**Abstract**

**Objectives:** This systematic review assessed whether Tuina (therapeutic massage) is more effective and safer than no treatment or routine medical treatment for irritable bowel syndrome (IBS).

**Methods:** Eleven databases were searched for randomized clinical trials of IBS diagnosed based on Manning or Rome criteria. Tuina with or without routine treatments (RTs) was tested against RTs. The Cochrane risk of bias was evaluated for each trial. RevMan 5.3 was used to conduct a meta-analysis.

**Results:**A total of 8 trials (5 IBS-diarrhea and 3 IBS-constipation) with 545 participants using 8 different manipulations were included. All trials were published in Chinese. For overall symptom improving rate ( > 30% improvement in overall symptom scores), it had not been shown that Tuina was significantly better than RTs (RR 1.23, 95% CI 0.94-1.60, 197 participants, 3 studies, *I*2 = 65%) for IBS-diarrhea, and Tuina combined with RTs showed more benefit than RTs alone (RR 1.29, 95% CI 1.08-1.54, 115 participants, 3 studies) for IBS-diarrhea. All trials did not report adverse effect in relation to Tuina. Risk of bias was generally unclear across all domains.

**Conclusions:** Tuina combined with RTs may be superior to RTs for improving overall symptom of IBS-diarrhea. Due to the existing methodological issues and the heterogeneity of Tuina manipulation, current findings need to be confirmed in large scale, multicenter, and robust randomized trials (especially on outcome assessing blinding and allocation concealment).

**Systematic review registration:** PROSPERO CRD42019132473

**Keywords:** Tuina, Massage, Irritable bowel syndrome, IBS, Functional intestinal disease, randomized trials, Systematic review, Meta-analysis

**Introduction**

Irritable bowel syndrome (IBS) is a functional intestinal disease characterized by recurrent abdominal pain accompanied by abnormal or altered defecation habits. Symptoms usually occur at least 6 months before diagnosis and will persist for 3 months. It is a common and frequently occurring disease which presents in gastroenterology departments, and there are no specific morphological changes and biochemical abnormalities that can explain the symptoms.

IBS occurs mostly between 20 and 30 years old, and the incidence in women is about twice that of men. 1 The prevalence is estimated to be 10%-15% in the general adult population. 2 IBS has a huge economic burden. One study showed that the estimated direct costs per patient per year ranged from $348 to $8,750, with indirect costs ranging from $355 to $3,344. 3 The pathological mechanisms of IBS include gastrointestinal motility changes, increased visceral sensitivity, central nervous system visceral paresthesia processing, psychological abnormalities, mucosal immune activation changes, and intestinal permeability or intestinal flora changes. 4 In Rome IV criteria, 5 IBS is classified into 4 subtypes according to bowel habits abnormalities: IBS with predominant diarrhea (IBS-D), with predominant constipation (IBS-C), with mixed bowel habits (IBS-M) and IBS unclassified (IBS-U). For treatment, the routine treatments (RTs) recommended by the guidelines are as follows 1,6-7: antidiarrheals, 5-HT3 receptor antagonist, antispasmodics, fiber supplements, laxative agents, prosecretory agents, antidepressants and probiotics.

Routine western medicine for IBS, as a chronic and relapsing disease, often lacks evidence of long-term effectiveness and safety, and medications have their respective side effects, most of which are concentrated in the gastrointestinal tract. 7 Nonpharmacological therapy may not aggravate the disease, and may help maintain a good physician-patient relationship. 8 In recent years, nonpharmacological therapy has received extensive attention.

Tuina is a therapeutic approach guided by the theory of traditional Chinese medicine (TCM) and used to treat diseases by massage techniques or some massage tools to act on certain parts or acupoints. 9 It belongs to the category of external treatment in TCM. Tuina is a natural and non-invasive therapy, without the side-effects compared with medicines. One bibliometric study has shown that the spectrum of diseases applicable to Tuina is mainly concentrated in musculoskeletal diseases, digestive diseases, pediatric diseases, nervous system diseases, etc. 10 According to the theory of TCM, Tuina can promote circulation of Qi and activating blood, regulate the spleen and stomach, promote blood circulation to remove blood stasis, relax muscles, treat and restore injured soft tissues and promote their recovery and renovation.9

No systematic reviews on Tuina for IBS has been conducted. Tuina is widely used in China, especially for digestive system functional diseases. Therefore, through systematically reviewing, integrating the existing evidence of the original Tuina studies, discovering the problems and making relevant recommendations is essential for the exploring the effectiveness of Tuina therapy for international use. Our research question focused on whether Tuina was more effective and safer than no treatment or routine medical treatment for IBS.

**Methods**

The protocol of the review was registered in PROSPERO (CRD42019132473) on 20th of May 2019 (Available from: <http://www.crd.york.ac.uk/PROSPERO/>).

**Eligibility criteria**

**Type of studies**

Randomized, parallel-group clinical trials were included, irrespective of blinding, publication status, and language.

**Type of participants**

Male or female patients, of any age or ethnic origin, who had a diagnosis of IBS. IBS were diagnosed on the basis of one of the following six international criteria: Manning criteria; Kruis criteria; Rome I criteria; Rome II criteria; Rome III criteria; or Rome IV criteria.

**Type of intervention**

All types of Tuina manipulation were included, without limitations on the manipulation technique used, the number of Tuina sessions administered, or the duration over which Tuina was used. The Tuina treatment could have been used alone, or in combination with RTs (i.e., Western active medicines, probiotics, synbiotics, antidepressants, anti-anxiety agents). RTs should be identical in the intervention and the control group.

**Type of outcomes**

The primary outcomes were measured at the end of treatment and at maximal follow-up after completion of the treatment were: (1) global improvements of symptoms: including overall symptom improving rate and overall symptom scores; (2) quality of life (QOL). Secondary outcomes included: (1) relapse rates; (2) the improvement of predominant symptoms: including the scores of abdominal pain, distension, diarrhea or constipation; (3) psycho-mental condition: including depression and anxiety; (4) cost-effectiveness; (5) numbers and type of adverse events.

This study defined the overall symptom improvement as more than 30% improvement in overall symptom scores or improved overall signs/symptoms.11 Overall symptom improvement rate = [(Pre-treatment symptom scores - Post-treatment symptom scores)/ Pre-treatment symptom scores] \* 100%. Overall symptom scores were defined as the following: the sum of symptom scores based on customize criteria; essential single symptom (at least including distension, abdominal pain, diarrhea or constipation) scores; scores of scales that reflected the overall condition of IBS, such as IBS-SSS.

**Search strategy**

Electronic databases were searched from their inception dates to the present for potentially relevant studies: China National Knowledge Infrastructure (CNKI); Wanfang database; Chinese Scientific Journal Database (VIP); SinoMed; The Cochrane IBD Group Specialized Register; The Cochrane Central Register of Controlled Trials (CENTRAL); MEDLINE; Embase. No language or publication type limitations were applied (**Appendix A**), there were no limitations on the date of publication or study settings. The following trials registers were also searched: International Standard Randomized Controlled Trial Number Register ([www.controlled-trials.com/](http://www.controlled-trials.com/)); US National Institutes of Health Ongoing Trials Register (www.ClinicalTrials.gov); and World Health Organization International Clinical Trials Registry ([www.who.int/ictrp/en/](http://www.who.int/ictrp/en/)). The reference lists of all identified studies were searched to find any further relevant trials for inclusion. Unpublished graduate thesis, conference proceedings and newspapers included in the CNKI, VIP and Wanfang databases were also searched.

**Study selection and data extraction**

Two review authors (FLB and MH) reviewed all titles, abstracts of the studies identified by the search strategy independently, to assess eligibility. If it was hard to assess eligibility based on the titles and abstracts, the full texts needed to be read for judging. Additionally, we had searched the references of included studies for potential studies. Any disagreements were discussed by two review authors (CLL and XHL) to achieve a consensus, or consulted a third author (JPL).

Two review authors (JLL and XHQ) then independently extracted data from the included studies, using standardized data extraction forms. Data from trials published in duplicate were included only once. Disagreements were resolved by discussion, or with the involvement of a third author (WGW). The following data was: first author, funding source, study setting, methodological characteristics, demographic characteristics, number of randomized patients, follow-up details, patient inclusion and exclusion criteria, predominant symptoms of IBS patients, the diagnostic criteria, intervention details, details of the comparison groups, outcome measures (end of treatment and follow-up), adverse events. Data on the number of patients with each outcome, by allocated treatment group, irrespective of compliance or follow-up, was sought to allow an intention-to-treat analysis. One author (HZ) entered the data into Review Manager (RevMan 5.3, 2014), and a second author (FLB) checked it.

**Quality assessment**

Two authors (FLB and BXH) assessed the risk of bias by Cochrane tool for each study. 12 Any disagreements were discussed and consensus reached through a third party (NR). Due to the particularity of Tuina therapy, it was not possible to blind researchers and subjects. The following domains were considered: (1) random sequence generation (selection bias); (2) allocation concealment (selection bias); (3) blinding of outcome assessment (detection bias); (4) incomplete outcome data (attrition bias); (5) selective outcome reporting (reporting bias); (6) Other bias: included explicit inclusion and exclusion criteria, baseline imbalance, and conflicts of interests.

**Data analysis**

Each type of Tuina manipulation was compared with no treatment or RTs individually regardless of route of administration, dose or preparation. Data from individual trials were combined for meta-analysis when the interventions are sufficiently similar. Dichotomous data was planned to be presented as relative risk (RR) and continuous outcomes as mean difference (MD), both with 95% confidence intervals (CI). Analyses was performed by intention-to-treat where possible. For dichotomous outcomes, patients with incomplete or missing data was included in a sensitivity analysis by counting them as treatment failures to explore the possible effect of loss to follow-up on the findings ('worst-case' scenario). Meta-analyses were performed if the study design, participants, interventions, control and outcome measures were similar.

*I*² test (a *P* value of < 0.10 is generally considered to be statistically significant) was used to assess heterogeneity. A *P* value of < 0.10 is considered to be statistically significant. When there was significant heterogeneity, the results of *I*² where be quantified in each of the studies, and could be interpreted as a percentage of the total variation between studies caused by heterogeneity rather than chance. 13 As recommended by the Cochrane Handbook 5.1.0, we had defined *I*² as follows: (1) less than 25%: may represent mild heterogeneity; (2) 25% to 50%: may represent moderate heterogeneity; (3) More than 50%: may represent severe heterogeneity. A random effect model was used when the heterogeneity more than 25%, otherwise the fixed effect model was used. Sensitivity analyses were intended to be conducted so that robustness can be tested, including quality of trials (high or low) and funding(commercial or uncommercial).

If sufficient studies were available (at least 10 trials), we intended to assess and find out potential publication bias by funnel plots. 14

If the number of included RCTs permitted, we intended to perform subgroup analyses based on the subcategories of Tuina manipulation, types of IBS (IBS-C, IBS-D, IBS-M, IBS-U), clinical course (duration of disease), different diagnostic criteria and treatment duration (short and long term).

**Results**

**Searching and Screening**

From the 11 databases searched, 696 articles were identified, including 667 in Chinese and 29 in English. After excluding duplications, the titles and abstracts of the remaining 357 citations, (334 Chinese and 23 English) were screened. After screening, 35 remained and were downloaded in full and screened. Finally, 8 studies 15-22 met the inclusion criteria, all of which were published in Chinese. Although 3 of them contained English abstracts, none of the 8 studies had been indexed in the Medline database. If readers are interested in the original literatures included, they can obtain it from the review authors. The flow diagram is shown in **Flow diagram** (**Fig. 1**).

**Study characteristics**

The details of the eight trials are summarized in **Table 1**. The sample size of these studies ranged from 46 to 90 participants, with an average age of 30.4 to 43.5 years. Two trials included IBS-C patients and others IBS-D patients. Only one trial reported syndrome differentiation of TCM. Follow-up time was reported in three trials, two trials for 1 month and one trial for 6 months. For the outcomes, seven trials reported overall symptom improving rate. Two trials showed relapse rates, and two trials reported overall symptom scores. Only one trial showed QOL by SF-36. Two trials reported abdominal pain scores. One trial reported bloating scores, and one trial reported diarrhea scores. Only one trial reported constipation effectiveness by Bristol Stool Form Scale scores (BSFS) and one trial reported depression by HAMD-24 scores. None of the trials showed cost-effectiveness outcomes or safety outcomes.

This review compared eight different Tuina manipulations (see in **Table 2** and **Appendix B**) with eight different RTs (including trimebutine maleate, bifid triple viable, mosapride citrate, cisapride, pinaverium bromide, live combined bifidobacteriu, lactobacillus and enterococcus, compound diphenoxylate, and oryzanol, used alone or in combination).

Tuina treatment in RCTs included were most frequently concentrated on RenMai (Conception Vessel). A total of 48 acupoints were used in all RCTs, which were listed in **Table 2**. There were 16 most frequent acupoints, which were GanShu (BL18), DanShu (BL19), PiShu (BL20), WeiShu (BL21), ShenShu (BL23), DaChangShu (BL25), BaLiao (BL31-34), GuanYuan (CV4), QiHai (CV6), ShenQue (CV8), ZhongWan (CV12), TianShu (ST25), ZuSanLi (ST36). The most common manipulations were: circular rubbing the abdomen and pressing or kneading or pushing with one-finger the relevant acupoints. Different locations required different manipulations, durations, or frequency. The frequency of the Tuina was usually once one or two days, and one course lasted for half a month to one month. Tuina was often used alone as an alternative or combined with RTs as a complimentary therapy.

**Risk of bias of included trials**

For incomplete outcome data, articles that were consistent with the number of cases enrolled and analyzed by statistical or that did not mention withdrawals and dropouts were evaluated as “unclear”. For selective outcome reporting, we defined that overall symptom improving rate, overall symptom scores and QOL were the most important outcomes. For the above three outcomes, none of them reported was rated as “high”. If only the overall symptom improving rate was reported as outcome, it should be included in the specific definition of the above individual symptoms to be rated “low”, otherwise rated as “high”. If the overall symptom scores at least included the sum of all the individual symptom scores mentioned above or the relevant scale was used, it was rated as “low”; otherwise, it was “high”. Other biases，included: (1) If the baseline data was presented in a text or presented in a form, it is rated “low”, without mentioning the relevant information as “high”. If only mentioned “balanced” without data to support was “unclear”. (2) It is explicitly reported that the inclusion and exclusion criteria was “low”, otherwise it was “unclear”. (3) Non-commercial funding supported research was “low”, and pharmaceutical companies funding was “high”. If all three of the above were “low” risk, it was judged to be “low” risk for other biases. However, if there was one “high” risk, it was judged as “high” risk, and the “unclear” assessment was the same.

For random sequence generation, three trials 15, 16, 19 reported on the randomization method used (random number table, drawing of lots, randomization system), which were judged to be a “low” risk, while the others only reported the " randomized" without further information was judged to be “unclear”. All trials did not report the allocation concealment, so they were judged to be “unclear” risk. Only one trial 19 reported the use of single-blinding, but did not mention the object of blinding, which we considered to be blind to the assessor. So it was judged as “low”. The remaining trials did not have the relevant information of blinding, so they were judged as “high” risk of bias for blinding of assessor. No cases of withdrawals and dropouts were provided in all trials and their risk of biases were judged to be “unclear”. Only one trial 16 reported QOL, and one reported 15 IBS-SSS scores, so they were rated as “low” risk. The overall symptom improving rate of one trial 21 reported did not describe individual symptoms and another trial 22 reported was only based on the scores of degree and frequency of abdominal pain, so were rated as “high” risk. The overall symptom improving rate of the remaining trials 17-20 reported clearly defined the individual symptoms involved, so they were rated as “low” risk. For other biases, two trials 15, 21 claimed that the baseline was balanced but did not provide data, so they were judged as “unclear” and the rest trials were “low”. Only two trials 18 that did not report inclusion criteria and exclusion criteria were rated “unclear”, and the others were “low”. Since funding information was not reported, the conflict of interest for all trials were judged to be “unclear” risk (**Fig. 2**).

**Effects of the interventions**

Eight different Tuina manipulations were tested in 8 trials and compared with 8 RTs. Due to the limitations of the data, we only performed meta-analyses for overall symptom improving rate. Sensitivity analyses were unable to conduct due to general low quality of randomized trials and no information about funding.

**Primary Outcomes**

**1 Global improvements of symptoms**

**1.1 Overall symptom improving rate**

In China, as a composite outcome, the overall symptom improving rate is usually based on the improvement rate of overall symptom scores. The overall symptom score was the sum of the individual symptom scores, one of or all the following three symptoms: distension, abdominal pain and diarrhea/constipation.

**1.1.1 Tuina vs Routine treatments**

**1.1.1.1 Overall symptom improving rate of IBS-D in Tuina vs Routine treatments**

In general, for IBS-D patients, it had not been shown that Tuina was significantly better than RTs (RR 1.23, 95% CI 0.94-1.60, 197 participants, 3 studies, *I*2 = 65%). A subgroup analysis according subtypes of IBS showed that for patients diagnosed by Rome II, there was no statistical difference between Tuina and RTs (RR 1.12, 95% CI 0.93-1.34, 119 participants, 2 studies, *I*2 = 11%). The sample size of both studies was small. Although for patients diagnosed by Rome III, Tuina might be superior to RTs (RR 1.63, 95% CI 1.20-2.21), only one small sample study was included. (**Fig. 3**)

**1.1.1.2 Overall symptom improving rate of IBS-C in Tuina vs Routine treatments**

Since the heterogeneity test showed *I*2 = 74%, so no meta-analysis was performed for the three included studies on IBS-C. The results of two studies using Rome II as diagnostic criteria were inconsistent (Pei XH 2007: RR 1.03, 95% CI 0.88-1.20; Zhang GZ 2010: RR 1.88, 95% CI 1.13-3.14); one study using Rome III as diagnostic criteria showed that Tuina was superior to RTs (RR 1.26, 95% CI 1.02-1.55), but the lower limit of the CI was almost ineffective and its sample size was small. (**Fig. 4**)

**1.1.2 Tuina + Routine treatments vs Routine treatments**

In this comparison, a meta-analysis by using the M-H fixed effect model was conducted (**Fig. 5**). The results indicated that Tuina combined with RTs might have certain advantages for IBS-D (RR 1.29, 95% CI 1.08-1.54, 115 participants, 2 studies). Since only two small sample sizes studies were included, it was necessary to be cautious about this conclusion.

**1.2 Overall symptom scores**

Two studies reported overall symptom scores, which 15 respectively showed IBS-SSS scores and symptom scores with reference to a criterion from a TCM monograph. One study 15 showed IBS-SSS scale in the Tuina combined group were lower than trimebutine maleate group (MD -43.90, 95% CI -62.25 to -25.55). The other study 19 showed that the Tuina group significantly reduced total symptom scores (including scores of BSFS, distension, difficulty in defecation, abdominal pain, incomplete defecation, and mentality) compared to the mosapride citrate group (MD -10.93, 95% CI -16.76 to -5.10).

**2 Quality of life (QOL)**

Only one study 16 reported QOL using SF-36, and showed that the trimebutine maleate combined with Tuina was 7.7 points higher than the trimebutine maleate alone (MD 7.70, 95% CI 5.19-10.21).

**Secondary Outcomes**

**1** **Relapse rates**

Two trials 15, 20 focused on relapse rate, one trial at 1 month was 6.7% (1/15) vs 44.4% (4/9) of the Tuina combined group vs trimebutine maleate group. However, there was no significant difference in relapse rates between the two groups (RR 0.15, 95% CI 0.02-1.14).

The other trial was at 6 months was 12.5% (5/40) vs 56.4% (22/39) in the Tuina group vs cisapride group. The Tuina group significantly reduced the relapse rate compared with the cisapride group (RR 0.22, 95% CI 0.09-0.53).

**2 Predominant symptom relief**

Two studies reported the outcome of abdominal pain relief. One 16 showed by the 7-point Likert scale (MD -1.10, 95% CI -1.35 to -0.85) and the other 19 with reference to a literature as its scoring criterion (MD -2.07, 95% CI -3.32 to -0.82). Only one study 19 reported the effectiveness of distension relief (MD -1.66, 95% CI -2.96 to -0.36). Only one study 16 reported the effectiveness of diarrhea relief by using the 7-point Likert scale scores (MD -1.10, 95% CI -1.28 to -0.92). One trial 19 reported the effectiveness of constipation relief, which was measured by the BSFS (MD -1.67, 95% CI -2.95 to -0.39).

**3 Psychological states**

Only one study 16 reported depression, which was measured by HAMD-24 (MD -5.50, 95% CI -6.70 to -4.30). No data was reported on anxiety in trials.

**4 Cost-effectiveness and adverse events**

No data were reported on cost-effectiveness and adverse events in trials.

**Discussion**

**Summary of findings**

In this review, 8 RCTs involving 545 participants (349 for IBS-D, 196 for IBS-C) and 8 different manipulations were included. Meta-analysis could only be performed on the overall symptom improving rate. Tuina combined with RTs may be superior to the RTs in overall symptom improving rate for IBS-D. There was very little information on the adverse events and relapse rates. In most domains of the risk of bias, almost trials had an unclear risk. Due to limitations to the risk of bias, it is hard to confirm the effectiveness and safety of Tuina.

**Compared with previous studies**

We identify no previous systematic review existed on Tuina for IBS.

**Limitations**

All studies included in this review are published in Chinese on Chinese journals that were not indexed in Medline. It had been pointed out that studies published in non-English and in journals that were not included in Medline may overestimate the effects 23, so our study may be affected by language bias. All trials included showed positive results for Tuina therapy, while more negative trials may be difficult to publish in peer-reviewed literature, which may lead to publication bias that overestimated effects.

Due to the insufficient reporting of the methodology in the included studies, almost domains of trials had an unclear risk, especially the serious shortcomings of blinding and allocation concealment. None of the included studies reported the outcome of adverse events, and we could not determine from the reporting whether it had been measured but it had not occurred or had not been measured at all. This makes it hard to draw the definitive conclusions of Tuina effectiveness and safety. This review is based on small sample size studies, ranging from 46 to 90 cases. Therefore, the results should be interpreted carefully. In addition, the difficulty of implementing blinding, the patient's expectations and cultural difference, which may make the results difficult to duplicate in other settings.

The heterogeneity of manipulations is a problem that cannot be ignored. Due to the influence of the concept of TCM syndrome differentiation and different Tuina genres, if the differences in Tuina techniques, strength, frequency and acupoints are considered strictly, most Tuina trials may be difficult to conduct a meta-analysis. The purpose of this study was to evaluate the effectiveness of Tuina therapy in a macroscopic way, so meta-analysis were still performed. But given the heterogeneity from Tuina manipulations and different control medications, this still carries a certain risk. Additionally, none of the studies included reported on the qualifications of Tuina doctors or therapists, which could cause variability in results.

**Recommendations/Implications for future research**

In the case of study design, blinding setting and placebo effects will be two major challenges in Tuina research. If patient reported outcomes (PROs) are used, blinding (whether for participants, investigators, or outcome assessors) is difficult to conduct in clinical trials of Tuina for IBS. It is reported 24 that the placebo effect can be as high as 84% in the IBS studies. The biases from the participants and investigators can be reduced by balancing the placebo effect between treatment group and control group, controlling the investigators biases, controlling the difference among the therapists and adopting on-demand treatment. Future designs should develop and validate methods for assessing the expected effects (eg, placebo, nocebo) of IBS, and try to explore and minimize the effect values. Larger sample sizes RCTs should be design to evaluate long-term effectiveness of Tuina, utility of on-demand treatment and related health economics outcomes (eg, cost-effectiveness, cost-utility).

For patients, since all the studies included were completed in China, multi-center and cross-cultural studies should be conducted to evaluate the effectiveness of Tuina with different ethnic patients in the future. For interventions, the therapist's Tuina techniques should belong to the same genre and receive standardized training before the trials. On-demand treatment should be used in IBS researches. The frequency of Tuina therapy is generally once every other day in clinical practice 9. A short-term effectiveness evaluation should be at least 4 weeks, and a long-term at least 6 months 5. For controls, future studies should set the treatments which is similar with the benefit expectations (placebo effect) of Tuina as control. For outcomes, PROs should be used and the recall period for a PRO is preferably no more than 1 day. Symptom assessment was recommended at any time 5. All adverse events should be observed and reported, even if they did not occur. The dose-response effect should be considered in the trials to explore the minimum and optimal effective "dose" of the Tuina therapy (including frequency, duration, dose and manipulations).

For reporting, details of Tuina therapy (including acupoints, manipulations, strength, dose, frequency, duration) and qualifications of Tuina therapists need to be sufficiently reported in a transparent and standardized manner to allow repetition. Future studies must explicitly report eligibility criteria. The CONSORT guidelines for non-pharmacological treatments (CONSORT-NPT) 25 and STRICTA checklist 26 have important guiding significance in protocols writing, trials performing and reporting. Also, standardized Tuina terms should be used in reporting.

**Implications for clinical practice**

Based on the evidence collected at present, the following acupoints can be considered in clinical treatment of Tuina for IBS: BL18, BL19, BL20, BL21, BL23, BL25, BL31-34, CV12, CV4, CV6, CV8, ST25, ST36, and the following manipulations: circular rubbing the abdomen, pressing/kneading/pushing with one-finger. The course of treatment can be 0.5 to 1 month, and the frequency can be once a day or once every other day.

**Conclusion**

This study shows that Tuina combined with RTs may be superior to RTs for improving overall symptom of IBS-D. However, due to the poor quality of the methodology and small sample size, the interpretation of the results should be cautious. In the future, studies with large samples, multicenter, and of high methodology quality (especially focusing on the blinding of the evaluators and the concealment of random sequence) of RCTs should be designed and performed.

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**Table 1 Characteristics of included randomized controlled trials on Tuina for IBS**

|  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| **Study ID** | **Sample Size** | **Diagnostic criteria** | **Age(y)** | **Sex M/F** | **Duration of disease** | **Subtype of IBS** | **TCM syndrome differentiation** | **Comparison** | **Outcomes** | **Follow up** |
| **Tuina + routine treatments *vs* routine treatments, 3 trials** |
| Lai SL 2017 | T: 27C: 33 | Rome III | T: 44.2C: 43.5\* | T: 10/17C: 14/19 | T: 8.8mC: 8.5m | IBS-D | NR | Tuina+Trimebutine Maleate dispersible tablets (dosage: 0.1g, tid, po) *vs* Trimebutine Maleate dispersible tablets (0.1g, tid, po) (4w) | ①Quality of life (SF-36);②Individual Symptom scores (abdominal pain, diarrhea);③Psychological states (HAMD-24) | NR |
| Chen Y 2018 | T: 34C: 34 | Rome III | T: 44.6C: 45.1 | T: 13/21C: 11/23 | T: 8.4m C: 7.9m | IBS-D | Syndrome of liver depression with spleen insufficiency (GanYuPiXu) | Tuina+Trimebutine Maleate tablets (0.1g, tid, po) *vs* Trimebutine Maleate tablets (0.1g, tid, po) (4w) | ①Global Improvement of symptoms (overall symptom improving rate, overall symptom scores);②Relapse rate (T: 1/15 1m; C: 4/9 1m) | 1m |
| Lu L 2008† | T: 24C: 23 | Rome II | T: 35.2C: 30.4 | T: 10/14C: 9/14 | T: 3-9y C: 3-11y | IBS-D | NR | Tuina+Bifid Triple Viable capsules Dissolving at Intestines (0.42g, tid, po) *vs* Bifid Triple Viable capsules Dissolving at Intestines (0.42g, tid, po) (2w) | Global Improvement of symptoms (overall symptom improving rate) | NR |
| **Tuina *vs* routine treatments, 6 trials** |
| Zhang GZ 2010 | T: 26C: 20 | Rome II | total: 42.5\*\* | T: NR/NRC: NR/NR | 4.5y | IBS-C | NR | Tuina *vs* Mosapride Citrate tablets (15mg, qd, po) (4w) | Global Improvement of symptoms (overall symptom improving rate) | NR |
| Pei XH 2007 | T: 45C: 45 | Rome II | T: 39.15C: 40.37 | T: 16/29C: 14/31 | T: 10.6y C: 11.2y | IBS-C | NR | Tuina *vs* Cisapride tablets (10mg, tid, po) (8w) | ①Global Improvement of symptoms (overall symptom improving rate);②Relapse rate (T: 5/40 6m; C: 22/39 6m) | 6m |
| Lian BL 2011 | T: 40C: 38 | Rome III | T: 35.7C: 34.9 | T: 17/23C: 17/21 | T: 1.7y C: 1.6y | IBS-D |  | Tuina *vs* Pinaverium Bromide tablets(50m, tid, po)+ Live Combined Bifidobacterium，Lactobacillus and Enterococcus capsules(210mg\*2, tid, po) (1m) | Global Improvement of symptoms (overall symptom improving rate) | NR |
| Zhang GZ 2004 | T: 36C: 36 | Rome II | T: 40C: 39\*\*\* | T: 17/19C: 16/20 | NR | IBS-D |  | Tuina *vs* Compound Diphenoxylate tablet(1s‡, tid, po)+ Oryzanol tablets(10mg, tid, po) (4w) | Global Improvement of symptoms (overall symptom improving rate) | NR |
| Lu L 2008† | T: 24C: 23 | Rome II | T: 33.1C: 30.4 | T: 9/15C: 9/14 | T: 3-9y C: 3-11y | IBS-D |  | Tuina *vs* Bifid Triple Viable capsules Dissolving at Intestines (0.42g, tid, po) (2w) | Global Improvement of symptoms (overall symptom improving rate) | NR |
| Pei JW 2012 | T: 30C: 30 | Rome III | T: 20-55C: 22-49# | T: 12/18C: 14/16 | T: 1-13yC: 1.5-10y | IBS-C |  | Tuina *vs* Mosapride citrate tablets (5mg, tid, po) (4w) | ①Global Improvement of symptoms (overall symptom improving rate, overall symptom scores);②Individual Symptom scores (abdominal pain, distension, and constipation) | 4w |

Note: T: treatment group; C: control group; y: year; m: month; w: week; d: day; IBS-D: diarrhea-predominant IBS; IBS-C: constipation-predominant IBS; NR: not report; po: by oral; qd: once a day; tid: three times a day

\**‾x*±*SD*; \*\**‾x*（*Min*-*Max*）; \*\*\*‾*x*; # *Min* to *Max*

‡ The specification of the medicine was unclear.

† This study is a three-arm trial, and the different arms belong to different comparisons.

This study defined the overall symptom improving rate of more than 30% improvement in overall symptom scores or improved signs and symptoms. Overall symptom improvement rate = [(Pre-treatment symptom scores - Post-treatment symptom scores)/ Pre-treatment symptom scores] \* 100%.

**Table 2 Description of Tuina manipulation**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Study ID** | **Manipulation** | **Frequency** | **Course** | **Location** |
| **Main acupoints involved** | **Main meridians involved** | **Main Regions involved** |
| Lai SL 2017 | ①Palm-pressing the abdomen (for 5min);②Circular palm-rubbing the abdomen (CV12 as center, making counterclockwise circular movements, slow action, 20-30 times/min, for 5min);③Circular pushing the abdomen (8 cycles, for 2min);④Thumb-pushing from CV14 to CV8 (push 36 times alternately, for 5min);⑤To-and-fro Rubbing LR4 and LR13 with palms (for 4min);⑥Pinching the Spine along EX-B2(especially BL17, BL-18, BL-19) (for 3min);⑦Grasping, Pressing and Kneading areas from vertex to GV16 (for 6min) | qod | 4w | CV4;CV6;CV8;CV12;CV14;LR4; LR13;EX-B2;EX-HN1;GV16;GV20;GB20;BL10 | Conception Vessel | Abdomen;Chest and hypochondrium; Spine and back; Head and nape |
| Chen Y 2018 | ①Palm-pressing abdomen;②Circular Palm-pushing CV8, finger-pushing from CV14 to CV8 and Kneading BL18 and BL19;③Pushing GV20 and GB20 with One-finger(alternately using ①-③ for 40min) | qod | 4w | CV4;CV6;CV8;CV12;CV14;BL18;BL19;GV20;GB20 | Conception Vessel | Abdomen;Spine and back; Head and nape |
| Lu L 2008 | ①Pressing-Kneading or Pushing with One-finger CV12, ST25, CV4 and SP15 (2min/acupoint);②Pushing with One-finger or Rolling BL18, BL20, BL21, BL23, BL25, BL31-34, GV1(to-and-fro, for 5min);③Pressing-Kneading BL18, BL20, BL21, BL25, GV1 (2min/acupoint) | qd | 2w | BL18; BL20; BL21; BL23; BL25; BL31-34;CV4;CV12;ST25;SP15;GV1 | Bladder Meridian | Abdomen;Back |
| Zhang GZ 2010 | ①Thumb-pressing CV15 and Pushing with One-finger or Finger-kneading CV6, CV11, CV12, ST25, SP15, CV8, CV4 and ST28 (1-3min/acupoint);②Circular Rubbing (clockwise, 3-5min);③Circular pushing the abdomen (for a few minutes);④Separate pushing from xiphoid to lower abdomen and iliac regions (repeated several times);(Repeated ①-④ three times)⑤Digital-pressing CV22, CV21, CV17, LI11, LU5, TE6, TE5, LI4, ST36, ST37, ST39 and BL57;⑥Rolling and Kneading the flowing regions of Bladder Meridians on both sides of the spine from top to lumbosacral portion (3-5 times);⑦Fist percussing (40-60 times) and To-and-fro Rubbing (take thermal penetration as the degree) BL31-34 | qd | 4w | CV4;CV6;CV8;CV11;CV12;CV15;CV17;CV21;CV22;BL18-20;BL21;BL23;BL25;BL31-34;BL57;ST25;ST28;ST36;ST37;ST39;SP15;LI4; LI11; LU5; TE5; TE6 | Conception Vessel; Bladder Meridian;Stomach Meridian | Abdomen;Back |
| Pei XH 2007 | *Passive Tuina*:①Circular Rubbing the abdomen (for 5min);②Pushing ST36, CV12, GB34, LR2 with One-finger (reduction manipulation, 2min/acupoint);③Pushing with One-finger from BL17 to BL25 (stimulating focused on BL17, 20, 23, 25, for 5min);④To-and-fro Rubbing BL20, 21, 23, 31-34, GV4 and Governor Vessel (take thermal penetration as the degree);⑤Palm-twisting hypochondrium (3-5 times*Initiative Tuina*:Self-Circular Rubbing the abdomen | NR | 2m | BL17;BL20;BL21;BL23; BL25;BL31-34;ST36;CV12;GB34;LR2;GV4 | Bladder Meridian;Governor Vessel | Abdomen;Hypochondrium |
| Lian BL 2011 | ①Pushing CV12 with One-finger (for 5min);②Pushing Conception Vessel from CV12 to CV4 (focus on CV8, CV6, CV4) with One-finger;③Pushing with One-finger from left to right ST25 (for 5min);④Pushing with One-finger and To-and-fro Rubbing from CV12 to CV4⑤Pushing with One-finger and To-and-fro Rubbing between left and right ST25(take warming and comfort as the degree);⑥Circular Palm Rubbing (CV8 as center, for 5min);⑦Pushing with One-finger LR13, LR4, LI11, ST36, ST37, SP6 and LR3 (1min/acupoint);⑧Pushing BL18, BL20, BL21, BL25 and BL27 with One-finger from the each left acupoint to right (3 times);⑨To-and-fro Rubbing BL25 and lumbosacral portion(The whole process is about 40 minutes.) | qod, tiw | 1m | CV4;CV6;CV8;CV12;BL18;BL20;BL21;BL25;BL27;LR3;LR4;LR13;ST25;ST36;ST37;LI11;SP6 | Conception Vessel;Bladder Meridian | Abdomen;Back;Lumbosacral portion |
| Zhang GZ 2004 | ①Thumb-pressing CV15 and Finger-kneading CV6, CV11, CV12, ST25, ST28 and ST29 (1-2min/acupoint);②Circular Rubbing (5-10min);③Circular pushing the abdomen (for 10 min);④Separate pushing from xiphoid to lower abdomen and iliac regions (repeated several times), then Combine pushing from outsides to center of abdomen (15 times);⑤Pushing with One-finger, Rolling and Kneading the flowing regions of Bladder Meridians on both sides of the spine from top to lumbosacral portion (3-5 times);⑥Fist percussing (30-60 times) and To-and-fro Rubbing (take thermal penetration as the degree) BL31-34;⑦For patients with severe abdominal pain and diarrhea: i. conducting the above manipulations on the abdomen to rotate clockwise with moving counterclockwise; ii. combing with Pressing-Kneading ST36, BL20, BL23, BL25 and SP6; iii. Fist percussing BL31-34 (60 times); iv. To-and-fro Rubbing GV4 and areas around umbilicus (30 times) | qd | 4w | CV6;CV11;CV12;CV15;BL18-21; BL23; BL25; BL31-34;ST25;ST28;ST29;ST36;SP6;GV4 | Bladder Meridian; Conception Vessel;Stomach Meridian | Abdomen;Back |
| Pei JW 2012 | ①Thumb-Pressing along Conception Vessel from CV15 to CV4 (1-3min/acupoint);②Pushing ST25 and SP15 with One-finger (1-3min/acupoint);③Circular Rubbing (CV8 as center, clockwise, 3-5min);④Circular pushing the abdomen (3-5 min);⑤Twisting and Rubbing like Plucking the String from CV15 to ilia;⑥Digital-pressing TE6, SP21, LR13, ST36, ST37, ST39 and BL57;⑦Rolling and Kneading the flowing regions of Bladder Meridians on both sides of the spine from top to lumbosacral portion;⑧Fist percussing the above acupoints; ⑨To-and-fro Rubbing (take thermal penetration as the degree) BL31-34 | ≥tiw, one day of weekends without treatment | 4w | CV4;CV6;CV12;CV15;BL18-21;BL23;BL25;BL31-34;BL57;ST25;ST36;ST37;ST39;SP5;CV8;TE6;SP21;LR13; | Conception Vessel;Bladder Meridians;Stomach Meridian | Abdomen;Hypochondrium;Back;Lumbosacral portion |

Note: qd: once a day;qod: once every other day; tiw: three times a week.

BL: Bladder meridian of foot-taiyang; BL10: Tianzhu; BL17: Geshu; BL18: Ganshu; BL19: Danshu; BL20: Pishu; BL21: Weishu; BL23: Shenshu; BL25: Dachangshu; BL31-34: Baliao (including Shangliao, Ciliao, Zhongliao and Xialiao); BL57: Chengshan.

 CV: Conception vessel; CV4: Guanyuan; CV6: Qihai; CV8: Shenque; CV11: Jianli; CV12: Zhongwan; CV14: Juque; CV15: Jiuwei; CV17: Tanzhong; CV21: Xuanji; CV22: Tiantu.

 EX: Extraordinary acupoints; EX-B2: Jiaji; EX-HN1: Sishencong.

 GB: Gallbladder meridian of foot-shaoyang; GB20: Fengchi; GB34: Yanglingquan.

 GV: Governor vessel; GV1: Changqiang; GV16: Fengfu; GV20: Baihui; GV4: Mingmen.

 LI: Large intestine meridian of hand-yangming; LI4: Hegu; LI11: Quchi.

 LR: Liver meridian of foot -jueyin; LR2: Xingjian; LR3: Taichong; LR4: Zhongfeng; LR13: Zhangmen.

 LU: Lung meridian of hand-taiyin; LU5: Chize.

SP: Spleen meridian of foot-taiyin; SP5: Shangqiu; SP6: Sanyinjiao; SP15: Daheng; SP21: Dabao.

 ST: Stomach meridian of foot-yangming; ST25: Tianshu; ST28: Shuidao; ST29: Guilai; ST36: Zusanli; ST37: Shangjuxu; ST39: Xiajuxu.

 TE: Triple energizer meridian of hand-shaoyang; TE5: Waiguan; TE6: Zhigou.

**Fig. 1. Flow diagram**

**Fig. 2. Risk of bias of included trials**

**Fig. 3. Subgroup analysis of forest plot of overall symptom improving rate for IBS-D according to diagnostic criteria (Tuina vs RTs)**

Notes: M-H: Mantel-Haenszel method, 95% CI: 95% confidence interval, RTs: routine treatments.

**Fig. 4. Subgroup analysis of forest plot of overall symptom improving rate for IBS-C according to diagnostic criteria (Tuina vs RTs)**

Notes: M-H: Mantel-Haenszel method, 95% CI: 95% confidence interval, RTs: routine treatments.

**Fig. 5. Forest plot of overall symptom improving rate (Tuina + RTs vs RTs)**

Notes: M-H: Mantel-Haenszel method, 95% CI: 95% confidence interval, RTs: routine treatments.

**Appendix A Search strategy examples**

**Appendix B The operation methods of Tuina manipulations in included studies**