Effect of Chinese herbal topical medicine, acupuncture, and moxibustion on pressure ulcer wound healing: A meta-analysis

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Abstract
We performed a meta-analysis to evaluate the effect of Chinese herbal topical medicine, acupuncture, and moxibustion on pressure ulcer wound healing. A systematic literature search up to January 2022 was done and 13 studies included 1073 subjects with pressure ulcer wound at the start of the study; 593 of them were using traditional Chinese medicine treatments, and 480 were control for pressure ulcer wound. We calculated the odds ratio (OR) with 95% confidence intervals (CIs) to evaluate the effect of Chinese herbal topical medicine, acupuncture, and moxibustion on pressure ulcer wound healing by the dichotomous methods with a random or fixed-influence model. Traditional Chinese medicine treatments had significantly higher complete healing (OR, 5.94; 95% CI, 3.94–8.95, P < .001), and curative ratio post-treatment (OR, 4.79; 95% CI, 2.62–8.76, P < .001) compared with control for subjects with pressure ulcer wound. Traditional Chinese medicine treatments had a significantly higher complete healing and curative ratio post-treatment compared with control for subjects with pressure ulcer wounds. Further studies are needed to validate these findings.

Keywords
acupuncture, Chinese herbal topical medicine, complete healing, curative ratio post-treatment, moxibustion

Key Messages
- We performed a meta-analysis to evaluate the effect of Chinese herbal topical medicine, acupuncture, and moxibustion on pressure ulcer wound healing.
- Traditional Chinese medicine treatments had a significantly higher complete healing, and curative ratio post-treatment compared with control for subjects with pressure ulcer wounds.
- Further, studies are needed to validate these findings.
**1 | BACKGROUND**

Pressure ulcers, which are recognized as bedsores or pressure sores are areas of localized injury to the skin and deeper layers of tissue affecting muscle, tendon, and bone as an outcome of continuous pressure due to impaired movement. The pressure causes poor circulation and ultimately donates to cell mortality, skin damage, and develops an open wound. If not sufficiently managed, open ulcers can develop into a cause of pain, disability, and infection. Pressure ulcers are usually graded according to the European Pressure Ulcer Advisory Panel and National Pressure Ulcer Advisory Panel as follows:

Grade I: Complete skin with non-bleachable erythema. Discoloration of the skin, warmth, edema, hardness, or pain might additionally be used as indicators with darkly pigmented skin that might not have visible bleaching; Grade II: Restricted thickness skin loss including epidermis, dermis, or both, with a red-pink wound bed, without slough. The ulcer might also exist as an abrasion or blister; Grade III: Full thickness tissue loss, but not exposing muscle, tendon, or bone. Some slough might exist, and may comprise undermining and tunnelling; Grade IV: Full thickness tissue loss with exposed bone, tendon, or muscle. Slough or eschar might exist. Frequently comprise undermining and tunnelling. Pressure ulcer occurrence differs extensively depending on subjects who have influencing risk factors for example, poor nutrition, confinement to a bed or wheelchair, and other medical complications, particularly spinal cord injury, hip fracture, or dementia. Common sites comprise the sacrum, back, buttocks, heels, back of the head, and elbows. Pressure ulcers are extensive, expensive, and painful health care complications, with frequency rates up to 53.2% and occurrence rates up to 71.6%. A multinational study including five countries showed that the overall incidence of pressure ulcers was almost 18% of hospitalized subjects. Pressure ulcer incidence was up to 32.1% in the UK, 29.7% in the USA and Canada. These ulcers are a major load of morbidity and decrease quality of life for subjects and their carers and are a substantial cost to both the subjects and the health care service. Management approaches for pressure ulcers frequently represent a great economic burden in the form of direct costs from the loss of work and medical expenses. Effective and sufficient management is a vital matter for subjects, clinicians, and policymakers. Pressure ulcer management is now an enormous industry and includes a range of interventions. In addition to traditional interventions for pressure ulcer for example, antimicrobial, mattress, dressing, hydrotherapy, skin substitutes, negative pressure therapy, electrical stimulation, ultrasound, electromagnetic treatment, laser treatment, and light treatment. Treatments collectively called traditional Chinese medicine treatments are usually used. Though, the influence of traditional Chinese medicine treatments for the management of pressure ulcers is not without argument. So, the present meta-analysis aimed to evaluate the effect of Chinese herbal topical medicine, acupuncture, and moxibustion, as types of traditional Chinese medicine treatments, on pressure ulcer wound healing.

**2 | METHODS**

This meta-analysis is organized according to the epidemiology statement after the established methodology.

**2.1 | Study selection**

The main objective of this study was to compare the effect of traditional Chinese medicine treatments to control on pressure ulcer wounds using the following tools for example, odds ratio (OR), mean difference (MD), frequency rate, or relative risk, and confidence interval of 95%.

The search was not narrowed to English, and inclusion criteria were not restricted by study type or size. Studies with no correlation were exempted from the study, for example, editorials, review articles letters, and commentary. Figure 1 exhibits the mode of analysis.

The article inclusion criteria were classified and integrated into the meta-analysis when

1. The study was a randomized control trial, prospective study, or retrospective study.
2. The target population was subjects with pressure ulcer wound
3. The intervention program was traditional Chinese medicine treatments
4. The study comprised comparisons between traditional Chinese medicine treatments to control on pressure ulcer wounds.

The next exclusion criteria were adopted among the intervention groups

1. Studies that did not determine the effect of Chinese herbal topical medicine, acupuncture, and moxibustion as types of traditional Chinese medicine treatments on pressure ulcer wound healing
2. Studies with management other than traditional Chinese medicine treatments and control.
3. Studies that did not concentrate on the influence of comparative outcomes.
2.2 Identification

PICOS principle was the protocol for the search strategy, and asserted the critical elements of PICOS as P (population): subjects with pressure ulcer wound; I (intervention/exposure): traditional Chinese medicine treatments; C (comparison): traditional Chinese medicine treatments compared to control in pressure ulcer wound; O (outcome): complete healing, and curative ratio post-treatment; and S (study design): had no limitation. We conducted a systematic and brief search on Embase, PubMed, Cochrane Library, OVID, China National Knowledge Infrastructure, WanFang databases, Chinese Biomedical Literature Database, and Google Scholar until January 2022, by a combination of keywords and correlated words for traditional Chinese medicine treatments, pressure ulcer wound, complete healing, curative ratio post-treatment, Chinese herbal topical medicine, acupuncture, and moxibustion as shown in Table 1. The selected studies were pooled in EndNote software to exclude the duplicates. Additionally, a thorough screening on the title and abstracts were done to erase any data that did not show any influence of traditional Chinese medicine treatments compared to control in subjects with pressure ulcer

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TABLE 1 Search strategy for each database

| Database       | Search strategy                                                                 |
|----------------|---------------------------------------------------------------------------------|
| Pubmed         | #1 ‘Chinese Medicine treatments’[MeSH Terms] OR ‘pressure ulcer wound’[MeSH Terms] OR ‘complete healing’[MeSH Terms] OR ‘curative ratio post treatment’[All Fields] OR ‘moxibustion’[MeSH Terms] OR ‘acupuncture’[All Fields] #3 #1 AND #2 |
| Embase         | ‘Chinese Medicine treatments’[exp OR ‘pressure ulcer wound’[exp OR ‘complete healing’[exp OR ‘curative ratio post treatment’[exp OR ‘moxibustion’[exp OR ‘acupuncture’[exp #3 #1 AND #2 |
| Cochrane library | #1 (Chinese Medicine treatments):ti,ab,kw OR (pressure ulcer wound):ti,ab,kw OR(complete healing):ti,ab,kw OR (curative ratio post treatment):ti,ab,kw (Word variations have been searched) #2 (Chinese herbal topical medicine):ti,ab,kw OR (moxibustion):ti,ab,kw OR (acupuncture):ti,ab,kw (Word variations have been searched) #3 #1 AND #2 |
wound on the outcomes studied. Related pieces of information were collected from the remaining studies.

### 2.3 | Screening

Subject-related and study-related data characteristics were considered for the collection and classification of data, and it was pooled into a standardized form. The categorization was made into the standard form like the surname of the first author, duration of the trial, place of practice, design of the study, subject type, sample size, categories, demography, treatment methodology, information source, method of evaluation (both qualitative and quantitative), statistical analysis, and primary outcome evaluation.\(^{21}\)

Methodological quality was assessed by the ‘risk of bias tool’ adopted from Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0. This meta-analysis recommended that if a trial with inclusion criteria is based on the standards mentioned earlier, any conflicts that arose during the data collection by two reviewers must be resolved through discussion and when necessary by the ‘corresponding author’ to ensure the quality of the methodology.\(^{21}\) When there were different data from one study based on the evaluation of the relationship, we extracted them separately.

### 2.4 | The level of risk of bias is counted in the assessment criteria

The level of risk was considered low if all quality parameters were met; it was considered moderate if one of the quality parameters was not met/or partially met and was considered high if one of the quality parameters was not met/or not included. A reexamination of the original article was addressed for any inconsistencies.

### 2.5 | Eligibility criteria

The main eligibility criteria concentrated on the effect of Chinese herbal topical medicine, acupuncture, and moxibustion as types of traditional Chinese medicine treatments on pressure ulcer wound healing. An evaluation of the influence of traditional Chinese medicine treatments compared to control in pressure ulcer wound on the complete healing, and curative ratio post-treatment.

### 2.6 | Inclusion

Studies reporting the effect of Chinese herbal topical medicine, acupuncture, and moxibustion as types of traditional Chinese medicine treatments on pressure ulcer wound healing were only included in the sensitivity analysis. In comparison, the impact of traditional Chinese medicine treatments compared to control in pressure ulcer wounds was considered as a subcategory of sensitivity analysis.

### 2.7 | Statistical analysis

The dichotomous methods were used to compute the odds ratio (OR) at a 95% confidence interval (CI) on a

| Study | Country | Total | Traditional Chinese medicine treatments | Control |
|-------|---------|-------|------------------------------------------|---------|
| Luo\(^{25}\) | China | 76 | 38 | 38 |
| Jing\(^{26}\) | China | 55 | 30 | 25 |
| Bao\(^{27}\) | China | 46 | 23 | 23 |
| Li\(^{28}\) | China | 132 | 67 | 65 |
| Li\(^{29}\) | China | 40 | 20 | 20 |
| Tao\(^{30}\) | China | 48 | 24 | 24 |
| Chen\(^{31}\) | China | 35 | 18 | 17 |
| Li\(^{32}\) | China | 308 | 200 | 108 |
| Zhao\(^{33}\) | China | 44 | 22 | 22 |
| Zhang\(^{34}\) | China | 109 | 57 | 52 |
| Zhan\(^{35}\) | China | 50 | 25 | 25 |
| Guo\(^{36}\) | China | 60 | 34 | 26 |
| Parizi\(^{37}\) | Iran | 70 | 35 | 35 |
| **Total** | | 1073 | 593 | 480 |
fixed-influence or random-influence model. First, the $I^2$ index range was established between 0% and 100%, when the $I^2$ index scale for heterogeneity was indicated as no, low, moderate, and high as 0%, 25%, 50%, and 75%, respectively. Random-influence was considered if $I^2$ was >50%, and if <50%, as fixed-influence. The initial evaluation of the result was stratified, and in sub-group analysis a $P$-value <.05 was reported statistically significant. Egger regression test was used quantitatively and qualitatively to assess the publication bias (if $P \geq .05$) by inspecting funnel plots of the logarithm of odds ratios compared with their standard errors. The entire $P$-values were two-tailed. The statistical analysis and graphs were done by ‘Reviewer manager version 5.3’ (The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark).

### RESULTS

A total of 1010 distinctive studies were found, of which 13 studies (between 2008 and 2022) satisfied the inclusion criteria and were comprised in the study. This meta-analysis study based on 13 studies included 1073 subjects with pressure ulcer wound at the start of the study; 593 of them were using traditional Chinese medicine treatments, and 480 were control for pressure ulcer wounds. All studies evaluated the effect of Chinese herbal topical medicine, acupuncture, and moxibustion on pressure ulcer wound healing. All studies were from China except one recent study from Iran. About 12 studies reported data stratified to the complete healing, and 11 studies reported data stratified to the curative ratio post-treatment. The information of the 13 studies is shown in Table 2.

**FIGURE 2** A forest plot of the complete healing of the traditional Chinese medicine treatments compared with the control for subjects with pressure ulcer wounds

**FIGURE 3** A forest plot of the curative ratio post-treatment of the traditional Chinese medicine treatments compared with the control for subjects with pressure ulcer wounds
Traditional Chinese medicine treatments had significantly higher complete healing (OR, 5.94; 95% CI, 3.94–8.95, \( P < .001 \)) with low heterogeneity (\( I^2 = 22\% \)), and curative ratio post treatment (OR, 4.79; 95% CI, 2.62–8.76, \( P < .001 \)) with moderate heterogeneity (\( I^2 = 66\% \)) compared with control for subjects with pressure ulcer wound as shown in Figures 2 and 3.

The stratified data did not examine the factors like age, gender, and ethnicity between the two groups because no studies adjusted or outlined these factors. No publication bias (\( P = .88 \)) was detected when the quantitative measurement was conducted using the Egger regression test and examination of the funnel plot. However, low methodological quality was observed in selected randomized controlled trials. No articles had selective reporting or incomplete data, which proved that selected articles devoid of selective reporting bias.

4 | DISCUSSION

This meta-analysis study based on 13 studies included 1073 subjects with pressure ulcer wound at the start of the study; 593 of them were using traditional Chinese medicine treatments, and 480 were control for pressure ulcer wounds.25–37 Traditional Chinese medicine treatments had significantly higher complete healing, and curative ratio post-treatment compared with control for subjects with pressure ulcer wounds. However, the analysis of outcomes should be performed with consideration because of the low number of selected studies and the low sample size of most of the selected studies found for the meta-analysis, 10 out of 13 studies with \( \leq 100 \) subjects as sample size; recommending the need for other studies to confirm these findings or perhaps to significantly impact confidence in the influence evaluation.

Traditional Chinese medicine treatments comprise Chinese herbal topical medicine, acupuncture, and moxibustion. Chinese herbal topical medicine is an oil-based ointment enclosing sesame oil, honey, and other small quantities of plant ingredients.25–37 Numerous studies showed that Chinese herbal topical medicine endorses epithelial repair, inhibits bacterial growth, soothes wounds, retains moisture, relieves pain from wound surface, offers the best physiological environment for healing, and outcomes in progress for scar creation.25–37 Acupuncture is based on the system of meridians. Moxibustion is an East Asian treatment technique that produces heat by burning herbal formulae enclosing Artemisia vulgaris, applied next to the acupuncture points.38 Moxibustion management was reported to have assistances for pressure ulcers,39 pain,40 and cancer care.41 The popular of pressure ulcers occurs from other illnesses for example, stroke,27–29,34 heart disease,27–29,34 sequelae of traumatic brain injury,26–29,34 paraplegia,27–29,34 bone fracture,26,29 diabetes28,34 and renal failure.27,28 The drugs for these diseases may also have influences on pressure ulcers. Most traditional Chinese medicine treatments suppliers are the local hospitals themselves. That may cause varying results with the same Chinese herbal topical medicine management. To get a good assumption of traditional Chinese medicine treatments on bedsores, randomized controlled trials must care to control traditional Chinese medicine treatments and placebo effects. Furthermore, other vital results for example, wound area and symptoms must also be used to evaluate the effects of traditional Chinese medicine treatments; though, only one of these trials described the wound area properly.34 Not a single trial sufficiently covered group allocation and 10 of 13 studies did not clearly define how randomization was accompanied. Furthermore, none of the 13 trials showed any blind or blinding processes. Neither short-term nor long-term follow-ups were defined in 10 randomized controlled trials, so we are not sure about the effectiveness of traditional Chinese medicine treatments after the intervention. Therefore, poor reporting and high risks of bias both made these studies less dependable. Few rigorous randomized controlled trials testing the influences of traditional Chinese medicine treatments for pressure ulcers are available nowadays, and the present studies do not deliver much information about the advantage of traditional Chinese medicine treatments over other interventions for subjects with a pressure ulcer. Hence, this meta-analysis showed the relationship between the effects of traditional Chinese medicine treatments compared to control in subjects with pressure ulcer wounds. However, further studies are needed to validate these potential associations. Also, further studies are needed to deliver a clinically meaningful difference in the results. This was suggested in another meta-analysis which showed similar effects.42 This needs additional examination and clarification because no clear reasoning was found to clarify these outcomes. Well-designed clinical trials are also required to evaluate these factors with the blend of diverse ages, gender, and ethnicity; as our meta-analysis study could not answer whether these factors are related to the outcomes. In summary, traditional Chinese medicine treatments had a significantly higher complete healing, and curative ratio post-treatment compared with control for subjects with pressure ulcer wounds.

4.1 | Limitations

There may be a collection bias in this meta-analysis since several studies found were excluded from the meta-
analysis. Though, the studies excluded did not satisfy the inclusion criteria of the meta-analysis. Furthermore, we could not decide if the results were linked to age, gender, and ethnicity or not. The study was designed to assess the relationship between the influences of traditional Chinese medicine treatments compared to control in pressure ulcer wounds on the outcomes of subjects with pressure ulcer wounds was depending on data from former studies, which may result in bias brought by incomplete details. The meta-analysis was depending on 13 studies; 10 studies of them were small, \( \leq 100 \). Features comprising the age, gender, obedience, nutritional status, and ethnicity of subjects were also likely bias-encouraging features. Several unpublished studies and lost data may result in a pooled influence bias. Subjects were using diverse chief pharmacological medicines, treatment schedules, doses, and health care schemes. The type of traditional Chinese medicine treatments used for pressure ulcer wound treatment of the included studies was varying. The comprised studies did not sufficiently assess the hospital costs of the subjects studied, which is a vital result.

5 CONCLUSIONS

Traditional Chinese medicine treatments had a significantly higher complete healing, and curative ratio post-treatment compared with control for subjects with pressure ulcer wounds. However, the analysis of outcomes should be done with consideration because of the low sample size of most of the selected studies found for the meta-analysis; recommending the need for added studies to confirm these results or perhaps to significantly influence confidence in the effect evaluation. More studies are essential to confirm these outcomes.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

DATA AVAILABILITY STATEMENT

The datasets examined during the present study are obtainable from the corresponding author on reasonable request.

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How to cite this article: Wang F, Chen M, Du J. Effect of Chinese herbal topical medicine, acupuncture, and moxibustion on pressure ulcer wound healing: A meta-analysis. *Int Wound J.* 2022;19(8):2031-2038. doi:10.1111/iwj.13803