performed by the Cochrane Collaboration’s RevMan 5.3 software.

RESULTS: We identified 12 studies involving 1150 patients aged between 40 and 78 years old. The pooled analysis indicated that acupotomy showed a significant improvement for short-term effect [cure rate: odds ratio (OR) = 2.04, 95% confidence interval (CI) (1.46, 2.85), P < 0.01; total effective rate: OR = 2.25, 95% CI (1.55, 3.28), P < 0.01; pain score: standard mean difference (SMD) = –1.02, 95% CI (–1.72, –0.31); P = 0.005; Western Ontario and McMaster Universities Questionnaire (WOMAC) score: SMD = –0.74; 95% CI (–1.11, –0.37); P < 0.01]; and also for long-term effect [total effective rate: OR = 2.99, 95% CI (1.88, 4.76), Z = 4.64, P < 0.01; pain score: SMD = –1.68; 95% CI (–2.14, –1.22); P < 0.001; WOMAC score: SMD = –0.91; 95% CI (–1.40, –0.41); P < 0.001]. In addition, there was no obvious difference between acupotomy group and control group in adverse events [OR = 2.13, 95% CI (0.14, 32.28), P = 0.58].

CONCLUSION: Acupotomy is a safe and effective treatment for KOA. However, due to the methodological deficiency of the included studies, well-designed randomized controlled trials are required to further confirm the findings.
Keywords: Osteoarthritis, knee; Hyaluronic acid; Acupuncture therapy; Review; Meta-analysis

INTRODUCTION

Knee osteoarthritis (KOA) is a common chronic and degenerative disease which is one of the leading cause of chronic disability in middle-aged and elderly people, characterized by knee pain, stiffness and dysfunction. According to statistics, the incidence of KOA increased with age, it reaches 50% in the people aged over 60, while it can reach 80% over 75s, and compared to male, female is obvious higher especially in postmenopausal women period. With the advent of an aging population in the world, KOA has become a major public health problem that threatens the health of the elderly and affects the patients’ quality of life, furthermore, the disability rate can reach 53%, being the second most significant disabling disease next to cardiovascular disease. At present, 10% of the world’s medical treatments are related to KOA. The annual treatment costs and other economic losses for KOA rose in line with annual growth, even up to $125 billion in the US. Therefore, finding a safe and effective treatment is of great significance to relieve pain, reduce disability, and alleviate family and social economic burden. Currently, the therapeutic methods for KOA mainly include exercise, physical therapy, medicine and surgery in terminal stage. These therapies can relieve symptoms and delay the onset of disease, but cannot stop the progression of KOA. Among them, the surgical treatment is generally effective, but patients may suffer from persistent pain and serious complications. In conventional therapy, the intra-articular injection of sodium hyaluronate (HA) is a commonly used treatment for KOA with good safety and effectiveness. It is a glycosaminoglycan that can be found within various soft connective tissues and epithelial and neural tissues, and the concentration of HA in the synovial fluid of healthy knee joint is approximately 3 mg/mL in a young man and 1 mg/mL in an old man. Studies shows it plays a role in lubricant, shock absorber, inhibiting inflammation and relieving pain.

With the continuous development of the traditional Chinese acupuncture therapy, it has formed two major branches: one is filiform needle therapy; the other is micro blade-edged needle therapy. A successful example of the latter is acupotomy, it was first introduced in 1976, based on the acupuncture of Traditional Chinese Medicine combining modern surgical principles, and exerted dual functions of acupuncture and knife. It can bring better economic and social benefits, and is favored among patients. According to the Chinese Academy of Chinese Medical Sciences research, 360 000 people receive acupotomy every day, and the practitioners of this therapy are existing in over thirty countries with overseas development of acupotomy. Acupotomy is mainly used to treat soft tissue injuries, nerve entrapment and bone hyperplasia. In recent years, acupotomy has been widely used in KOA patients and has been trusted by a considerable number of patients. Besides, many basic researches have been completed and reported positive efficacy of acupotomy for the treatment of arthritis and pain.

In 2012, Liu et al. completed a Meta-analysis of six RCTs comparing acupotomy with HA treatment for KOA, whereas the long-term clinical efficacy and the other secondary outcomes among studies were not discussed, and the safety of acupotomy was not assessed. Recently, more articles with larger sample sizes or longer follow-up have emerged to evaluate the efficacy and safety of acupotomy for KOA, so an updated Meta-analysis is urgently required.

METHODS

Search strategy

We developed a study protocol based on Cochrane Reviews’ Handbook for this systematic review and Meta-analysis. Electronic searches were performed in PubMed, EMBASE, Cochrane library (Issue 5, 2017), Chinese Biomedical Literature Database, China National Knowledge Infrastructure Database, China Science and Technology Journal Database and Wanfang Database up to May 31, 2017. Using following terms: acupotomy, acupotome, needle-knife, needle scalpel, knee osteoarthritis, KOA, osteoarthritis, gonarthritis, gonitis, and knee arthritis, and the same terms in Chinese were searched in Chinese databases. We did not impose any language restriction. Additionally we also manually searched bibliographies and contacted relevant study authors for additional data when necessary. The search strategy for PubMed as follows: 1# Mesh term: ((acupotomy) or (acupotome) or (needle-knife) or (needle scalpel)): ti, ab, kw; 2# Mesh terms: ((knee osteoarthritis) or (KOA) or (osteoarthritis) or (gonarthrosis) or (gonitis) or (cervical disc) or (knee arthritis)): ti, ab, kw 3# Mesh terms: ((clinical trials) or (randomized controlled trials))

Inclusion criteria and exclusion criteria

We chose the PICOS principle (population, intervention, comparison, outcome, and study design) as the inclusion criteria. P: people diagnosed with KOA using clear diagnostic criteria that Guiding Principles of Clinical Research on New Drugs (GPCRND)-knee osteoarthritis, Guidelines for the Diagnosis, Treatment of Osteoarthritis (GDTOA), American College of Rheumatology (ACR) and Kallgren-Lawrence Criteria Condition (KLCC) were included. Patients’ gender, age, the
source of the case and duration of illness are not limited. I and C: the treatment group and the control group were treated with single acupotomy and injection intra-articular HA independently. Studies with other complementary treatments in the two groups were ruled out. O: we assessed the total effective rate and cure rate (total effective rate = (total number-invalid number) / total number, cure rate = cure number/total number) as primary outcomes, the pain score, adverse effects and Western Ontario and McMaster Universities Questionnaire (WOMAC) score regarded as secondary outcomes. All outcomes were assessed with definitive assessment instrument, such as WOMAC, the GPCRND, visual analogue scale (VAS) and numeric rating scale (NRS). S: randomized controlled trials (RCTs) were included. The exclusion criteria were shown as following: duplicate studies; wrong interventions: studies were excluded which used open surgery or acupotomy was manipulated in both two groups.

Data extraction
Two of us (Fang Ting and Zhou Fanyuan) independently extracted relevant data from the eligible studies according to a predefined standardized protocol, and then cross checked. Discrepancies were resolved through discussion or by consulting the other reviewer (Liu Fushui). The key information was collected systematically using a standardized form. From the references mainly extracted were the first author, year of publication, case source, study design, baseline characteristics for participants (age, sex, number of participants, intervention), diagnostic criteria of KOA, efficacy evaluation criteria, outcome assessments, duration of intervention, adverse events, follow-up and withdrawal. Where possible, clarification would be sought from the first author regarding the ambiguity in the information provided in some studies.

Quality assessment
Methodological quality and risk of bias in included studies were assessed on the basis of Cochrane collaboration’s tool, which is based on seven items: (a) randomization sequence generation; (b) allocation concealment; (c) blinding of participants or personnel; (d) blinding of outcome assessment; (e) incompleteness bias; (f) reporting bias; (g) other sources of bias. Each item was recorded as high, low, or unclear risk of bias that is represented as high (H), low (L), and unclear (U) respectively. The risk of bias was assessed by two reviewers (Fang Ting and Zhou Fanyuan) independently. Disagreements would be settled by discussing and analyzing between reviewers.

Data analysis
Data analysis was performed according to the RevMan5.3 statistical software (Copenhagen: the Nordic Cochrane Centre, the Cochrane Collaboration, 2014) for Meta-analysis. For the categorical data (clinical effect and frequency of adverse events), we calculated combined odds ratio (OR) with 95% confidence intervals (CI); as regards to continuous variables, the weighted mean difference (WMD) or standard mean difference (SMD) combined with 95% CI were applied. χ² test and Higgins I² test were used to evaluate the heterogeneity between the studies, if I² ≤ 50%, P ≥ 0.10, the fixed effect model was applied; otherwise the random effect model was used. In this Meta-analysis, P value smaller than 0.05 was considered statistically significant. Forest plot was performed using Revman 5.3, funnel plot, Begg’s test and Egger’s test were used to evaluate the publication bias using Stata 12.0 (Stata Corp., LP, College Station, TX, USA).

Ethical statement
All analyses were based on previously published studies, so ethical approval was superfluous.

RESULTS

Search results
A total of 1423 potential literature citations were obtained in the initial examination, including 1398 Chinese literatures and 25 English literatures. It remained 959 literatures after we eliminated 464 duplicates with EndNote software. Then, 813 literatures were excluded after scanning the title and abstracts. Finally, in accordance with the prespecified exclusion and inclusion criteria, 12 eligible RCTs31-32 were included in the review, which were all Chinese literatures (Figure 1).

Basic characteristics of eligible studies
The basic characteristics of all eligible studies were provided in Table 1. All studies were single center clinical RCTs and were published between 2007 and 2017 in China. There were two studies31,32 were 3-arm design, we divided it into two RCTs and selected a combination that met the inclusion criteria. Sample size of each study ranged from 40 to 316 and the sum was 1150 included 410 male patients and 631 female patients (The remaining 109 cases were uncertain because one study32 did not report the gender in detail).

Patients in acupotomy group received only acupotomy, the treatment point selection was based on obvious tenderness point or tubercule around the patella. And patients in control group only received intra-articular HA. Two RCTs21-22 used GPCRND, six RCTs22,25,26,29,31 adopted GDTOA, four RCTs23,26,30,32 received KLCC and three RCTs22,26 utilized ACR as their diagnostic criteria respectively. One RCT30 only calculated VAS score, the others all calculated clinical effects. Long-term effect (it referred to additional follow-up evaluation that patients received at least 4 weeks after treatment): only one RCT30 reported the long-term clinical effects, one RCT30 reported the long-term VAS score and one
within half a year and the control group was 53%.

Six RCTs reported adverse events, the incidence of adverse events calculated the WOMAC score totally. Five RCTs reported long-term WOMAC score after half a year and three months respectively. Four RCTs calculated the WOMAC score totally. Five RCTs reported adverse events, the incidence of adverse events of the experimental group was 4.3%, while the control group was 2.2%. Six RCTs recorded the level of pain and one of them selected NRS to assess pain, the others utilized VAS to assess pain. One RCT reported the recurrence rate of acupotomy group was 25.0% within half a year and the control group was 53.4%.

**Quality assessment**

Quality and risk of bias of included trials were assessed by the Cochrane collaboration’s tool. Except the two RCTs didn’t describe the method of randomization sequence generation in detail, the rest all mentioned appropriately randomization sequence generation with software-generated randomization table or random number table, judged to low risk of bias. Two RCTs were judged to low risk of bias for using proper opaque envelopes to achieve allocation concealment. As for the

---

**Table 1 Characteristics of included studies**

<table>
<thead>
<tr>
<th>Study</th>
<th>Population (T/C)</th>
<th>Treatment</th>
<th>Control</th>
<th>Age (T/C)</th>
<th>Female/Man</th>
<th>Duration (T/C) (week)</th>
<th>Outcome</th>
<th>Adverse events</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yang DW et al 2007</td>
<td>56/53</td>
<td>Acupotomy</td>
<td>HA, 2 mL</td>
<td>42-78</td>
<td>NR</td>
<td>5/5</td>
<td>CE</td>
<td>NR</td>
</tr>
<tr>
<td>Wang LK 2009</td>
<td>30/30</td>
<td>Acupotomy</td>
<td>HA, 2 mL</td>
<td>41-74</td>
<td>40/20</td>
<td>5/5</td>
<td>CE, WOMAC</td>
<td>NR</td>
</tr>
<tr>
<td>Lu D et al 2010</td>
<td>182/134</td>
<td>Acupotomy</td>
<td>HA, 2 mL</td>
<td>62.51±3.35</td>
<td>150/166</td>
<td>5/5</td>
<td>CE</td>
<td>NR</td>
</tr>
<tr>
<td>Zhu JS 2011</td>
<td>40/40</td>
<td>Acupotomy</td>
<td>HA, 2 mL</td>
<td>40-75</td>
<td>55/25</td>
<td>5/5</td>
<td>CE</td>
<td>NR</td>
</tr>
<tr>
<td>Xu CH et al 2013</td>
<td>28/28</td>
<td>Acupotomy</td>
<td>HA, 2 mL</td>
<td>59.6±6.8</td>
<td>25/31</td>
<td>5/5</td>
<td>CE</td>
<td>NR</td>
</tr>
<tr>
<td>Zhu DY 2013</td>
<td>20/20</td>
<td>Acupotomy</td>
<td>HA, 2 mL</td>
<td>53.55±7.46</td>
<td>27/13</td>
<td>5/5</td>
<td>CE, WOMAC</td>
<td>NR</td>
</tr>
<tr>
<td>Niu SJ 2013</td>
<td>40/40</td>
<td>Acupotomy</td>
<td>HA, 2 mL</td>
<td>50.1±9.12</td>
<td>42/38</td>
<td>2/2</td>
<td>CE, PS</td>
<td>NR</td>
</tr>
<tr>
<td>Zhang P et al 2015</td>
<td>50/50</td>
<td>Acupotomy</td>
<td>HA, 2 mL</td>
<td>57.5±4.91</td>
<td>58/42</td>
<td>3/3</td>
<td>CE</td>
<td>NR</td>
</tr>
<tr>
<td>Zheng ZW 2015</td>
<td>40/40</td>
<td>Acupotomy</td>
<td>HA, 2 mL</td>
<td>62.47±10.23</td>
<td>58/22</td>
<td>5/5</td>
<td>CE,NRS</td>
<td>Yes</td>
</tr>
<tr>
<td>Zhou L et al 2015</td>
<td>50/50</td>
<td>Acupotomy</td>
<td>HA, 2 mL</td>
<td>58.18±12.0</td>
<td>64/36</td>
<td>4/4</td>
<td>VAS</td>
<td>Yes</td>
</tr>
<tr>
<td>Zhong TH 2016</td>
<td>30/30</td>
<td>Acupotomy</td>
<td>HA</td>
<td>50-80</td>
<td>37/23</td>
<td>3/3</td>
<td>CE, WOMAC, VAS</td>
<td>Yes</td>
</tr>
<tr>
<td>Meng F et al 2017</td>
<td>36/33</td>
<td>Acupotomy</td>
<td>HA, 2 mL</td>
<td>56.46±13.25</td>
<td>31/38</td>
<td>5/5</td>
<td>CE, WOMAC, PS</td>
<td>Yes</td>
</tr>
</tbody>
</table>

Notes: T: treatment; C: control; NR: not reported; CE: clinical effect; NRS: numeric rating scale; VAS: visual analogue scale. HA: hyaluronate; WOMAC: Western Ontario and McMaster Universities Questionnaire; PS: pain score.
blinding of participants and personnel, all RCTs were judged to high risk of bias as it was impossible to carry out in our included studies. Only one RCT\(^{31}\) just referred the blinding of outcome assessment, others didn’t mention it, so all RCTs were judged to unclear risk of bias. When it comes to incomplete data, three RCTs\(^{31,27,31}\) reported no missing data, four RCTs\(^{22,26,28,32}\) provided the number of dropout and reason for withdrawal, those all judged to low risk of bias, two RCTs\(^{23,10}\) were judged to high risk of bias because they missed the primary data. Regarding selective reporting, protocols of these trials conducted in China are not published, it is hard to assess the selective reporting bias of these trials, and therefore all RCTs were judged to unclear risk of bias. Estimate of each risk of bias item for all included studies were revealed in Figures 2 and 3.

**Short-term outcomes**

Cure rate: except two RCTs\(^{22,28}\) the rest included studies employed clinical effect as outcome assessment. Analysis of data from cure rate at short-term showed no heterogeneity \((I^2 = 0\%)\) in all included RCTs, the fixed effect was applied. Meta-analysis showed that the cure rate of acupotomy group was higher than that of HA group \([OR = 2.04, 95\% CI = (1.46, 2.85), Z = 4.21, P < 0.01]\) (Figure 4).

Total effective rate: data extracted from eleven individual RCTs showed that no heterogeneity existed \((I^2 = 0\%)\), the fixed effect was applied for statistical analysis. Results from the pooled data supported the clinical significance of the total effective rate of acupotomy group \([OR = 2.25, 95\% CI (1.55, 3.28), Z = 4.24, P < 0.01]\) (Figure 4).

Pain score: pain scores were available in eight of the studies included VAS and NRS score. Data extracted showed obvious heterogeneity in the consistency of study results \((I^2 = 92\%; P < 0.01)\), the random effects model was utilized for statistical analysis. The combination of results showed that acupotomy could further alleviate pain associated with KOA \([SMD = −1.02; 95\% CI (−1.72, −0.31); P = 0.005]\) (Figure 5).

WOMAC rating scale score: four RCTs\(^{22,26,31-32}\) reported the WOMAC score. The overall results revealed that the acupotomy group had the lower WOMAC score \([SMD = −0.74; 95\% CI (−1.11, −0.37); P < 0.01]\).

The heterogeneity between these studies was moderate \((I^2 = 48\%; P = 0.12)\), the random effects model was utilized (Figure 5).

**Long-term effect**

Total effective rate, pain score and WOMAC score: only one RCT\(^{33}\) reported the total effective rate, furthermore, two RCTs\(^{31,32}\) described the pain and WOMAC score respectively. The Meta-analyses all showed a significant difference that the long-term effect of acupotomy group were higher than that of HA group \([total effective rate: OR = 2.99, 95\% CI (1.88, 4.76), Z = 4.64, P < 0.001]; pain score: SMD = −1.68; 95\% CI (−2.14, −1.22); P < 0.001; WOMAC score: SMD = −0.91; 95\% CI (−1.40, −0.41); P < 0.001]\) (Figures 6, 7).

**Adverse effect**

The rate of adverse effect was obtained from four RCTs\(^{29,32}\). One RCT\(^{33}\) demonstrated no adverse effects happened in the study period; another study\(^{30}\) described that the patient’s joints showed redness and swelling after HA was injected; Zhong\(^{34}\) recorded the pain, bleeding, hematomata, swelling of the joint and infection of the incision after treatment with acupotomy; Meng\(^{35}\) described the occurrence of palpitation, chest tightness and cold sweat after the end of acupotomy treatment. The heterogeneity test revealed a moderate difference \((I^2 = 60\%, P = 0.08)\). However, the combined data indicated no significant difference in reducing adverse effects between the two groups \([OR = 2.13, 95\% CI (0.14, 32.28), P = 0.58]\) (Figure 8).

**Publication bias**

Funnel plots were utilized to estimate publication bias (Figure 9). Cure rate was selected as an example as an outcome in most of the studies for publication bias was generally performed only when at least 10 studies were included. The resulting graphs showed no obvious asymmetry in this Meta-analysis, Begg’s test \((z = 0.72, P = 0.474)\) and Egger’s test \((t = 1.40, P = 0.200)\) also showed no statistically significant publication bias.

---

**Figure 2** Risk of bias graph: review authors’ judgements about each risk of bias item presented as percentages across all included studies.
Generally recognized as a safe and effective treatment for KOA, so we can suggest that acupotomy is as safe as HA for KOA. In any event, none of the adverse events for acupotomy was serious, and most of them could resolve spontaneously without medical intervention. Those adverse events can be avoided by reinforcing the aseptic operation specification, strengthening the operator’s clinical experience, and enhancing the patient’s confidence in the operator. Besides, it is essential that the operator acquaint with the extent of anatomical knowledge. Based on the findings of our included studies, we propose that acupotomy is an effective and safe therapy for KOA patients. Furthermore, a safer method was reported that acupotomy can be visible by ultrasound-guided, X-ray, CT and MRI in recent years. They could reduce the risk of blind sight of traditional acupotomy, maybe visualization of acupotomy is a trend and well worth for further investigation.

At present, the pathogenesis of KOA has not been acquainted entirely, and is generally believed to be related to age, sex, endocrine dysfunction, cumulative small trauma, intracellular hypertension, cytokines, genetic tendency, and other factors. The mechanism of acupotomy in KOA may include inhibiting the apoptosis of chondrocytes in articular cartilage, promoting the recovery of articular cartilage morphology, restoring the biomechanical balance of knee joint, regulating the central analgesic substance and other aspects. Our study also found that acupotomy could inhibit the release of inflammatory cytokine, such as tumor necrosis factor-α and interleukin-1, block the high-level expression of matrix metalloproteinases (MMPs) induced by them, suppress the degradation of cartilage matrix, protect cartilage cells, and thus carry out the therapeutic effects on KOA. Moreover, some scholars have proved the above conclusions by animal experiments, they treated KOA rabbits with acupotomy, and concluded that acupotomy can inhibit the expression of matrix metalloproteinase, protein and reduce the level of tumor necrosis factor in synovial fluid, so as to achieve therapeutic effects on KOA.

Our current study analyzed materials from twelve RCTs involving 1150 patients that aimed to evaluate the therapeutic effect and safety of acupotomy for KOA. According to the findings, acupotomy could further improve the clinical effective rate, lower WOMAC and pain score when compared with HA treatment for KOA. Just three RCTs reported long-term effects of acupotomy in KOA for one year, six months, and three months respectively. Meta-analysis indicated that the long-term effect of acupotomy for KOA might have a better potential benefit, but it still need more studies with long-term clinical effects to demonstrate. In the study only four RCTs reported relevant adverse events. The combined data indicated no significant difference in reducing adverse effects between acupotomy group and HA group.

DISCUSSION

Our study found that acupotomy could inhibit the release of inflammatory cytokine, such as tumor necrosis factor-α and interleukin-1, block the high-level expression of matrix metalloproteinases (MMPs) induced by them, suppress the degradation of cartilage matrix, protect cartilage cells, and thus carry out the therapeutic effects on KOA.

Figure 3 Risk of bias summary: review authors’ judgments about each risk of bias item for each included study

Lu D et al 2010
Meng F et al 2017
Niu SJ 2015
Wang LK 2009
Xu CH et al 2013
Yang DW et al 2007
Zhang P et al 2015
Zheng ZW 2015
Zhong TH 2016
Zhou L et al 2015
Zhu JS 2011
Zhu DY 2013

Random sequence generation (selection bias)
Allocation concealment (selection bias)
Blinding of participants and personnel (performance bias)
Blinding of outcome assessment (detection bias)
Incomplete outcome data (attrition bias)
Selective reporting (reporting bias)
Other bias

At present, the pathogenesis of KOA has not been acquainted entirely, and is generally believed to be related to age, sex, endocrine dysfunction, cumulative small trauma, intracellular hypertension, cytokines, genetic tendency, and other factors. The mechanism of acupotomy in KOA may include inhibiting the apoptosis of chondrocytes in articular cartilage, promoting the recovery of articular cartilage morphology, restoring the biomechanical balance of knee joint, regulating the central analgesic substance and other aspects. Our study also found that acupotomy could inhibit the release of inflammatory cytokine, such as tumor necrosis factor-α and interleukin-1, block the high-level expression of matrix metalloproteinases (MMPs) induced by them, suppress the degradation of cartilage matrix, protect cartilage cells, and thus carry out the therapeutic effects on KOA. Moreover, some scholars have proved the above conclusions by animal experiments, they treated KOA rabbits with acupotomy, and concluded that acupotomy can inhibit the expression of matrix metalloproteinase, protein and reduce the level of tumor necrosis factor in synovial fluid, so as to achieve therapeutic effects on KOA.

However, several limitations had existed in our study as following: firstly, unable to assess racial difference in effect of acupotomy because all the included studies were published in Chinese, it also limited the dissemination of scientific researches on acupotomy, so studies within western context are encouraged in future. Secondly, the methodological qualities of included studies were confirmed to be deficiency, only few RCTs described details about allocation concealment that might limit the value of conclusions about the clinical efficacy and safety of acupotomy. Then, the control groups of included studies all utilized HA that making the blinding of participants impossible, and perhaps a sham acupotomy control is preferable. Next, most of included studies estimated “cure”, “effective” and “ineffective” by the feeling of participants but lacked of quantitative standard, it remained debatable. As for secondary outcome measures, the measurement criteria were diverse, resulting in the heterogeneity and bias of RCTs, which need further study to improve the reliability of RCTs. Besides, the measurement of KOA is not exactly defined, the inclusion criteria varied among included studies, which may lead to the difficulties in evaluation of acupotomy for KOA. However, several limitations had existed in our study as following: firstly, unable to assess racial difference in effect of acupotomy because all the included studies were published in Chinese, it also limited the dissemination of scientific researches on acupotomy, so studies within western context are encouraged in future. Secondly, the methodological qualities of included studies were confirmed to be deficiency, only few RCTs described details about allocation concealment that might limit the value of conclusions about the clinical efficacy and safety of acupotomy. Then, the control groups of included studies all utilized HA that making the blinding of participants impossible, and perhaps a sham acupotomy control is preferable. Next, most of included studies estimated “cure”, “effective” and “ineffective” by the feeling of participants but lacked of quantitative standard, it remained debatable. As for secondary outcome measures, the measurement criteria were diverse, resulting in the heterogeneity and bias of RCTs, which need further study to improve the reliability of RCTs.
Fang T et al. / Systematic Review

that the definite conclusion couldn’t be drawn. And then, none of the included studies mentioned cost-effectiveness analysis or economic evaluation which was important for consumers choosing acupotomy, and cost is a frequent reason for stopping treatment. Last, few included studies reported adverse events, and the safety of acupotomy for KOA still remains to be further explored.
In conclusion, our study showed acupotomy’s potential for KOA treatment in alleviating knee pain or related symptoms for short-term and long-term. The adverse effects of primary studies were infrequently mentioned, and acupotomy may be as safe as HA treatment. However, the potential beneficial effect of acupotomy might be exaggerated due to the methodological deficiency of included studies. More reliable studies are needed to further confirm our findings.

REFERENCES


29 Zheng ZW. Acupotomy lysis effect on content of IL-1B and TNF-A in serum of patients with knee osteoarthritis. Hefei: Anhui University of Chinese Medicine, 2015: 9-29.


41 Liang CX, Guo Y, Tao L, et al. Effects of acupotomy intervention on regional pathological changes and expression of


