ISSN 2618-1584 Vol. 5, Issue 3: 14-23, DOI: 10.25236/FMSR.2023.050303

A Systematic Review and Meta-analysis of the Use of Simmering Pus and Growing Flesh Method to Promote Postoperative Wound Healing in Anorectal Diseases

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Abstract: *Objective: To systematically review the clinical efficacy and progress of Chinese medicine's external treatment method guided by the theory of simmering pus and growing flesh to promote postoperative wound repair in anorectology. Methods: Clinical randomized controlled trials (RCTs) of simmering pus and growing flesh method to promote postoperative wound healing in anorectology were collected by a computer search of China Knowledge Network (CNKI), Wanfang (WANGFANG DATA), VIP (VIP), China Biomedical Literature Database (CBM) and other means, and the screening of articles and the extraction of article data were performed according to the inclusion and exclusion criteria.Meta-analysis of the extracted data was also performed using Stata14 software, to compare the overall efficacy, mean wound healing time, and other clinical observations of patients with postoperative wounds in anorectal medicine by the external Chinese medicine method of simmering pus and growing flesh with the non-simmering pus and growing flesh method. Results: The final 12 publications were included, with a total of 931 study participants, and the Meta results showed that the TCM external treatment of simmering pus and growing flesh method helped to shorten the mean wound healing time [WMD=-3.791 , 95% CI (-4.629 , 2.952), P<0.05], improve the 14-day wound healing rate [WMD=9.341 , 95% CI (6.951 , 11.731), P<0.05], and improved postoperative wound recovery efficiency in anal diseases [RR=3.099, 95% CI (1.898, 5.060), P<0.05].Conclusion: The simmering pus and growing flesh method helps to improve the average healing time and wound healing rate of postoperative wounds in anal diseases, thus improving the efficiency of postoperative wound repair in anal diseases.*

Keywords: *Simmering pus and growing flesh; anal disease; postoperative wound repair; Meta-analysis*

1. Introduction

Anorectal diseases are usually divided into hemorrhoids, anal fistulas, perianal abscesses, anal fissures, hidden hair sinuses, and other diseases, and the disease types can be subdivided according to different principles of differentiation. However, the final treatment of anorectal diseases is mainly surgical. Since anorectal surgical wounds are located in the perianal and perineal areas, blood circulation is poorer than other wounds, and they are open wounds with a higher wound infection rate than other wounds, so postoperative wound dressing changes and care are particularly important.

According to TCM, the slow repair of trauma is due to the patient's deficiency, stagnation of the meridians, stagnation of the veins and veins, and the transformation of decay into pus. The words "deficiency" and "stasis" run through the whole process of chronic trauma [1].The slow repair of post-operative trauma is not only due to the special anatomical location of the trauma, but more importantly, its pathogenesis is in the case of weakness of the viscera and lack of regulation of yin and yang, and the evil stagnates in the couples and veins, and over time stagnates into pus and rot. Therefore, it is necessary to break the stasis, drain the pus and dispel the decay, open the trauma, and cause the evil to be consumed as well. Among them, simmering pus and growing flesh believe that in the late stage of sore healing, applying topical Chinese herbal ointment (scattering), through the absorption of drugs on the skin and trauma, promotes local qi and blood circulation, enhances its defense function, increases pus exudation from the trauma, and carries the evil out, thus achieving the purpose of promoting the repair of the trauma [2].However, randomized controlled clinical trials of the

ISSN 2618-1584 Vol. 5, Issue 3: 14-23, DOI: 10.25236/FMSR.2023.050303

simmering pus and growing flesh method for postoperative wound repair in anorectal surgery have been reported rarely, and the use of the simmering pus and growing flesh method for postoperative dressing changes and care of anorectal diseases has not been promoted in a timely manner, nor has there been a systematic evaluation of this aspect. This article is an evaluation of the efficacy of the external Chinese medicine method of simmering pus and growing flesh for postoperative wound repair in anorectal diseases, thus providing an evidence-based basis for the widespread use of the simmering pus and growing flesh method for postoperative wound repair in anorectal surgery at a later stage.

2. Materials and Methods

The clinical randomized controlled trials (RCTs) of simmering pus and growing flesh method to promote postoperative wound healing in anorectology were collected by a computer search of China Knowledge Network (CNKI), Wanfang (WANGFANG DATA), Vipers (VIP), China Biomedical Literature Database (CBM) and other means to build the database to date. Additional literature on the same topic was manually searched to supplement relevant information. The search terms include simmering pus and growing flesh, simmering pus and raising flesh, snug pus and growing flesh, external Chinese medicine, debridement and growth, anorectal disease, postoperative trauma, trauma repair, randomized control, RCT, etc.

2.1 Inclusion and exclusion criteria

2.1.1 Inclusion criteria

Subjects: the study subjects were patients with postoperative anal diseases, meeting the diagnostic criteria of mixed hemorrhoids, anal fissures, perianal abscesses, and anal fistulas in the Diagnostic Efficacy Criteria for Chinese Medical Evidence [3]. Interventions: Treatment group: Simmering pus growing flesh theory guided by the external route of administration, including Chinese ointments, oils, and compresses. Interventions do not include other TCM treatments such as oral tonics, acupuncture, and red light therapy.Western drugs with the ability to promote postoperative wound repair cannot be combined. Control group: Use of petroleum jelly gauze or other conventional topical treatments not guided by the theory of simmering pus and growing flesh in Western or Chinese medicine.

2.1.2 Exclusion criteria

Exclude pregnant, postpartum and lactating patients.Exclude patients with other serious medical and surgical diseases in combination.Exclude patients with diseases that affect postoperative healing of the trauma.Exclusion of literature for which full text is not available or data is missing.

2.2 Filtering method

Literature screening and data selection were performed by 2 researchers independently for literature screening,and data extraction and then exchanged and checked. If after carefully reading the original article you decide that the data cannot be analyzed, try to contact the original author to obtain the missing information. Data extraction method: After excluding literature with apparently irrelevant titles and abstracts, the full text was read further to determine inclusion. If there is any dispute in the above process, both parties will discuss the differences and exchange arguments, and if there is still no consensus, a third party (the third author of this paper) will assist in the decision.

The quality assessment method "RCT risk of bias assessment" tool provided in the Cochrane 5.1.0 manual was selected for analysis. Including seven aspects of random assignment sequence generation, whether the random assignment sequence was hidden, implementation bias, measurement bias, follow-up bias, reporting bias, and other sources of bias.The evaluation process was conducted independently by two researchers, and any disagreement was decided through discussion.

Statistical methods software applied Stata14 for systematic analysis of each statistic. Weighted mean difference (WMD) or standardized mean difference (SMD) was selected for the measurement data, relative risk ratio (RR) was selected for the count data, and 95% confidence intervals were calculated. A heterogeneity test was subsequently performed and a fixed effects model was selected for analysis when heterogeneity test results: $p > 0.05$ and $I\ 2 < 50\%$.When the heterogeneity test results: $p \leq 0.05$ and $I\ 2 \geq 50\%$, a random effects model was selected for analysis ,and a sensitivity analysis was performed to find the causes of large heterogeneity.

ISSN 2618-1584 Vol. 5, Issue 3: 14-23, DOI: 10.25236/FMSR.2023.050303

3. Results

3.1 Literature search results

Through the inclusion and exclusion criteria, a total of 48 Chinese papers were initially retrieved from various databases across the web, 0 papers were obtained through other resources, and 18 duplicate papers were excluded.By browsing titles, and abstracts, excluding reviews, systematic reviews, and animal experiments 2. By reading the full text, 15 papers with inconsistent or inconsistent study contents were excluded, and one paper with a poor experimental design was excluded.Twelve papers [4-15], with a total of 931 subjects, were eventually included, and the specific literature search flow chart is shown in Figure 1.

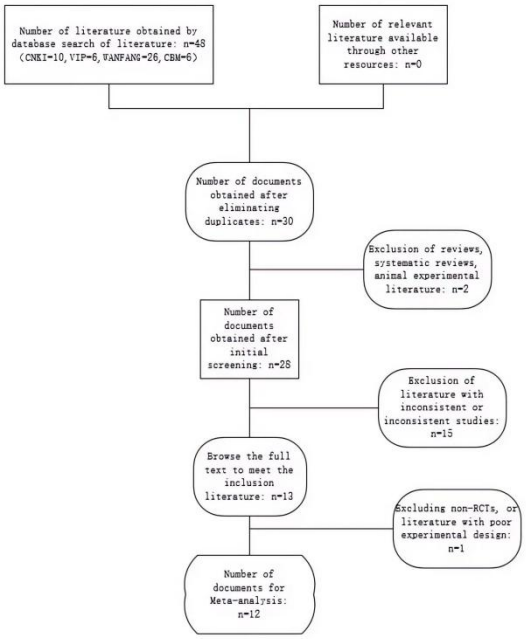

Figure 1: Flowchart of literature search

3.2 Basic characteristics and quality assessment of the literature

Since the simmering pus growing flesh method was not involved in foreign countries, the 12 included papers were all in Chinese, and the quality evaluation method "RCT risk of bias assessment" tool provided by the Cochrane Handbook was chosen for the analysis, and the results of the risk of bias assessment are shown in Figures 2 and 3. Twelve studies were generated by a "randomized allocation sequence", three of which were allocated according to the randomized number table method, while the remaining nine studies did not describe the randomized grouping method.And none of the 12 studies indicated that the investigators and subjects were blinded.Of the 12 included studies, 1 study involved missing data but did not analyze the reasons for missing data, the remaining 11 studies had complete data,the remaining risk of bias indicators was not reported, and the quality of the literature was average.

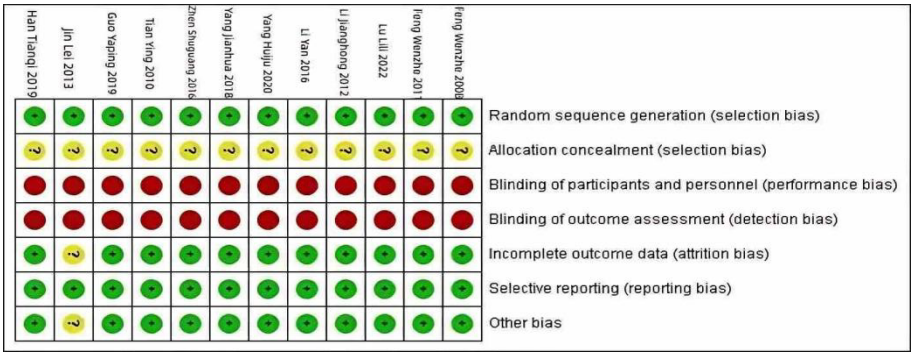

Figure 2: Risk of bias assessment

ISSN 2618-1584 Vol. 5, Issue 3: 14-23, DOI: 10.25236/FMSR.2023.050303

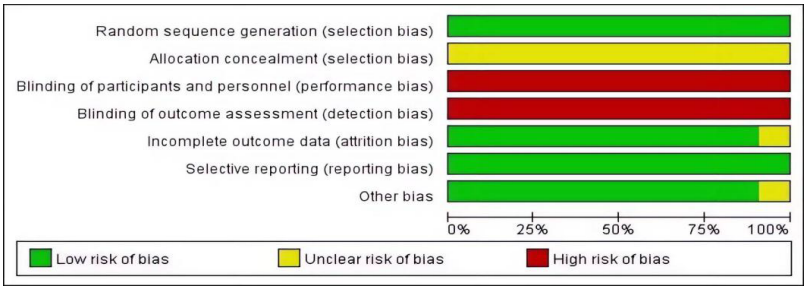

Figure 3: Risk of bias assessment

3.3 Meta-analysis results

3.3.1 The average healing time of postoperative wounds in anorectal diseases

Five original studies [7,8,10,12,14] reported the mean postoperative wound healing time. A total of 201 study subjects in the simmering pus growing flesh method group and 196 study subjects in the control group were included. After the heterogeneity test, I2=0.0%<50%, and P=0.925>0.1 for the Q test, suggesting that there is no heterogeneity between the literature selected for this study, and fixed effects can be selected for meta-analysis. As shown in Figure 4, the difference was statistically significant, [WMD=-3.791 , 95% CI (-4.629 , 2.952), p<0.05].Therefore, the use of the simmering pus and growing flesh method to guide postoperative wound repair in anorectal medicine can shorten the average healing time of postoperative wounds.The five included papers were also analyzed for bias, and it can be clearly seen from Figure 5 that the funnel plot of this study is basically symmetrical, while the Begg's bias test was conducted to conclude that: P= 0.806>0.05, so it can be judged that there is no publication bias in the literature of this study.

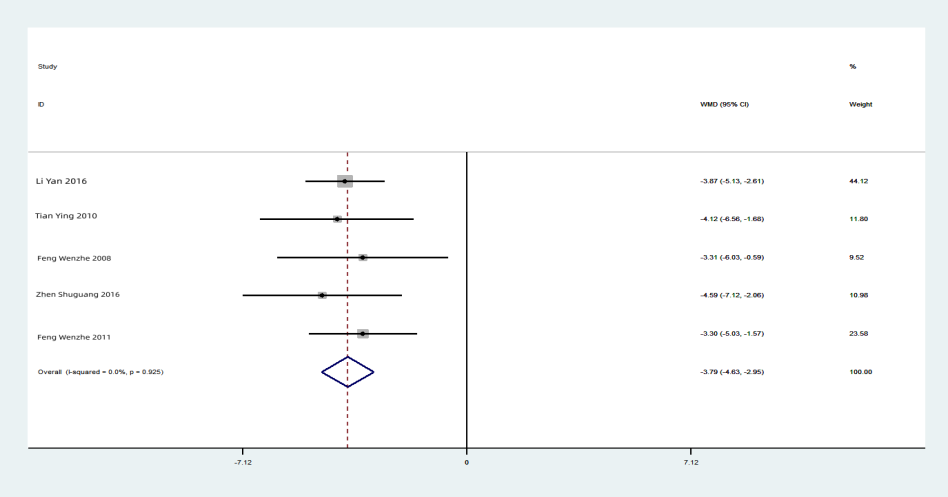

Figure 4: Forest plot of mean wound healing time

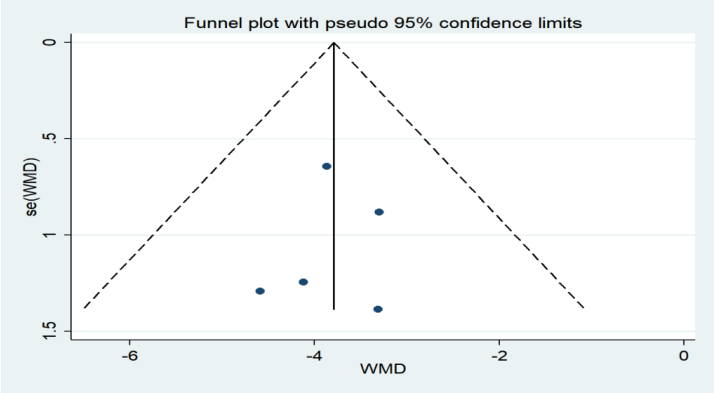

Figure 5: Funnel plot of mean wound healing time

ISSN 2618-1584 Vol. 5, Issue 3: 14-23, DOI: 10.25236/FMSR.2023.050303

3.3.2 Postoperative wound healing rate at day 14 for anorectal diseases

Five original studies [6,10,11,12,14] reported wound healing rates on day 14 after surgery for trauma in anorectal diseases. After testing for heterogeneity, I2=91.7%>50% and P=000<0.1 for Q-test, suggesting that the heterogeneity between the literature selected for this study is statistically significant. As in Figure 6, a heterogeneity lookup is required.To address the research heterogeneity in the literature and to ensure the accuracy and stability of the study, a sensitivity analysis of the current five papers is required. The sensitivity analysis is shown in Figure 9, and Yang 2018[11] was found to have a large effect on heterogeneity, and after removing that study, the meta-analysis combined a large effect variable, as shown in Figure 7. Therefore, the article was removed and the heterogeneity test was performed again after removing the study, and the results showed that there was no heterogeneity in the remaining four papers. (I2=2.6%<50%,p=0.379>0.1)

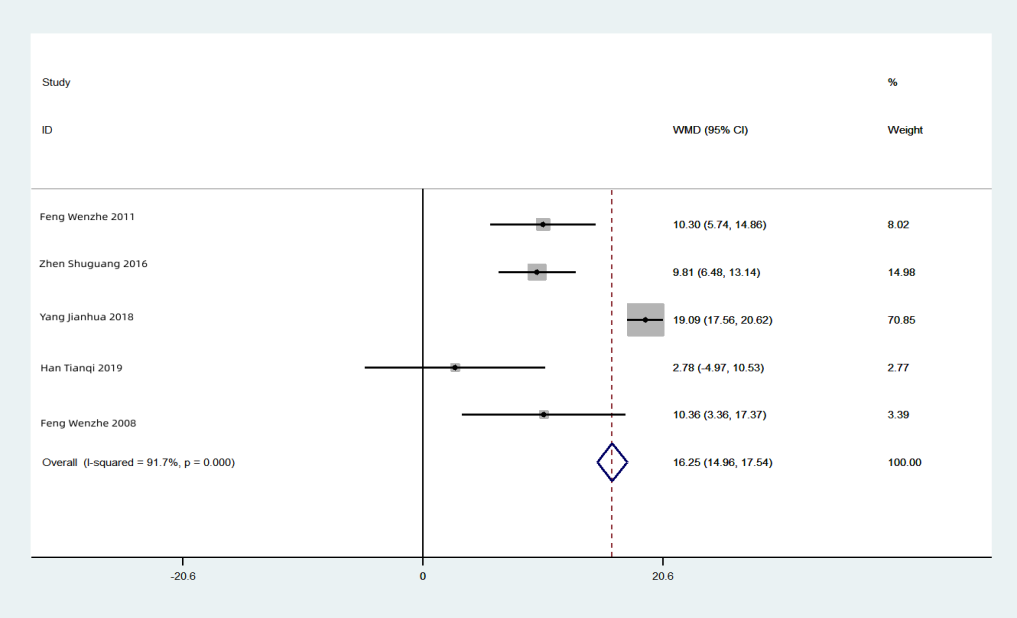

Figure 6: Forest plot of wound healing rate at day 14

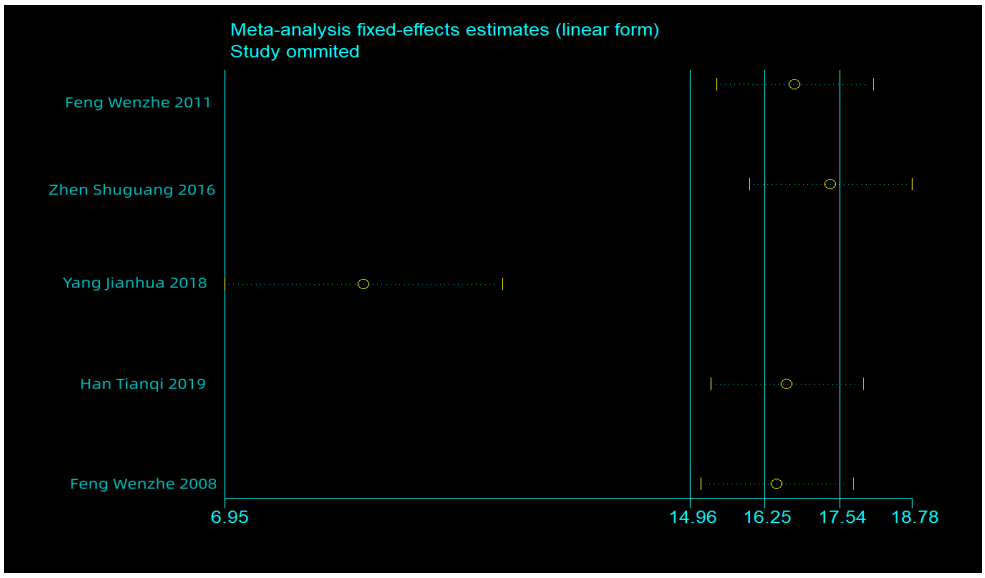

Figure 7: Sensitivity analysis of wound healing rate at day 14

ISSN 2618-1584 Vol. 5, Issue 3: 14-23, DOI: 10.25236/FMSR.2023.050303

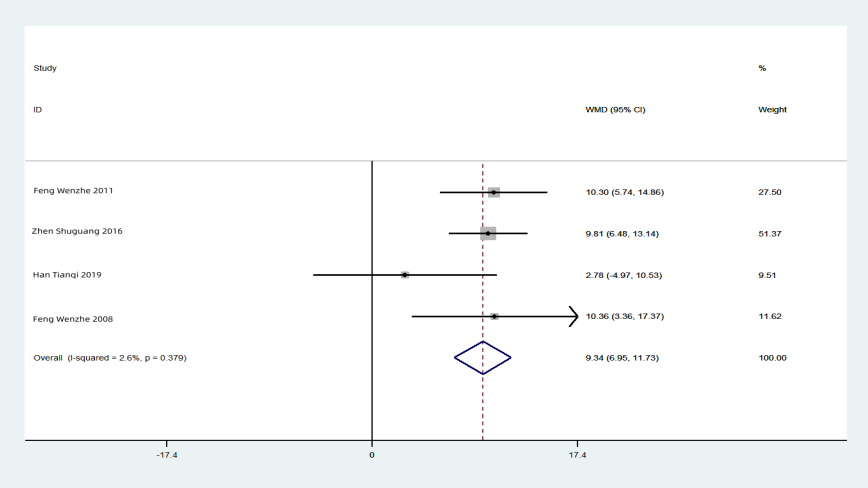

Figure 8: Forest plot of wound healing rate on day 14 after exclusion of Yang Jianhua 2018

Therefore a fixed effects model can be chosen for meta-analysis, as shown in Figure 8[WMD=9.341, 95% CI (6.951, 11.731), p<0.05]. Bias analysis was performed on the original literature included on postoperative day 14. As can be seen from Figure 9, the funnel plots for the original studies that included trauma healing rates at day 14 postoperatively were essentially symmetrical, while an Egger's bias test was performed to yield: P= 0.073>0.05. Therefore, it can be judged that there is no publication bias in the literature of this study. It can be concluded that the theory of simmering pus and growing flesh guiding wound repair in anorectal diseases can significantly increase the wound healing rate.

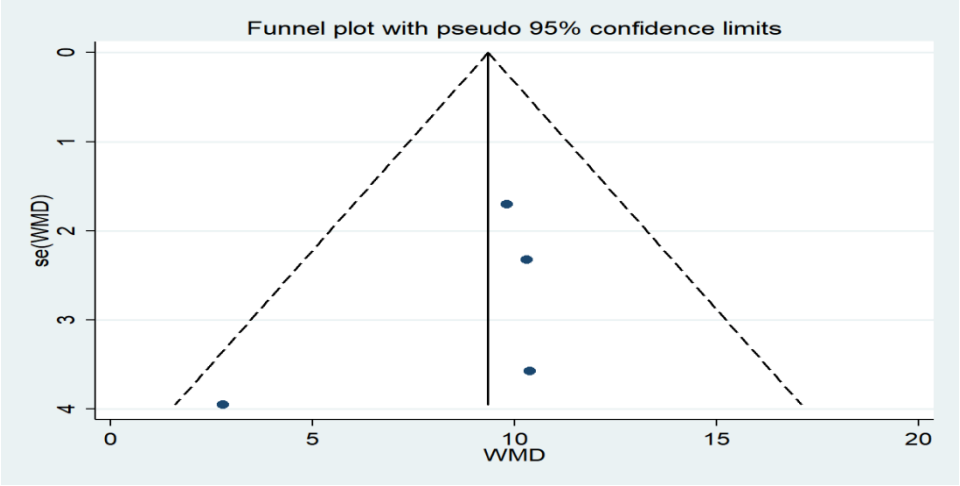

Figure 9: Funnel plot of day 14 wound healing rate

3.3.3 Postoperative wound healing efficiency in anal diseases

Five original studies [4,6,9,10,15] reported on wound healing efficiency and included a total of 233 study subjects in the simmering pus and growing flesh method group and 233 study subjects in the control group. After the test of heterogeneity, I^2=65.8%>50% and P=0.020<0.1 for the Q-test, as shown in Figure10, suggesting that the heterogeneity between the literature selected for this study is statistically significant and requires heterogeneity finding. To address the research heterogeneity in the literature and to ensure the accuracy and stability of the study, a sensitivity analysis was performed on five papers, as shown in Figure 11. It was found that Han Tianqi 2019 [6] had a large effect on heterogeneity, and after removing the study, the meta-analysis combined a large effect variable, as shown in Figure 12. Therefore, the article was removed and the heterogeneity test was performed again after removing the study, and the results showed that there was no heterogeneity in the remaining four papers (I2=0%<50%,p=0.894>0.1). Fixed effects could be selected for meta-analysis [RR=3.099, 95% CI (1.898, 5.060), P<0.05], suggesting that the efficacy of Chinese medicine external treatment of simmering pus and growing flesh to promote postoperative wounds in anorectal diseases is significantly better than that of non-simmering pus and growing flesh method.Bias analysis of the four

ISSN 2618-1584 Vol. 5, Issue 3: 14-23, DOI: 10.25236/FMSR.2023.050303

original papers, as shown in Figure 13, clearly shows that the funnel plots for the original studies incorporating trauma healing rates at day 14 postoperative are largely symmetrical, and a Begg's bias test yielded P=0.734>0.05, implying no publication bias in the four papers selected for this study.

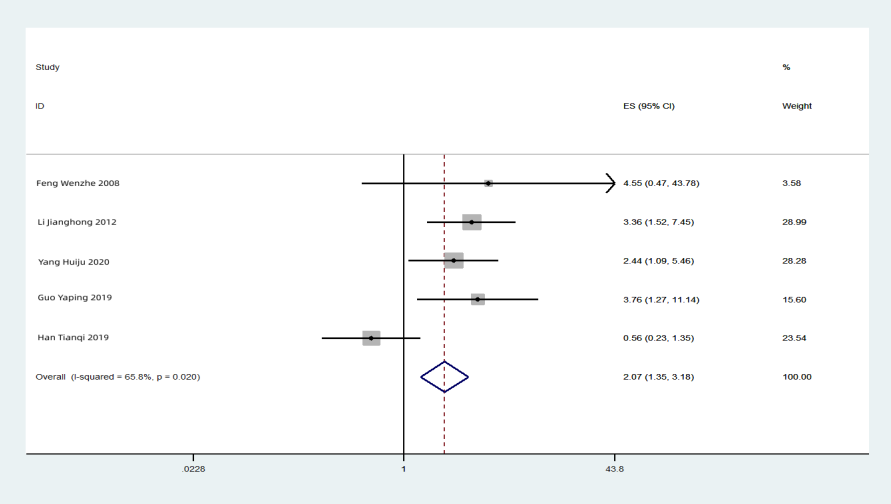

Figure 10: Wound healing efficiency forest plot

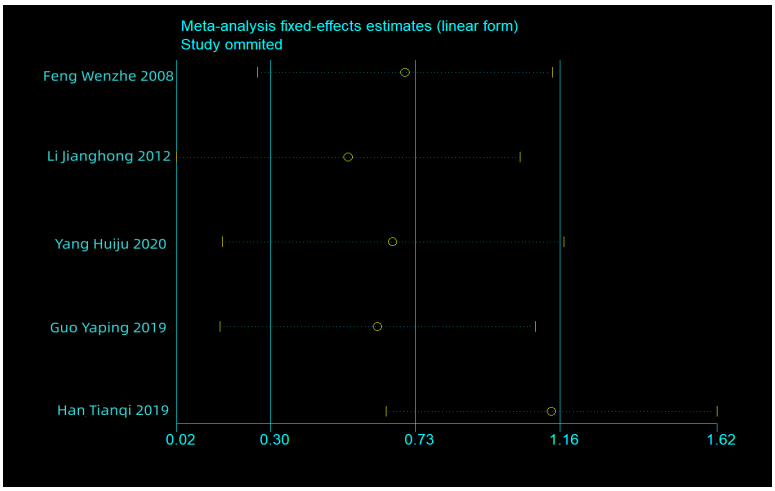

Figure 11: Sensitivity analysis of wound healing efficiency

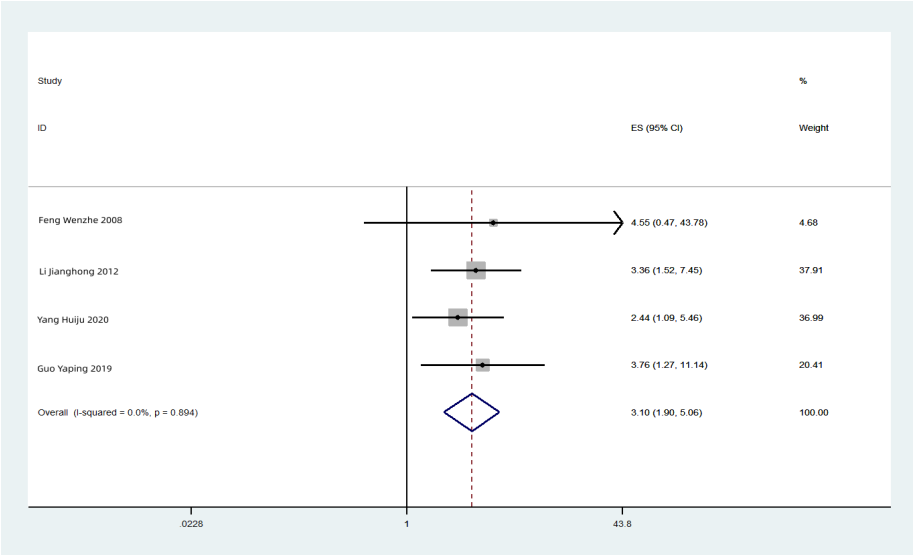

Figure 12: Forest plot of Wound healing efficiency after exclusion of Han Tianqi 2019

ISSN 2618-1584 Vol. 5, Issue 3: 14-23, DOI: 10.25236/FMSR.2023.050303

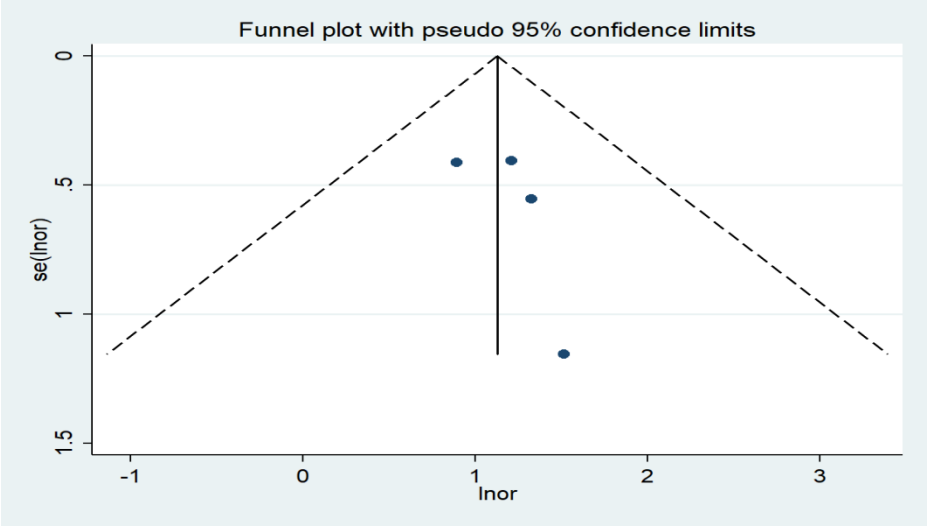

Figure 13: Funnel plot of wound healing efficiency

4. Discussion

With continuous in-depth research on anorectal diseases, surgery has become the main treatment for specialist anorectal diseases. Postoperative wound care and wound medication are also receiving more attention and can be considered as one of the key steps in postoperative wound recovery in anorectology. Shen Duoguan [16] in "Surgery Qixuan" said, "In where sores and toxins have been pacified ..... Can it not lead to defeat?". Here, for the first time, the method of simmering pus and growing flesh was proposed. The pus here is not the pathological product of the accumulation of necrotic cells and bacteria referred to in Western medicine, but the manifestation of the body's fullness of qi and blood, heat and flesh decay, and the fierce struggle between good and evil.The pus at this time is full of qi and blood, bright and moist in color, thick in quality, and slightly fishy in taste, which can protect the safety of the trauma and increase the opportunity for the growth of muscle and flesh. Therefore, Chinese medicine surgery believes that suitable pus covering the wound not only plays the role of protecting the wound but also promotes the growth of wounded flesh buds.

The method of simmering pus and growing flesh needs to be decaying and growing muscle. The anorectal specialist disease in abscesses, anal fistula after surgery, the rotten meat has gone, new meat has not been born, which is the key time to decay, and muscle, simmering pus and growing meat. Therefore, it is necessary to simmer pus and grow flesh on the theory of TCM, using TCM prescriptions, prescription creams or now using growth dressings to act on the postoperative anorectal wounds to achieve the purpose of simmering pus and growing flesh by the interaction of medicinal sores[17]. The pus acts as a medium in the drug sore interaction, and the "pus" promotes the growth of the wound or granulation, and the "pus" also promotes the release of the drug's active substances into the wound. The drug also undergoes biochemical changes in the pus, making it easier to release the drug's efficacy, and the wound undergoes a series of changes after absorbing the active substances in the pus, continuing to produce "pus. The changes in "pus" reflect the microenvironment and key substances for the repair of the sore surface. It can be said that the "good pus" produced here is also the "medicinal pus" of the medicinal sore interaction[18].

The "pus" on the surface of postoperative anorectal wounds is more accurately described as wound exudate. The exudate here includes not only the cellular debris metabolized from the trauma surface and the bacteria removed, but also the physiological exudate after the change of the vascular osmotic pressure of the trauma surface [19]. Trauma exudate also serves as a bridge between intercellular communication, trauma, and drug communication. Trauma dressing or Chinese ointment maintains proper moistening of the trauma surface, allowing endogenous enzymes to decompose apoptotic tissues, thus promoting autolysis of necrotic tissues, accelerating autolytic debridement of the trauma surface, and promoting collagenase synthesis of the trauma surface, accelerating the absorption of trauma nutrients such as growth factors and cytokines, and accelerating healing of the trauma surface. The simmering pus - that is, the wound exudate - is rich in phagocytic, anti-inflammatory factors, which happen to form a biological barrier that creates a closed, slightly acidic, low-oxygen environment on the wound surface. This not only isolates external bacteria and reduces the chance of infection, but also

ISSN 2618-1584 Vol. 5, Issue 3: 14-23, DOI: 10.25236/FMSR.2023.050303

promotes the differentiation and migration of fibroblasts in a relatively low-oxygen environment.

In this systematic evaluation, the mean trauma healing time and day 14 trauma healing rate, and trauma repair efficiency directly reflected that the postoperative trauma recovery of anal diseases was significantly better than other control groups under the guidance of simmering pus and growing flesh theory. However, the original literature included in this article is relatively small. And the quality of the original literature was average, and some experimental designs were deficient. The evaluation criteria of the outcome indicators in the original literature included in this article were inconsistent and the evaluation criteria were not standardized, such as exudate scores and pain scores, resulting in the inability to systematically evaluate these indicators and considerable heterogeneity. Therefore, this article also did not do a systematic evaluation of this indicator, and the need to standardize industry standards for the evaluation of outcome indicators is a long way off. And nowadays, most of the clinical studies on the simmering pus and growing flesh method to promote post-anorectal wound repair focus on basic indicators such as exudate, pain, wound healing rate and wound healing time, and very few clinical studies on molecular biological indicators such as traumatic inflammatory factors, growth factors, or macrophage and exosome catalysis. This is one of the main reasons why the original literature included in this systematic evaluation was of average quality and could not be evaluated in depth. Therefore, more and better quality primary studies need to be included in later studies to provide a better evidence-based basis for the study of simmering pus and growing flesh to promote postoperative trauma in anorectal diseases.

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