REVIEW ARTICLE

Effectiveness of Chuna (or Tuina) Manual Therapy for Temporomandibular Disorder: A Systematic Review

Nam-Woo Lee, KMD; Sook-Hyun Lee, PhD; Koh-Woon Kim, KMD, PhD; In-Hyuk Ha, KMD, PhD; Jae-Heung Cho, KMD, PhD; Yoon Jae Lee, KMD, PhD

ABSTRACT

Background • Temporomandibular disorder (TMD) affects patients' quality of life (QoL) because of the resulting structural and functional impairment and pain.

Objective • This study aimed to evaluate the evidence regarding the effectiveness, safety and improvement in QoL in patients who underwent Chuna manual therapy (CMT) for TMD.

Methods • We searched 11 databases and included randomized controlled trials (RCT) on CMT for TMD published before March 2020. A meta-analysis was conducted, and the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method was used to evaluate the evidence level. We included 12 RCTs that compared CMT and conventional care.

Results • CMT showed significantly better patient pain reduction, functional improvement and QoL. A superior result was seen in the use of CMT in conjunction with Traditional Chinese Medicine (TCM) or conventional care. CMT showed no minor or serious adverse events compared with medical treatments. The evidence level was low for all outcomes, except QoL.

Conclusions • We found that CMT for TMD resulted in functional improvement, pain reduction and improvement in QoL, with fewer adverse events. However, since the evidence level varied from very low to moderate due to imprecision and the risk of bias with the included studies, we are limited in determining the efficacy of Chuna therapy using these studies. High-quality, well-designed and large-scale RCTs are needed to conclusively determine the clinical efficacy of CMT in TMD. (*Altern Ther Health Med.* 2023;29(1):258-268).

Nam-Woo Lee, KMD, Korean Rehabilitation Medicine, Jaseng Hospital of Korean Medicine, Seoul, South Korea. **Sook-Hyun Lee, PhD; In-Hyuk Ha, KMD, PhD; Yoon Jae Lee, KMD, PhD;** Jaseng Spine and Joint Research Institute, Jaseng Medical Foundation, Gangnam-daero, Gangnam-gu, Seoul, South Korea**. Koh-Woon Kim, KMD, PhD; Jae-Heung Cho, KMD, PhD;** Department of Korean Rehabilitation Medicine, College of Korean Medicine, Kyung Hee University, Seoul, South Korea.

Corresponding author: Yoon Jae Lee, KMD, PhD
E-mail: goodsmile8119@gmail.com
Corresponding author: Jae-Heung Cho, KMD, PhD
E-mail: vetkong95@hanmail.net

INTRODUCTION

Temporomandibular disorders (TMD) are characterized by various structural disorders or dysfunctions of the jaw muscles; tenderness and persistent/recurrent pain in the temporomandibular joint (TMJ), masticatory muscles and associated myofascial structures; headaches; crepitus at the TMJ site, limited mouth movement; and tinnitus.[1,2] TMD involves various TMJ problems associated with masticatory muscle actions and is the main musculoskeletal cause of orofacial pain.[3,4]

Studies with different target populations and research methods have reported a TMD prevalence rate of 11% to 50%.[5] Data from the health insurance claims of the South Korea National Health Insurance Service from 2010 to 2015 revealed a 40.5% increase in the number of patients (248 052 in 2010 to 348 413 in 2015) with TMD as the principal diagnosis in individuals who visited the hospital for treatment.[6] The annual incidence of TMD is approximately 3.5%; moreover, approximately 25% of adults present with signs or symptoms of TMD more than once in their lifetime.[7,8] The reported TMD incidence is high among women age between 20 and 40 years[8]; in addition, it affects more women than men at a 2.5:1.5 ratio.[9]

Since the pathophysiology of TMD remains unclear, non-invasive, reversible and conservative treatments are generally preferred. Surgery is only performed when the conservative treatment for TMD is considered ineffective.[10]

Conservative treatment methods for TMD include intraoral appliances[11]; psychological interventions[12]; acupuncture treatment[13]; physical therapy, including transcutaneous electrical nerve stimulation (TENS) and laser[14]; and manual therapy using biofeedback training, including muscular awareness relaxation therapy and active exercises.[15] Manual therapy improves circulation, decreases muscle spasm, induces relaxation, re-aligns soft tissue, breaks adhesions, increases the range of motion of the jaw and reduces pain. Therefore, it is increasingly applied in patients with TMD who present with pain and dysfunction.[16]

Chuna manual therapy (CMT) is a traditional method of musculoskeletal manipulation combining biomechanical function, diagnostics and pathology theories to achieve a balance in orthopedic structure and function. In South Korea, CMT has been actively used by Korean medical doctors to treat various musculoskeletal diseases, including TMD; moreover, there have been reports on its effects and efficacy.[17] CMT is a discipline that combines anatomy, pathology and physiology of modern medicine with the theoretical background of Korean medicine and focuses on treating body balance. It emphasizes meridian theory and muscle concepts, which are not usually applied in chiropractic therapy or osteopathic medicine.[18] Currently, CMT is used in clinical practice as a treatment encompassing Tuina in China, chiropractic and osteopathic therapy in the United States and Shiatsu in Japan.[19] Since the establishment of the Korean Society of Chuna Manual Medicine (KSCMM) in 1991, there has been active academic and clinical progress in CMT. Recently, its effects and safety have received national recognition; it has also been incorporated for coverage under South Korea National Health Insurance since April 2019.[20]

Several clinical studies have been conducted on TMD treatment with CMT, but no systematic literature review on the effectiveness of CMT in TMD has been performed. In the United States, there have been systematic reviews on the effects of manipulative therapy performed by physical therapists in TMD.[21-26] However, there is a need for studies exclusively on CMT as treatment in TMD; it involves treatment principles that are different from manipulative therapy with respect to functional improvement and pain relief.

Thus, we performed a systematic review of domestic and international clinical studies on CMT for TMD according to the Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) reporting guidelines, in terms of safety, effectiveness of pain relief, and improvement in functionality and quality of life (QoL).

MATERIALS AND METHODS

Data Sources and Searches

We searched for studies in 4 English-language databases (CENTRAL, Ovid Medline, Ovid-EMBASE, and AMED), 1 Chinese database (China National Knowledge Infrastructure [CNKI]), 1 Japanese database (CiNii), and 5 South Korean databases (KoreaMed, Korean Medical Database [KMBASE], Korean Studies Information Service System [KISS], National Discovery for Science Leaders [NDSL], and Oriental Medicine Advanced Searching Integrated System [OASIS]).

The search terms for the English-language databases were: "Tuina OR Chuna" AND "Randomized Controlled Trial" OR "Randomised Controlled Trial" OR "RCT" OR "Randomized" OR "Randomised" AND "TMJ" OR "TMD" OR "CMD" OR "temporomandibular" OR "craniomandibular." The end search date was March 20, 2020.

The study protocol registration number was CRD42020190730, registered on 15 August 2020.

Study Selection

Inclusion criteria. We included parallel or crossover randomized controlled trials (RCTs) on the clinical effects of CMT on functional and pain improvement, efficacy and QoL in adult patients with TMD.

We screened for RCTs on adult patients (age ≥19 years) with TMD who received CMT as their intervention. We performed a search without restrictions on the application site or CMT method. In addition, we included studies evaluating the combined effect of CMT plus other interventions only when the same supplementary intervention was applied to both the CMT and control groups. Furthermore, to determine the combined effect of CMT application, we included studies comparing CMT with conventional medicine (including traditional Chinese medicine [TCM]) and a control group involving monotherapy using other types of interventions. The control group received usual care, including physical therapy and medication such as analgesics.

We included all indicators for evaluating TMJ function, pain and QoL in patients with TMD, including maximum mouth opening (MMO) and the Visual Analog Scale (VAS). In addition, we included results regarding the effect rate and complication outcomes for safety, as well as scales for evaluating QoL, including the 12-Item Short Form Survey (SF-12) and EuroQol-5 Dimension (EQ5D).

Exclusion criteria. We excluded studies with any of the following patient characteristics: age <18 years; without a formal TMD diagnosis; and with TMD with psychogenic, neurological or other non-musculoskeletal causes (ie, TMD was not the primary diagnosis).

Furthermore, we excluded studies using a manual therapy other than CMT or studies with insufficient descriptions of the treatment method used. We excluded RCTs comparing different CMTs since the effect of a single CMT method cannot be clearly analyzed in such cases.

Data Extraction

A total of 2 independent researchers performed the initial screening of each article title and abstract, followed by a full-text review of the article. One researcher, who holds TCM licenses for both China and South Korea, performed detailed analysis of all Chinese articles, while the other reviewed English, Korean, and Japanese articles.

Both researchers then shared the analysis results and performed cross-evaluation. Disagreements were resolved

Table 1. Summary of Randomized Controlled Trials of Chuna (or Tuina) Manual Therapy in TMD

Study ID	Study design	Sample size	Age	Intervention	Comparison	Type of C(T)MT	Duration	F/U	Outcome measurements	Adverse events
C(T)MT vs Usual Care										
Kim, et al. (2019)	RCT (unpublished)	80 (EG:40; CG:40)	EG (35.63 ± 10.16) CG (36.10 ± 10.41)	C(T)MT	Usual care (UC) [thermotherapy, ultrasound therapy, TENS, ICT, etc.]	Sitting TMJ distraction with thumb technique; sitting lateral pterygoid pushing with index finger technique; sitting TMJ manipulation with thumb technique	8 sessions for 4 weeks	1st, 3rd, 5th, and 7th treatment visits (weeks 1 to -4) and 5 weeks, 3 months and 6 months	1) VAS 2) NRS 3) ROM 4) BDI 5) JFLS 6) PGIC 7) SF-12 8) EQ5D-5L 9) EQVAS	Total 6 events (EG: 3, CG:3) EG: headache, tinnitus, oral mucosal edema. CG: intensifying ear, neck and TMJ pain.
Shen, et al. (2012)	RCT	78 (EG:39, CG:39)	EG (33.2 ± 10.4) CG (35.1 ± 11.5)	C(T)MT	Western medication (meloxicam tablets and composite chlorzoxazone tablets)	Kneading technique on LI4, ST6, SI18, GB3, ST7 and Rubbing technique	1 session per a day for 2 weeks	2 weeks	1) ER 2) ROM 3) VAS	Digestive symptoms such as nausea, loss of appetite, upper abdominal discomfort and stomach pain in the comparison group
Su, et al. (2014)	RCT	60 (EG:31, CG:29)	19-61	C(T)MT	Ultrashort wave therapy	Pushing and Pressing techniques on Ashi point, TE22, ST7, GB3, ST6 for 5 minutes; Grasping technique on LI4 for 1 minute.	3 sessions per week for 2 weeks	2 weeks	1) ROM	NR
Su, et al. (2013)	RCT	60 (EG:30, CG:30)	19-61	C(T)MT	Ultrashort wave therapy	Pushing and Pressing techniques on Ashi point, TE22, ST7, GB3, ST6; Grasping technique on LI4, SJ5.	3 sessions per week for 2 weeks	2 weeks	1) VAS	A small number of patients in the treatment group experienced local swelling, skin redness and other symptoms; the symptoms disappeared after adjusting the technique intensity.
Gu, et al. (2015)	RCT	60 (EG:30, CG:30)	EG (37.40 ± 13.25) CG (35.27 ± 11.29)	C(T)MT	Semiconductor laser	Kneading technique; Pushing manipulation with one-finger technique on GB3 ST7, ST6 GB2, SI19 TE21, TE17, GB20, LI4, GB21	Each treatment is about 20 minutes, every other day; 6 sessions as course of treatment	Immediately after treatment	1) ER 2) Fricton's Craniomandibular Index: DI, PI,CMI 3) ROM	NR
C(T)MT with TCM vs TCM alone										
Ding, et al. (2016)	RCT	120 (EG:60, CG:60)	EG (25-32) CG (24-34)	C(T)MT + Acupuncture with moxibustion	Acupuncture with moxibustion	Kneading technique on GB20, TE17, SI19, GB2, EX-HN5, ST7, TE21, ST6, LI4; Reduction technique on TMJ	20 sessions for 20 days	Immediately after treatment	1) ER 2) VAS	NR
Liu, et al. (2013)	RCT	15 (EG:5, CG1:5, CG2:5)	NR	C(T)MT + Xuefu zhuyu decoction	1) Xuefu Zhuyu decoction 2) C(T)MT	Pressing, Kneading, Pulling techniques and Pushing manipulation with one-finger technique on GB2, GB3, ST7, ST6, SI19, TE21, TE17, GB20, TE20, LI4	1) TID for 2 weeks 2) 1 session per a day for 2 weeks	1 week and 2 weeks	1) ER	NR
Wan, et al. (2014)	RCT	105 (EG:35, CG1:35, CG2:35)	EG (32.0±0.5) CG1 (33.0±1.2) CG2 (34.0±0.6)	C(T)MT + acupuncture	1) acupuncture 2) acupoint injection	Pushing and Kneading techniques and Pushing manipulation with one-finger technique on GB3, ST7, SI19, TE17, GB2; Reduction technique on TMJ	1 session per day for 10 days	Immediately after treatment	1) ER	NR
Bu, et al. (2011)	RCT	96 (EG:48; CG:48)	19-67	C(T)MT + electro-acupuncture	Electro-acupuncture	Pushing technique on GB3, ST7, ST6, SI19; Rotating technique on TMJ	1 session a day, 10 sessions as a course of treatment, 2 days apart; 4 courses total	Immediately after treatment	1) ER 2) Efficacy for myofascial pain 3) Efficacy for external pterygoid muscle spasm	NR
Jin, et al. (2011)	RCT	52 (EG:26; CG:26)	EG (30.19 ± 9.02) CG (33.23 ± 9.97)	C(T)MT + acupuncture, pharmaco-puncture	Acupuncture, pharmaco-puncture	Pushing technique on lateral pterygoid muscle; Stretching technique on TMJ	2 sessions a week for 4 weeks	Immediately after treatment	1) VAS 2) FPSC	NR

Table 1. (continued)

Study ID	Study design	Sample size	Age	Intervention	Comparison	Type of C(T)MT	Duration	F/U	Outcome measurements	Adverse events
C(T)MT with Usual care vs Usual care										
Gu, et al. (2008)	RCT	61 (EG:30; CG:31)	EG (19-63) CG (21-67)	C(T)MT + TDP	TDP	Pushing technique on Ashi point, GB3, ST7, TE17, ST6, LI4 Kneading, Rubbing techniques; Pushing manipulation with one-finger technique and Reduction technique on TMJ.	2 courses conducted with 1 course of treatment once a day for 10 days. Rest for 5 days in the middle of the course.	Immediately after treatment	1) ER	NR
Li, et al. (2008)	RCT	77 (EG:40; CG: 37)	EG (19-54) CG (21-52)	C(T)MT + Ultrashort wave	Ultrashort wave	Pressing, Kneading, Pushing and Rubbing techniques on Ashi point, ST7, TE17, ST6, SI18, LI4; Rotating technique on TMJ.	1 session per day for 10 days	Immediately after treatment	1) ER	NR

Abbreviations: BDI, Beck's Depression Inventory; C(T)MT, Chuna (or Tuina) manual therapy; CG, control group; CMI, craniomandibular index; DI, dysfunction index; EG, experimental group; EQ5D-5L, 5-Level EuroQol-5 Dimension; EQVAS, EQ-Visual Analog Scale; ER, effective rate; Ex-HN, extra Points, head and neck; FPSC, Facial Pain Score Scale; GB, gallbladder meridian; JFLS, Jaw Functional Limitation Scale; LI, large intestine meridian; MD, mean difference; NR, not reported; NRS, Numeric Rating Scale; PGIC, Patient Global Impression of Change; PI, palpation index; RCT, randomized controlled trial; ROM, range of motion; RR, relative risk; SF-12, Short Form-12 Health Survey; SI, small intestine meridian; ST, stomach meridian; TCM, Traditional Chinese Medicine; TDP, Te Ding Dian Zi Bo Pu; TE, triple energizer meridian; TID, 3 times a day; TMD, temporomandibular joint TMD disorder; TMJ, temporomandibular joint; UC, usual care; VAS, Visual Analog Scale.

by requesting additional information from the original author(s) via e-mail. After selecting eligible papers, we extracted the following data: author, year of publication, study design, sample size, intervention, follow-up period, outcome measures and adverse events (see Table 1).

Assessment of Risk of Bias

The quality of the included studies was evaluated using the Cochrane risk of bias (ROB) criteria tools.[27] ROB was assessed as "low" when the randomization method and process; allocation concealment, including sealed envelope or central randomization; and blinding of patients and assessors were clearly described. ROB was considered "unclear" if the outcome was assessed using a scale reflecting both the subjective and objective perspectives of the assessor or if it was difficult to clearly determine the blinding status. Regarding the completeness of outcomes, ROB was assessed as "low" if the included study satisfied the following 3 conditions: a clear description of the number and cause of dropouts in each group; between-group similarity in the dropout rate; and a dropout rate of ≤20% and ≤30% for short-term and long-term follow-up, respectively.[28] Regarding the selective reporting bias, we evaluated papers with published and confirmable protocols by comparing the protocols and published papers. In studies in which it was difficult to check the protocol, ROB was assessed as "unclear" when there was no report of adverse events status. Regarding other biases, we assessed the ROB by checking publication status and co-intervention. Between-researcher disagreements were resolved by discussion and consensus with a third-party researcher.

Data Analysis

All outcomes of the included studies were extracted as mean ± standard deviation (SD) or the total number of participants and occurrences. Data analysis was performed using the outcome measurement at the end of treatment. Relative risk (RR) was used for binary variables; moreover, the mean difference (MD) were used for the same and different (but comparable) continuous variables, respectively. Meta-analysis was performed with the calculation of 95% CI using the Fixed Inverse Variance method. Among-study heterogeneity was evaluated using the chi-square test and Higgins I^2 [29]; moreover, sub-group analysis was performed to identify the heterogeneity cause through subgroup analysis. Meta-analysis was performed using Cochrane Review Manager (RevMan) version 5.4.

Level of Evidence

The Grading of Recommendations Assessment, Development, and Evaluation (GRADE) method was used to evaluate the evidence level, as follows: high, moderate, low and very low. Specifically, the evidence level was determined by evaluating the ROB, inconsistency, indirectness, imprecision, publication bias, large effect magnitude and dose-response. However, only 1 to 4 studies were included in each analysis. We did not evaluate the publication bias.[30,31]

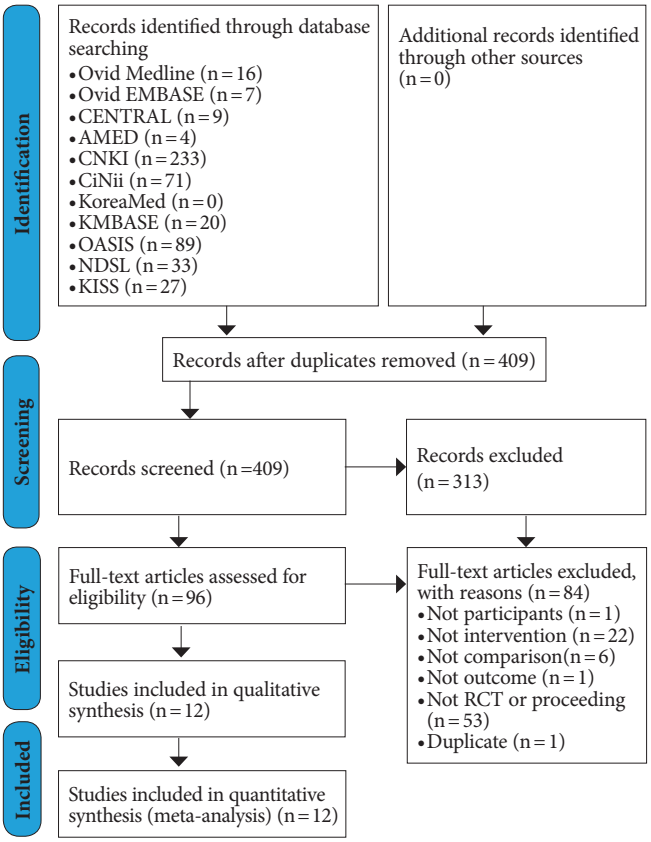
RESULTS

Study Selection

We identified 409 papers: 16 from OVID-Medline, 7 from OVID-EMBASE, 9 from CENTRAL, 4 from AMED, 233 from CNKI, 71 from CiNii, 0 from KoreaMed, 20 from KMBASE, 89 from OASIS, 33 from NDSL and 27 from KISS. After excluding duplicate papers, we included 409 papers for abstract review; of these, 313 papers were excluded for being unrelated. After a full-text review of the remaining 96 papers, 84 papers were excluded for not satisfying the Population, Intervention, Comparison, and Outcomes (PICO) criteria;

being a non-RCT study. Finally, we included 12 RCTs (see Figure 1)[32-43] published between 2008 and 2019; of these, one was an unpublished paper.[37] Figure 1 shows the PRISMA flow chart of the literature search process. Table 1 summarizes the details of the included studies.

Figure 1. PRISMA flow diagram of the literature search.



Abbreviations: PRISMA, Preferred Reporting Items for Systematic reviews and Meta-Analyses.

Study Characteristics

The included RCTs involved 863 patients with TMD. The average number of individuals in the CMT and control groups in each study was 34.5 ± 12.6 and 34.16 ± 12.62, respectively. Most of the studies included patients in their 30s (see Table 1).

The included RCTs were classified as follows: CMT vs usual care (5),[34,37,40-42] CMT + conventional care vs conventional care only (2)[35,38] and CMT + TCM vs TCM only (5)[32,33,36,39,43] (see Table 1).

The conventional treatment methods used in the control group were physical therapy, including heat therapy, ultrasound therapy, laser therapy, transcutaneous electrical nerve stimulator (TENS) and interferential current therapy (ICT)[34,35,37,38,41,42] and medication, including meloxicam and chlorzoxazone[40] (see Table 1).

Regarding the indicators for outcome assessment, common indicators for TMJ function and pain assessment were used, as all the included papers investigated the same condition. For TMJ functional assessment, 4 studies assessed range of motion (ROM),[34,37,40,42] while 1 study used Friton's Craniomandibular Index, including dysfunction, palpation, and craniomandibular indices.[34] Regarding pain assessment tools, the VAS and Facial Pain Score Scale were used in 4[33,37,40,41] and 1 study,[36] respectively. Moreover, 1 study[32] used the pain scale for individual muscles. One study assessed QoL using the SF-12 and EQVAS[37]; additionally, eight studies used the effective rate as a measure of the total effect rate.[32-35,38-40,43] The effect rate allows comprehensive evaluation of subjective symptoms, ROM, MMO, crepitus, masticatory functions and tenderness, among others, based on 4 levels: no effect, effective, remarkably effective and cured (see Table 1).

All included RCTs used CMT; however, there were slight differences in the application methods. The primary techniques used included pressing, kneading, rubbing, grasping, pulling, rotating, mobilization and corrective techniques for the TMJ. Specifically, 11 studies[32-36,38-43] employed pressing and kneading techniques using acupoints around the TMJ, while 8 studies used distal acupoints.[33-35,38-42] In addition, 3[33,35,43] and 2 studies[32,38] used corrective and rotating mobilization techniques for TMJ, respectively. Regarding the treatment acupoints, such as GB2, GB3, GB20, ST7, ST6, TE17, TE20 and TE21 located in the proximal TMJ, as well as distal acupoints located in the upper limbs, such as SJ5 and LI4, were used. The treatment duration varied from 10 days to 4 weeks and the average number of CMT sessions was 13.5 ± 9.31; the follow-up period ranged from 0 days to 6 months (see Table 1).

ROB Assessment

Most of the included studies were assessed as having "high" or "unclear" ROB (see Figure 2). Only 3 studies (25%)[37,41,42] reported using adequate randomization methods, including a random number table, computer random number generators, randomization codes or coin toss. Regarding allocation concealment, only 1 study (8.3%)[37] used sealed opaque envelopes or central assignments. One study reported blinding of study participants and investigators. Moreover, only 2 studies[33,37] reported blinding of outcome assessors, in which an independent assessor evaluated the treatment outcomes. There were 2 studies[37,41] that were assessed as having "low" ROB. Both studies had little/no missing data in the outcomes report, with dropout rates of ≤20% and ≤30% in the short-term and long-term follow-up periods, respectively; each group in these studies had similar dropout numbers and reasons cited for dropping out. The ROB of the remaining 10 studies were assessed as "unclear" due to the non-report of processing of the missing values. Regarding the selective outcome report, only 1 study[37] had published its protocol; moreover, the missing values in the report could be confirmed from the planned outcome measurement. However, protocols could not be identified and compared for the remaining studies. Of the studies, 2[40,41] reported the adverse event status and were assessed as having "low" ROB. The remaining studies did not describe adverse events; therefore, they were considered to have "unclear" ROB. Kim, et al[37] published their protocol, but the results are yet to be

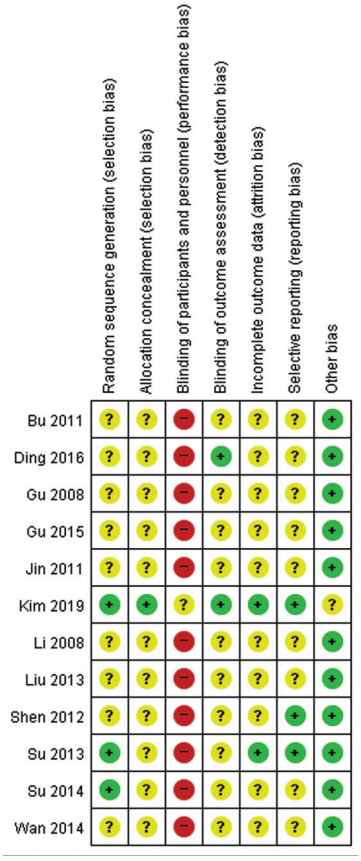
Table 2. Meta-Analysis of Outcomes and Quality of Evidence

Variable	Overall effect						# of Studies	Sample size (n)	Level of evidence
	RR or MD	95% CI	*P* value	I^2	χ^2	Statistical method			
CMT vs Usual Care Alone									
Effect rate	1.15	1.05, 1.27	.004	7	0.34	Fixed Inverse Variance	3	191	Low[a,b]
Pain (VAS)	-1.17	-1.71, -0.64	<.0001	48	0.15	Fixed Inverse Variance	3	211	Low[a,b]
Maximum mouth opening	2.34	0.82, 3.85	.003	89	0.0002	Fixed Inverse Variance	3	218	Very low[a,b,c]
Quality of life (EQVAS)	13.35	5.33, 21.37	.001	NA	NA	Fixed Inverse Variance	1	80	Moderate[b]
SF-12 PCS	4.59	1.75, 7.43	.002	NA	NA	Fixed Inverse Variance	1	80	Moderate[b]
CMT with TCM vs TCM Alone									
Effect rate	1.21	1.10, 1.32	<.0001	0	0.47	Fixed Inverse Variance	4	296	Low [a,b]
Pain (VAS change)	0.24	0.12, 0.35	<.0001	20	0.26	Fixed Inverse Variance	2	175	Low [a,b]
CMT with Usual Care vs Usual Care Alone									
Effect rate	1.28	1.08, 1.52	.004	52	0.15	Fixed Inverse Variance	2	138	Low[a,b]

[a]risk of bias
[b]imprecision (small sample size)
[c]inconsistency (heterogeneity)

Abbreviations: CI, confidence interval; CMT, Chuna manual therapy; EQVAS, EuroQol Visual Analog Scale; MCS, Mental Component Summary; MD, mean difference; NA, not applicable; PCS, Physical Component Summary; RR, relative risk; SF-12, Short Form-12 Health Survey; TCM, Traditional Chinese Medicine; VAS, Visual Analog Scale.

Figure 2. Risk of bias in included studies



+: high risk
?: unclear risk
-: low risk

published. They had an unpublished report with detailed study outcomes that was assessed as "other bias unclear."

Quantitative Data Synthesis

Figures 3 and 4 and Table 2 show the meta-analysis results.

CMT vs Conventional Care

Effect rate. Of the 5 studies comparing CMT and conventional care, 3 RCTs[34,40,41] assessed the effect rate of CMT on TMD. Compared with conventional care, CMT showed a significantly better effect rate (risk ratio [RR]: 1.15; 95% confidence interval [CI] 1.05-1.27; Figure 3 and Table 2).[34,40,41] In terms of the effect rate, sub-analysis revealed that CMT possessed a significant effect compared with the control group that received conventional medication (RR: 1.19; 95% CI 1.00-1.42; Figure 3A)[40] and the control group that underwent physical therapy (RR: 1.14; 95% CI 1.01-1.28; Figure 3A)[34,41], respectively.

Pain (VAS). Of the 5 studies comparing CMT and conventional care, 3 RCTs[37,40,41] used VAS for pain assessment. Combined analysis of the control group revealed that CMT showed a superior effect to conventional treatments (mesn difference [MD]: -1.17; 95% CI-1.71 to -0.64; heterogeneity: $P = .15$; $I^2 = 48\%$; Figure 3B and Table 2).[37,40,41] Subgroup analysis revealed that CMT showed superior and similar pain improvement compared with the conventional medication control group (MD: -1.46; 95% CI -2.15 to -0.77; Figure 3B.1)[40] and physical therapy control group (MD: -0.72; 95% CI -1.59 to 0.14; Figure 3B.2),[37,41] respectively.

Maximum mouth opening (MMO). Moreover, the 3 aforementioned RCTs[37,40,42] that reported the pain scale

Figure 3. Forest plots demonstrating the effect of CMT as the sole intervention for TMD.
Figure 3A. Effect of Chuna (or Tuina) vs usual care alone on effect rate.

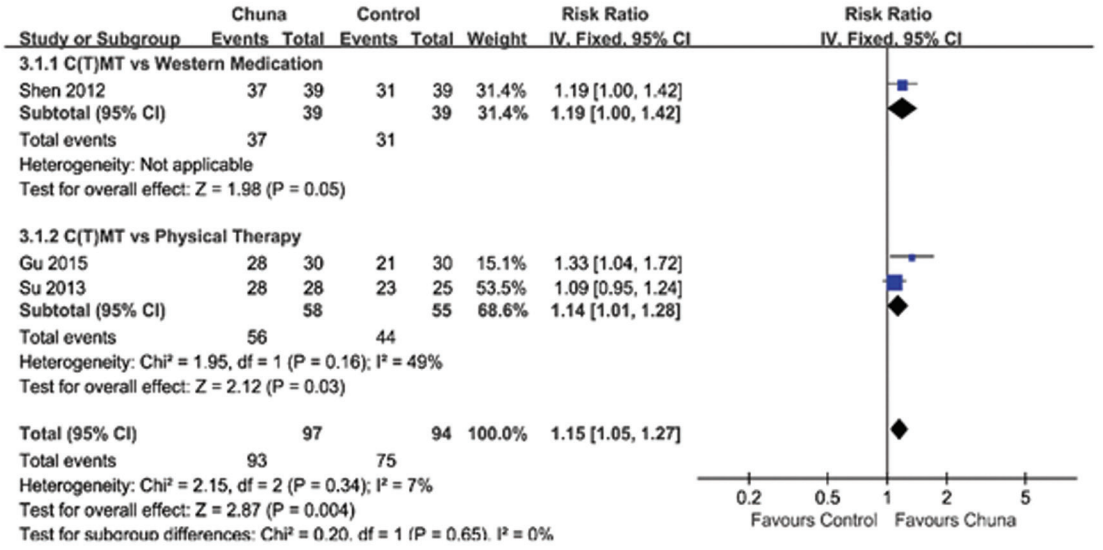


Figure 3B. Effect of Chuna (or Tuina) vs usual care alone on pain.

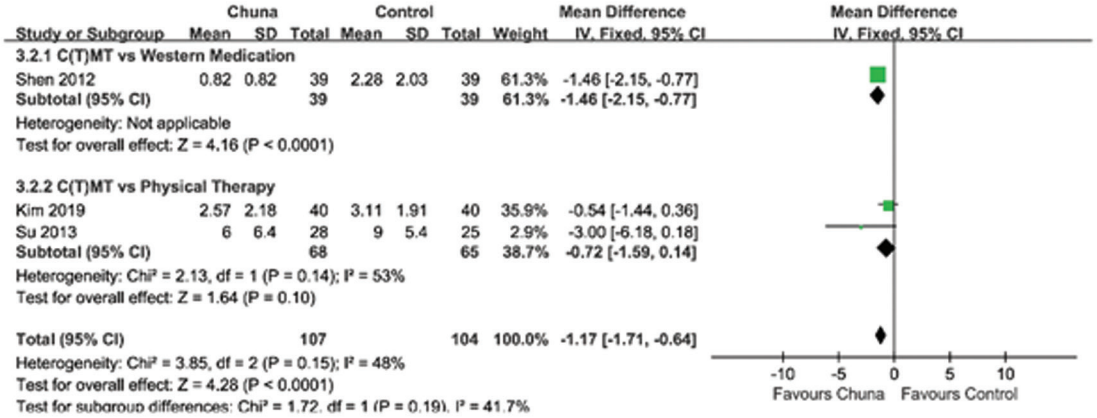


Figure 3C. Effect of Chuna (or Tuina) vs usual care alone on maximum mouth opening.

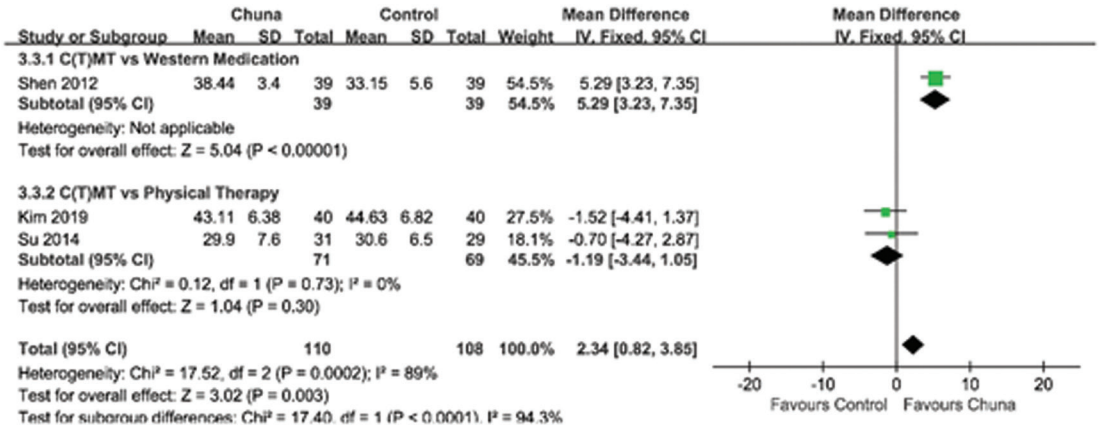


Figure 4. Forest plots demonstrating the effect of CMT as an add-on intervention for TMD.
Figure 4A. Effect of Chuna (or Tuina) plus traditional Chinese Medicine vs Traditional Chinese Medicine alone on effect rate.

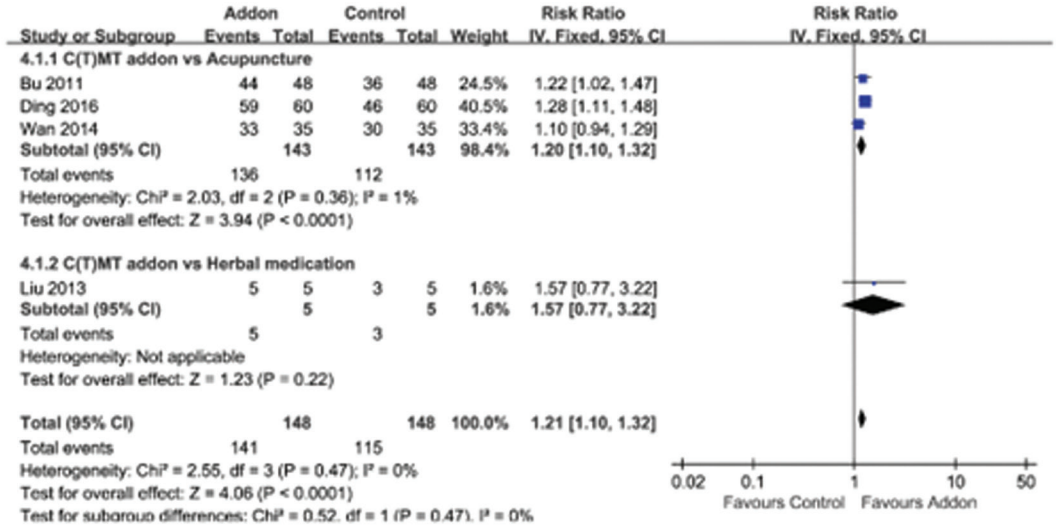


Figure 4B. Effect of Chuna (or Tuina) plus traditional Chinese Medicine vs Traditional Chinese Medicine alone on change in pain level.

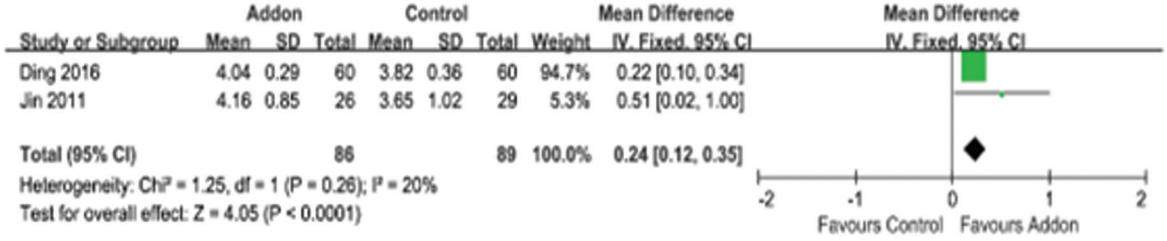
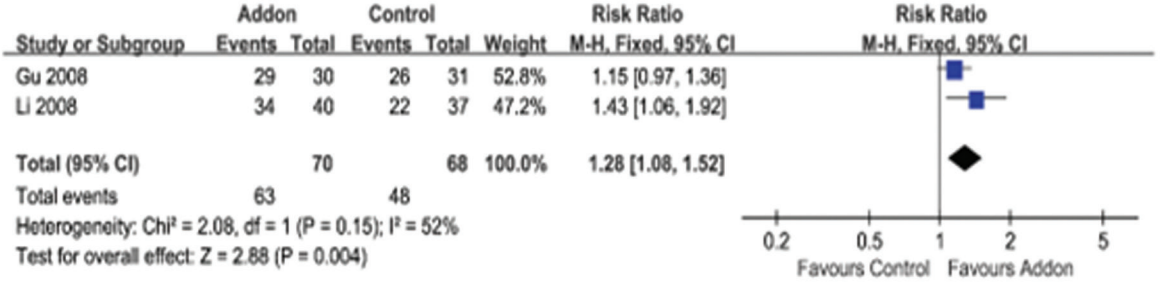


Figure 4C. Effect of Chuna (or Tuina) with usual care vs usual care alone on effect rate.



outcome evaluated TMJ functional improvement through pre- and post-treatment range of motion (ROM) measurements. There were significant differences in the MMO outcome; however, there was significant among-study heterogeneity (MD: 2.34; 95qo% CI 0.82-3.85: heterogeneity: P =.0002; I^2 = 89%; Figure 3C and Table 2).[37,40,42] Sub-analysis for resolving the heterogeneity revealed that CMT had a significant effect on ROM improvement in the TMJ (MD: 5.29; 95% CI, 3.23-7.35; Figure 3C.1)[40] compared with the conventional medication control group. However, compared with the physical therapy control group, there was no significant difference in outcome; heterogeneity was resolved (MD: -1.19; 95% CI, -3.44 to 1.05; Figure 3C.2).[37,42]

Quality of life. Only 1 RCT[37] evaluated the pre- and post-treatment QoL. QoL was assessed with the EuroQol-5 Dimension (EQ5D), EQVAS and SF-12, with the SF-12 divided into physical and mental component summary (Physical component summary, Physical component score and Mental component summary, Mental component score, respectively). Compared with the control group, the CMT group showed a significant effect on EQVAS (MD: 13.35; 95% CI, 5.33-21.37; Table 2) and SF-12 PCS (MD: 4.59; 95% CI, 1.75 to 7.43; see Table 2) but not EQ5D (MD −0.02; 95% CI, −0.06 to 0.02; data not shown) and SF-12 MCS (standardized mean difference [SMD]: 1.07; 95% CI, −2.54 to 4.68; data not shown).

CMT + TCM vs TCM Alone

Effect rate. Of the 5 studies comparing CMT + TCM with TCM alone, 4[32,33,39,43] assessed the effect rate of the combined CMT therapy on TMD. Each study performed CMT with

acupuncture and moxibustion,[33] acupuncture alone,[43] electroacupuncture,[32] or Hyulbuchuko-tang (herbal medicine for blood stasis relief).[39] Integrated analysis of all the included TCM methods showed that CMT + TCM had a significantly superior effect rate compared with TCM alone (RR: 1.21; 95% CI, 1.10-1.32; see Figure 4A and Table 2).[32,33,39,43] Sub-group analysis revealed that CMT combined with acupuncture treatment, including general acupuncture, pharmacoacupuncture and electroacupuncture, had a significantly superior effect compared with acupuncture treatment alone (RR: 1.20; 95% CI ,1.10-1.32; see Figure 4A.1).[32,33,43] However, there was no difference in the effect rate between CMT combined with herbal medicine treatment and herbal medicine alone (RR: 1.57; 95% CI, 0.77 to 3.22; Figure 4A.2).[39]

Pain (change in VAS score). Of the 5 studies comparing CMT + TCM with TCM alone, 2 RCTs[33,36] assessed pain improvement by comparing the pre- and post-treatment VAS scores. CMT + TCM showed a significant effect on pain improvement compared with TCM alone (MD: 0.24; 95% CI, 0.12-0.35; see Figure 4B and Table 2).

CMT + Conventional Care vs Conventional Care Alone

Effect rate. A total of 2 studies[35,38] compared the treatment effects of C(T)MT + conventional care with conventional care alone. In both studies,[35,38] the pre- and post-treatment effects were compared by assessing the effect rate. Both studies[35,38] applied physical therapy, which is commonly used in combination with CMT; 1 study[35] used Te Ding Dian Zi Bo Pu, while the other study[38] used a microwave diathermy system for treatment. CMT + conventional care showed a significant effect on the effect rate compared with conventional care alone (RR: 1.28; 95% CI, 1.08-1.52; see Figure 4C and Table 2).[35,38]

Adverse Events. Only 3 included studies presented safety-related reports.[37,40,41] Shen, et al.[40] reported no adverse events in the CMT group; however, the medication (control) group had 13 cases of adverse events, including nausea, loss of appetite, epigastric discomfort and stomach pain. Su, et al.[41] reported no serious adverse events in either group; however, local swelling and skin redness occurred in the CMT group. Kim, et al.[37] reported 3 cases of treatment-related adverse events each in the CMT and conventional care groups. In the CMT group, headaches, tinnitus and oral swelling occurred, while in the conventional care group, earache, neck pain and increased TMJ pain were reported, which are all minor adverse events. There were no reports regarding adverse events in the remaining 9 studies.

Level of Evidence. The GRADE approach was used to evaluate the evidence level concerning the outcome measures. There was a moderate evidence level regarding the comparison of QoL between CMT and conventional monotherapy. However, there was a low evidence level regarding the effect rate and pain improvement due to the ROB and imprecision. There was a very low evidence level with regard to MMO due to the ROB, imprecision and inconsistency. CMT + TCM showed a low evidence level concerning the effect rate and pain improvement due to the ROB and imprecision. The comparison between CMT + conventional care vs conventional care only showed a low evidence level due to the ROB and imprecision.

DISCUSSION

This meta-analysis of RCTs comparing the effects of CMT and conventional care found that CMT was effective in the functional improvement, pain reduction and enhancement of QoL in patients with TMD.

Pain Reduction, Functional Improvement and QoL

The groups that underwent CMT had greater pain reduction compared with groups that received medication and physical therapy, which generally comprise the usual care administered in various countries.[37,40,41] Patients who underwent CMT had greater functional improvement based on MMO[37,40,42] and QoL compared with patients who received usual care; poor functional improvement was closely associated with aggravated disease progression.[37]

In East Asian countries, including South Korea, China and Japan, greater pain reduction was observed when acupuncture and herbal medicine for musculoskeletal diseases were used in combination with CMT.[33,36]

Effect Rate

Regarding the effect rate, which comprehensively assesses the patient's overall condition, such as pain and function, CMT combined with conventional care showed superior effect compared with either conventional care[34,35,38,40,41] or TCM alone.[32,33,39,43] Subgroup analysis of the control groups showed that the effect was insignificant or ineffective. Specifically, CMT showed a non-significant effect in functional and pain improvement compared with conventional medication.[40] Given that the included studies assessed outcome measures upon treatment completion without a follow-up period, CMT characteristically showed an immediate therapeutic effect through manual intervention. Compared with medication alone, it demonstrated a superior short-term improvement in pain and functionality. In contrast, there was no significant difference in the effect rate, with various indicators comprehensively considered. No significant difference between physical therapy and CM[37,41,42] in pain and functional improvement was observed. This was attributed to their similarities as manual therapies involving physical manipulation. The combination of CMT and physical therapy showed an effect rate superior to physical therapy alone.[35,38] Therefore, CMT can be regarded as a safe and effective treatment and can be combined with physical therapy. In a similar fashion, a sub-analysis of TCM revealed that CMT showed a superior effect when combined with various acupuncture treatment methods (electroacupuncture, pharmacoacupuncture and general acupuncture).[32,33,43] However, CMT with herbal medicine was less effective compared with herbal medicine alone.[39] This could be attributed to the inclusion of 1 small-scale study in this analysis, which could not yield a definite conclusion.

Adverse Events

None of the included RCTs reported severe adverse events associated with CMT; however, local swelling, redness at the skin-contact site,[41] minor headaches, tinnitus and intraoral swelling were reported,[37] which were all minor adverse events with quick recovery. Compared with medication, CMT showed fewer adverse events. These results suggest that CMT is safer than other types of intervention, including medication. However, only 3 studies[37,40,41] reported adverse events; therefore, more studies reporting on the adverse events of CMT are warranted in order to yield more definitive conclusions on safety.

Study Strengths

The strength of this study is the systematic search of databases, the application of strict methodology for the analysis of RCT studies published up until March 20, 2020, and the evaluation of the evidence level. Furthermore, our findings are significant since this is the first systematic literature review of CMT for TMD. We included all RCTs on the effects of CMT on TMD published worldwide. In addition, to ensure that the effect was obtained from CMT alone, the included interventions were limited to Chuna and Tuina, with all other similar manual therapies excluded. This approach allowed examination of the effect of CMT application only.

To incorporate more up-to-date evidence, we included a paper reporting the protocol only[37] and conducted ROB evaluation by contacting the original author to obtain additional information about the outcomes and research progress, although the outcomes are yet to be published. We extensively attempted to overcome the limitations of obtaining results within published papers and presented better evidence for the analysis.

Study Limitations

Nevertheless, most of the included studies had methodological drawbacks. Only 1 study[37] reported appropriate allocation concealment. However, there were 2 concerns. First, therapeutic effect overestimation could arise from the concealment of inadequate allocation or improper randomization methods,[44,45] resulting in a significant bias.[46] Second, in 11 RCTs,[32-36,38-43] there was no blinding of the therapist/doctors and patients, which could be an RCT limitation. However, given the nature of CMT, it is practically difficult to perform blinding of the therapist/doctor and patients. Therefore, allocation concealment should be properly implemented with blinded assessors; however, most of the included RCTs did not employ such complementary measures. Only 2 studies[33,37] performed blinding of the assessors; therefore, there may be an overestimation of their results compared with studies without blinding. Therefore, the results from these studies should be carefully interpreted.

Nevertheless, 1 Korean study[37] achieved low ROB in all ROB assessment items, including randomization, allocation concealment and assessor blinding, except for the blinding of therapists/doctors and patients, which is methodologically impractical. Therefore, an appropriate study design could allow high-quality research and analysis in future RCTs on CMT.

Furthermore, we observed a lack of variations among the included studies. CMT is practiced as a part of traditional medicine in East Asia, including China, South Korea and Japan. Although it has methodological similarities with osteopathic and chiropractic therapy, it is based on different principles. Therefore, CMT is not a universally applied treatment modality worldwide; consequently, although we searched databases and published studies worldwide, all the included studies except for 2[36,37] were written in Chinese and published in a Chinese journal, which cannot be searched using Medline. It has been suggested that studies written in non-English and published in journals not registered in Medline present overestimation of the effects; therefore, the results should be carefully interpreted since there could be a language bias.[47] One of the remaining papers[37] was written in Korean; however, this paper contained unpublished data, and its findings should be interpreted carefully.

In addition, between-study heterogeneity underwent limited analysis in this study.[48] There can be various causes of heterogeneity. The MMO comparison between the CMT and conventional care groups showed the greatest heterogeneity, variations in the types of usual care, and CMT could have been among the most influential factors. The various included control groups were collectively analyzed as usual care; however, they contained differences in the detailed treatment methods, which may yield clinical heterogeneity. Further, there may be differences in the CMT administered depending on the doctor/therapist; moreover, the included studies did not employ a similar method for CMT, thus leading to substantial heterogeneity. To increase statistical/clinical homogeneity, we performed additional sub-analysis and made efforts to present a high evidence level by including similar study types. However, there was a limited number of published RCTs that would meet the exact population, intervention, control and outcomes (PICO). Therefore, a careful approach should be applied when comparing the effects of specific treatment methods in the control group. High-quality RCTs with appropriate blinding should be conducted; studies conducting comparative analyses of the effects may also be helpful.

We found that CMT for TMD was effective in pain reduction, functional improvement and QoL improvement; however, the evidence level was not high. Few studies were included in the analyzed outcome scale. Each group in the RCTs contained up to 60 patients. Therefore, we included small-scale studies that lowered the evidence level in the imprecision domain. In addition, most of the studies showed a "high" or "unclear" ROB, while most studies were evaluated as having a low evidence level. Future large-scale and better-designed studies in terms of ROB could yield results with a high evidence level, which could further elucidate the effect of CMT.

Only 3 included studies[37,40,41] reported mild adverse events. Given the clinical characteristics of CMT, it is expected to have a low incidence of adverse events and be clinically

safe. However, limitations remain regarding the evidence on safety since none of the remaining studies reported on adverse events. Future studies should provide clear evidence regarding the clinical safety of CMT by evaluating adverse events.

CMT is a reversible conservative treatment with a safety advantage over surgery and is considered among the most useful treatments for TMD.[49] Although all 12 included RCTs were limited in terms of being conducted in a single country and having a high ROB, we employed the methodological process of systematic literature review. Regarding meta-analysis, we analyzed study outcomes with similar indicators of pain, function and QoL, as well as effect rate, to derive results on the effectiveness and safety of CMT as a single and combined therapy. Future well-designed large-scale RCTs on CMT should elucidate its clinical efficacy in TMD.

CONCLUSIONS

Our findings showed that CMT had a significant effect on improving TMJ function, pain reduction, and QoL; moreover, we found that it was safe with fewer adverse events. However, it is difficult to conclusively determine the effectiveness of CMT since the included studies showed low quality and evidence levels. There is a need for future well-designed large-scale RCTs to elucidate the clinical effectiveness of CMT for TMD.

FUNDING

This work was supported by a grant from the Traditional Korea Medicine R&D Program through the Korea Health Industry Development Institute (KHIDI), funded by the Ministry of Health and Welfare, Republic of Korea (grant number: HB16C0059).

CONFLICT OF INTEREST

None.

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