## <u>Original research</u>

# Clinical Study on the Treatment of Complex Anal Fistula by Phased Chinese Herbal Sitz Bath Based on "Fuzheng Quxie" Theory

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## **ABSTRACT**

**Objective** • To evaluate the clinical efficacy of a phased Chinese herbal sitz bath for the treatment of complex anal fistula based on the traditional Chinese medicine theory of "Fuzheng Quxie."

Methods • We enrolled 200 patients with complex anal fistula who were hospitalized and treated surgically in the Department of Anorectal Medicine of Suining Central Hospital from June 2021 to December 2022. The patients were randomly divided into 2 groups of 100 patients each: sitz bath group 1 (postoperation, the patients used a sitz bath with a self-formulated decoction of "Qingre Zaoshi Zhitong" formula, once in the morning and once in the evening) and sitz bath group 2 (postoperation, the patients used the same decoction as the sitz bath group 1, and when the incision began to heal, the patients then used a sitz bath with a self-formulated decoction of "Yiqi Fuzheng" formula, once in the morning and once in the evening). Both groups were treated for 6 weeks. The assessments included wound symptom score, incision healing time, clinical efficacy after treatment, and serumrelated growth factor concentrations and anorectal dynamics indicators before and after treatment.

**Results** • After treatment, sitz bath group 2 had less wound pain, edema, exudate, and granulation growth

scores than sitz bath group 1 (P<.05). Postoperative incision healing time was faster in sitz bath group 2 22.96 (1.96) d than in sitz bath group 1 26.19 (2.62) d (t = 9.872,P < .001). The total effective rate after treatment was higher in sitz bath group 2 96% (96/100) than in sitz bath group 1 88% (88/100) ( $\chi^2 = 4.4$ , P = .04). Serum transforming growth factor  $\beta$ , epidermal growth factor, and basic fibroblast growth factor concentrations were higher in both groups after treatment than before treatment, and the concentrations of the growth factors after treatment were higher for sitz bath group 2 than for sitz bath group 1 (P<.001). Anal rest pressure and anal maximum contraction pressure were higher in both groups after treatment than before treatment, and the pressures after treatment were higher for sitz bath group 2 than for sitz bath group 1 (P < .05).

**Conclusion** • Based on the theory of Fuzheng Quxie, the effectiveness and superiority of a phased Chinese herbal sitz bath for the treatment of complex anal fistula were remarkable, which could promote the improvement of wound symptoms and anal function. This may be related to increases in growth factor concentrations and anorectal dynamics indicators. (*Altern Ther Health Med.* [E-pub ahead of print.])

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## INTRODUCTION

Anal fistula is a difficult anorectal disease, characterized by recurrent swelling, pain, and pus. It can occur after spontaneous rupture or incision and drainage of a perianal abscess followed by incomplete wound healing.<sup>1</sup> Complex anal fistula is a rare subtype of anal fistula that is also known as refractory anal fistula because of the large number of internal and external openings and ease of recurrence. Surgery is the main treatment for complex anal fistula, but complications can occur, such as severe pain, slow wound healing, or postoperative dysuria.<sup>2</sup> One unique, advantageous way to promote wound healing and reduce complications after anorectal surgery is to combine surgery with a traditional Chinese medicine herbal sitz bath.

In traditional Chinese medicine, all factors that can cause disease are collectively called "Zhengqi," and the disease resistance of the human body is called "Xieqi." The disease process corresponds to the struggle between Zheng and Xie. The rise and fall of Zheng and Xie determine the occurrence,

development, and outcome of the disease. Therefore, one of the basic principles for treating diseases is "Fuzheng Quxie," which can promote disease resolution and rapid bodily recovery. Complex anal fistula belongs to the category of "anal fistula" in traditional Chinese medicine. According to traditional Chinese medicine theory, anal fistula is mainly caused by damp heat gathering in the lower jiao (refers to the lower abdomen from the lower mouth of the stomach to the external genitalia and the perianal area) and tormenting the blood and flesh of the rectum and anus. Moreover, after anal fistula surgery, the damp heat's toxicity remains; coupled with knife blade trauma, this results in qi stagnation and blood stasis, which leads to damaged veins and reduced blood flow. The damp heat's toxicity stagnates outside the veins and accumulates in the skin, delaying postoperative wound repair. Treatments based on traditional Chinese medicine focus on clearing heat and dampness, using common formulas such as nitrate alum lotion, Sophora flavescens Ait decoction, and Chinese gall decoction. However, in long-term clinical practice, we have observed that, in the late stage of the disease (ie, when the postoperative incision secretion is reduced, the rotten flesh is falling off, and the granulation tissue is fresh and red), patients can gradually show signs of Zheng deficiency and Xie stagnation due to the depletion of qi and blood. At this time, excessive use of the previously mentioned cold herbal formulas can damage the patient's vital energy, prolonging recovery time after surgery. Therefore, to improve the clinical efficacy of surgical treatment of complex anal fistula and accelerate the postoperative recovery of patients, we aimed to use Fuzheng Quxie combined with a Chinese herbal sitz bath to treat complex anal fistula. We divided the Chinese herbal sitz bath treatment into 2 phases: Fuzheng and Quxie, to avoid damaging the Zhengqi by excessive coldness and to avoid stagnation of Xieqi caused by the premature use of some herbal formulas.

## **MATERIALS AND METHODS**

## Research participants

We enrolled 200 patients with complex anal fistula who were hospitalized and treated surgically in the Department of Anorectal Medicine of Suining Central Hospital from June 2021 to December 2022. The patients were divided using the random number table method into 2 groups of 100 patients each: sitz bath group 1 and sitz bath group 2.

Western medicine diagnostic criteria. We enrolled patients who met the diagnostic criteria for complex anal fistula in the Consensus of Chinese experts on the diagnosis and treatment of anal fistula (2020)<sup>4</sup>: this includes extra-sphincteric fistula, supra-sphincteric fistula, trans-sphincteric fistula involving >30% of the external anal sphincter range, horseshoe fistula, anterolateral transperineal complex in female patients, and anus fistula in combination with inflammatory bowel disease, radiation enteritis, malignant tumors, anorectal insufficiency of modulation, and chronic diarrhea.

Chinese medicine identification criteria. We enrolled patients who met the diagnostic criteria for complex anal fistula in the Guidelines for Diagnosis and Treatment of

**Table 1.** Patient Characteristics

Characteristics	Sitz bath group 1	Sitz bath group 2	Statistics	
	(n=100)	(n=100)		
Continuous data	Mean (SD)	Mean (SD)	t	P value
Age, y	42.3 (12.35)	44.3 (9.20)	1.273	.20
Weight, kg	64.99 (8.23)	65.14 (9.12)	0.122	.90
Disease duration, mo	11.50 (3.44)	12.08 (4.38)	1.041	.30
Distance of external opening from anus, cm	6.44 (0.31)	6.50 (0.33)	1.325	.19
Wound area, cm <sup>2</sup>	5.65 (1.02)	5.50 (1.06)	1.020	.31
Categorical data	No.	No.	$\chi^2$	P value
Sex			0.5	.48
Male	82	78		
Female	18	22		
Anal fistula site			1.1	.29
High	72	65		
Low	28	35		
Park classification of anal fistula			1.6	.67
Inter-sphincter fistula	46	40		
Trans-sphincter fistula	37	42		
Supra-sphincter fistula	12	15		
Extra-sphincteric fistula	5	3		
History of perianal abscess			0.8	.68
Yes	24	32		
No	76	68		

Common Diseases of Coloproctology in Traditional Chinese Medicine<sup>5</sup>: symptoms of damp heat diffused downward (perianal ulceration, flowing pus, thick pus, localized redness, swelling, heat and pain, unpleasant stool, low volume of urine in a single pass, reddish in color, red tongue body with yellow and greasy tongue coating, and smooth pulse) and symptoms of Zheng deficiency and Xie stagnation (thin pus around the anus, vague anal pain, perianal ulcers that heal from time to time, dull surrounding skin, fatigue, pale tongue body with thin and yellow tongue coating, and moist pulse).

Inclusion criteria. (1) Met the above Western medicine diagnostic and Chinese medicine identification criteria; (2) had anal fistula treated by a cutting, drainage, and suturing operation and had 2 or more postoperative traumatic incisions; (3) had normal previous anal morphology and function; (4) were 18 to 87 years old; (5) signed consent forms after being informed of the study; and (6) had good compliance and could effectively cooperate with the study.

Exclusion criteria. (1) Allergy-prone body, scarring-prone body; (2) had an infectious disease, such as tuberculosis, a venereal disease, or an inflammatory bowel disease, such as Crohn disease; (3) had a serious underlying disease (eg, diabetes, renal disease, hematologic disorders, or other immune system disorders that seriously affect incision healing) or psychiatric or cognitive or communication disorders; (4) were pregnant, lactating, or menstruating women; (5) had incomplete clinical data; or (6) withdrew from treatment in the middle of the study for any reason.

## Sitz bath treatments

The patients in both groups were closely observed for postoperative wound bleeding and were treated with the appropriate antibiotics according to bacterial culture results. A postoperative semiliquid diet was maintained for 24 hours, and soft stools were maintained. The Chinese herbs were obtained from the herbal pharmacy of Suining Central Hospital and were distributed after decoction by the hospital's Decoction Room. Both groups were evaluated for efficacy after 6 weeks of sitz bath treatment.

**Sitz bath group 1.** Starting on the first postoperative day, the patients used a self-formulated decoction of "Qingre Zaoshi Zhitong" in a 38 to 42°C sitz bath, once in the morning and once in the evening for 15 minutes each time, with routine cleaning and dressing changes. The Qingre Zaoshi Zhitong formula consisted of 20 g *Coptis chinensis* Franch, 20 g *Phellodendron chinense* Schneid, 12 g *Gentiana macrophylla* Pall, 12 g *Atractylodes chinensis* (DC) Koidz, 20 g talc, 30 g *Sophora flavescens* Ait, 15 g *Paeonia lactiflora* Pall, and 6 g *Glycyrrhiza uralensis* Fisch.

**Sitz bath group 2.** Starting on the first postoperative day, the patients used a self-formulated decoction of Qingre Zaoshi Zhitong in a 38 to 42°C sitz bath, once in the morning and once in the evening for 15 minutes each time, with routine cleaning and dressing changes. When the supervising physician observed that the postoperative incision secretion was significantly reduced, the rotten flesh was falling off, and the granulation tissue was fresh and red, the patients used a self-formulated decoction of "Yiqi Fuzheng" in a 38 to 42°C sitz bath, once in the morning and once in the evening for 15 minutes each time, with routine cleaning and dressing changes. The Yiqi Fuzheng formula consisted of 30 g Astragalus membranaceus, 20 g Angelica sinensis (Oliv) Diels, 20 g Codonopsis pilosula (Franch) Nannf, 15 g Atractylodes macrocephala Koidz, 20 g talc, 30 g Sophora flavescens Ait, 15 g Paeonia lactiflora Pall, 6 g Glycyrrhiza uralensis Fisch, and 15 g Sepiella maindroni Rochebrune.

## **Evaluation metrics**

Patients were evaluated by the following 5 metrics.

Wound symptom score. The patients' trauma recovery was assessed after 6 weeks of treatment, in which trauma pain was assessed using the numerical rating scale NRS (0-10 points)<sup>6</sup>, and the lower the score, the better the recovery, and the details of the scores for trauma edema (0-3 points), trauma exudate (0-3 points) and granulation growth (0-3 points) are shown in Table 2.

**Incision healing time.** Time to complete healing of the incision after the operation was recorded. The healing criteria were complete epithelial coverage of the wound, a firm scar, and continued observation of the wound for 1 week without recurrence of ulceration.

Clinical efficacy after treatment. Treatment efficacy was evaluated after 6 weeks, the efficacy criteria i.e.: *Healing*, the wound epithelium was completely covered, the scar was solid, and there was no recurrence of ulceration after observation for 1 week; *Apparently effective*, the wound area was reduced by 75%, the granulation tissue was fresh, and the patient's symptoms were obviously relieved; *Improved*, the wound area was reduced by 25%, the granulation tissue was relatively fresh, and the symptoms were improved; and *Ineffective*, not up to the standard of improvement. Total effective rate = (healing + apparently effective + improved) persons / total persons × 100%.

**Serum-related growth factor concentrations.** We collected 4 mL fasting peripheral blood from patients before

**Table 2.** Rules for scoring wound edema, wound exudate and granulation growth

Scores	Wound edema	Wound exudate	Granulation growth
0	Edema-free	Exudation-free	The wound has been completely covered by
			neoplastic epithelial tissue
1	Edema width	A small amount of	The granulation tissue on the wound is bright
	<l cm<="" td=""><td>exudate, pale</td><td>red in color and bleeds easily when touched</td></l>	exudate, pale	red in color and bleeds easily when touched
2	1cm <edema< td=""><td>The wound has obvious</td><td>The granulation tissue of the wound is dark</td></edema<>	The wound has obvious	The granulation tissue of the wound is dark
	width<3 cm	exudate, pale and slightly	red in color and does not bleed easily when
		yellow in color	touched
3	Edema width	Exudate on the wound is	The granulation tissue of the wound is dull in
	>3 cm	heavy, thick and yellowish	color and does not bleed on palpation

Table 3. Wound Symptom Scores, scores

Characteristics	Sitz bath group 1 (n=100)	Sitz bath group 2 (n=100)	Statistics	
Continuous data	Median (P25, P75)	Median (P25, P75)	Z	P value
Pain	2 (1, 2)	1 (1, 2)	-6.000	<.001
Edema	0 (0, 1)	0 (0, 0)	-2.828	.01
Exudate	1 (0, 1)	0 (0, 1)	-3.979	<.001
Granulation growth	0 (0, 1)	0 (0, 0)	-2.369	.02

and 6 weeks after treatment in the early morning, and the serum was extracted by centrifugation. The concentrations of the serum-related growth factors transforming growth factor  $\beta$  (TGF- $\beta$ ), epidermal growth factor (EGF), and basic fibroblast growth factor (bFGF) were measured by enzymelinked immunosorbent assay kits (Shanghai Xinyu Biotechnology Co, Ltd).

Anorectal dynamic indicators. Anorectal pressure was measured before and 6 weeks after treatment using a digestive tract dynamic detector (XDJ-S8, Hefei Kelly Optoelectronic Technology Co, Ltd), including rectal rest pressure (RRP), anal rest pressure (ARP), anal maximum contraction pressure (AMCP), and anal longest contraction time (ALCT).

#### Statistical analysis

Data analysis was performed with SPSS version 22.0 (IBM Corp). All continuous data passed the 1-sample Kolmogorov-Smirnov test. For normal distribution, paired or grouped t tests were used for inter group comparisons, while for skewed distribution, non-parametric tests were used for inter group comparisons. All categorical data were analyzed by  $\chi^2$  test. P < .05 indicates a statistically significant difference.

### **RESULTS**

#### **Patient characteristics**

General patient characteristics for sitz bath group 1 and sitz bath group 2 were statistically analyzed and were comparable ( $P_{\rm all}$  > .05) (Table 1).

## Wound symptom score

After treatment, sitz bath group 2 had less wound pain, edema, exudate, and granulation growth scores than sitz bath group 1 (P<.05) (Figure 1).

## **Incision healing time**

Postoperative incision healing time was faster in sitz bath group 2 22.96 (1.96) d than in sitz bath group 1 26.19 (2.62) d (t = 9.872, P < .001) (Figure 1).

Figure 1. Incision Healing Time, d

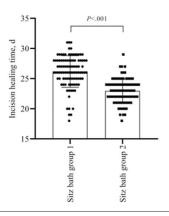
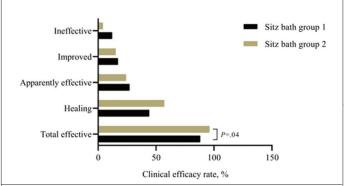
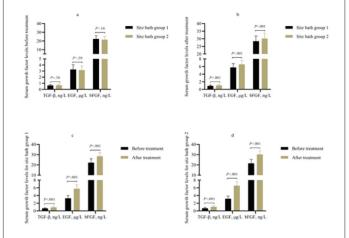


Figure 2. Clinical Efficacy Rate, %



**Figure 3.** Serum-Related Growth Factor Concentrations. A, Serum growth factor levels before treatment. B, Serum growth factor levels after treatment. C, Serum growth factor levels for sitz bath group 1. D, Serum growth factor levels for sitz bath group 2.

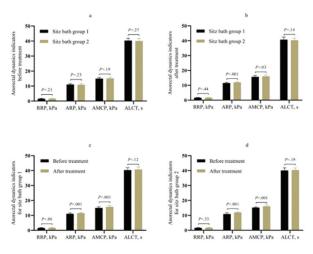


**Abbreviations**: bFGF, basic fibroblast growth factor; EGF, epidermal growth factor; TGF, transforming growth factor.

## Clinical efficacy rate

The total effective rate after treatment was higher in sitz bath group 2 96% (96/100) than in sitz bath group 1 88% (88/100) ( $\chi^2$  = 4.4, P = .04) (Figure 2).

**Figure 4.** Anorectal Dynamics Indicators. A, Anorectal dynamics indicators before treatment. B, Anorectal dynamics indicators after treatment. C, Anorectal dynamics indicators for sitz bath group 1. D, Anorectal dynamics indicators for sitz bath group 2.



**Abbreviations**: ALCT, anal longest contraction time; AMCP, anal maximum contraction pressure; ARP, anal rest pressure; RRP, rectal rest pressure.

## Serum-related growth factor concentrations

Serum TGF- $\beta$ , EGF, and bFGF concentrations after treatment were higher in both groups than before treatment, and the concentrations after treatment were higher in sitz bath group 2 than in sitz bath group 1 (P<.001) (Figure 3).

## Anorectal dynamics indicators

ARP and AMCP after treatment were higher in both groups than before treatment, and ARP and AMCP after treatment were higher in sitz bath group 2 than in sitz bath group 1 (P<.05) (Figure 4).

## **DISCUSSION**

Complex anal fistulas are mostly associated with deep dead space, complex distribution of hemorrhoidal ducts, and large numbers of fistulas, which increases the difficulty of treatment, prolongs the treatment period, and leads to a high recurrence rate, so it is important to effectively improve the cure rate of complex anal fistulas. Anal fistulas cannot be eradicated without surgery, but the wound after surgery remains open, and the anal position is particularly difficult to treat, it is difficult to keep the wound dry and clean after surgery. Improper treatment is likely to cause slow healing or even nonunion, inconvenience to the patient's life, and even cause sequelae. The re-epithelization of the wound after surgery has become an important factor in the successful wound repair of patients with complex anal fistula.

Chinese herbal sitz baths are a part of the characteristic methods of traditional Chinese medicine for the treatment of anorectal diseases; they have advantages compared with other drug-delivery methods.<sup>7</sup> Sitz baths can directly apply medicines to the anal lesion to improve medicine delivery; with their dual effects of medicine delivery and heat, sitz

baths can unclog meridians and relieve pain, move qi and dispel knots, coordinate the perianal muscles, improve local blood circulation, promote wound healing, and shorten the treatment course.8 Moreover, the localized effect can avoid the stimulation of medicines on the stomach and intestines and is mild and long-lasting. Shen et al<sup>9</sup> treated postoperative hemorrhoidectomy patients with a traditional Chinese medicine sitz bath, which significantly reduced the pain levels and saved the amount of pain medication. In our study, we compared a traditional Chinese medicine herbal sitz bath with a phased sitz bath approach for postoperative treatment of patients with complex anal fistula. Postoperative wound pain, edema, exudate, and granulation growth scores were lower for the phased approach in sitz bath group 2 than in sitz bath group 1, postoperative incision healing time was faster in sitz bath group 2 than in sitz bath group 1, and the clinical efficacy was better in sitz bath group 2 than in sitz bath group 1. This indicates that the treatment of complex anal fistula with a phased traditional Chinese medicine herbal sitz bath based on the theory of Fuzheng Quxie is more helpful than using a sitz bath with a single formula to relieve postoperative trauma symptoms and promote postoperative trauma repair.

We believe that, in the early stage of pathogenesis, patients with complex anal fistula mainly gather damp-heat toxin in the anus, and the treatment approach should focus on eliminating the damp-heat toxin; therefore, we formulated our own Qingre Zaoshi Zhitong formula, in which Coptis chinensis Franch and Phellodendron chinense Schneid are used to clear heat and dry dampness and to remove fire and detoxify toxins10; Gentiana macrophylla Pall dispels wind dampness, clears dampness and heat, soothes tendons and collaterals, and relieves paralysis and pain11; Atractylodes chinensis (DC) Koidz dries dampness and strengthens the spleen, dispels wind, and disperses cold12; talc dispels dampness and astringent sores; Sophora flavescens Ait clears heat and dampness, kills worms, and suppresses diuresis<sup>13</sup>; Paeonia lactiflora Pall nourishes blood and regulates menstruation, nourishes the liver, and relieves pain<sup>14</sup>; and Glycyrrhiza uralensis Fisch harmonizes all the herbs to clear heat and dry dampness, relieves fire and detoxifies, reduces swelling and pain, and has an astringent effect.

In the late postoperative period, most of the damp-heat internal toxins of the patient are resolved and the disease declines, so it is advisable to change to a method of herbal formula support that sustains righteousness and eliminates evil and that promotes wound healing. So, we chose to use a self-formulated Yiqi Fuzheng decoction, based on the self-formulated Qingre Zaoshi Zhitong decoction, that removed the heat-clearing and damp-drying herbs *Coptis chinensis* Franch, *Phellodendron chinense* Schneid, *Gentiana macrophylla* Pall, and *Atractylodes chinensis* (DC) Koidz and added the qi-enhancing herbs *Astragalus membranaceus*, *Codonopsis pilosula* (Franch) Nannf, and *Atractylodes macrocephala* Koidz.

Among them, Astragalus membranaceus and Codonopsis pilosula (Franch) Nannf can nourish the qi of the lung and

spleen to promote the biochemical source of gi and blood, and Astragalus membranaceus can promote the elimination of pus and toxins, the healing of the sore surface, and the movement of granulation growth toward the surface.15 Atractylodes macrocephala Koidz benefits the qi and strengthens the spleen, improves free-radical scavenging, protects cell structure and function, and promotes hematopoiesis.<sup>16</sup> Modern pharmacological studies have shown that Yiqi medicine can accelerate microvascular circulation near trauma and increase the growth rate of granulation tissue, so it is suitable for wound healing after anal fistula surgery. 17,18 In the Yiqi Fuzheng formula, Angelica sinensis (Oliv) Diels can tonify and invigorate the blood, dispel stasis, and generate new blood, so that the herbal formula is not stagnant<sup>19</sup>; Sepiella maindroni Rochebrune collects dampness and treats astringent sores, treats pus without drying, and further accelerates wound healing.<sup>20</sup>

Postoperative wound repair after anal fistula is both a continuous and complex process and is the result of the combined regulation of multiple cytokines and growth factors. In this context, TGF-β is able to promote fibroblast proliferation and differentiation and extracellular matrix synthesis, which in turn promotes granulation tissue proliferation at the wound surface.21 EGF is the most abundant mitogen in epithelial cells, and it has a significant role in promoting epidermal cell division, accelerating epithelialization of wounds, and stimulating matrix formation and connective tissue contraction.<sup>22</sup> bFGF can promote vascular and granulation tissue development by stimulating cell proliferation and collagen synthesis, among other pathways.23 In this study, based on the theory of Fuzheng Quxie, we used the self-formulated Yiqi Fuzheng decoction in the late stage of treatment to clear heat and dampness and, more importantly, to benefit qi and nourish blood, remove necrosis, and promote granulation, which promotes healing of postoperative wounds. Astragalus membranaceus, Phellodendron chinense Schneid, Angelica sinensis (Oliv) Diels, Sepiella maindroni Rochebrune, and other medicines used in the Yiqi Fuzheng formula all regulate the secretion of TGF-β, EGF, and bFGF, and the bioavailability of the formula was significantly increased using the sitz bath route of administration.<sup>24-27</sup> In this study, serum TGF-β, EGF, and bFGF concentrations were higher in sitz bath group 2 than in sitz bath group 1 after treatment, so the Yiqi Fuzheng formula may accelerate postoperative wound tissue repair in patients at the later stage of treatment.

Anorectal dynamics indicators are important parameters for the objective evaluation of conscious and unconscious anal function.<sup>28</sup> ARP is a passive barrier that blocks the overflow of feces and gas from the rectum and mainly represents the function of the internal sphincter in the resting state.<sup>29</sup> Both AMCP and ALCT reflect anal self-control during stress and mainly represent external sphincter function.<sup>30</sup> Previous studies have found that, after anal fistula surgery, the anatomical continuity of the patient's sphincter is interrupted, which consequently affects the closing function

of the anal canal and leads to anal incontinence; the results of rectal manometry in patients mainly show a decrease in ARP and AMCP after anal fistula surgery.<sup>31</sup> In our study, ARP and AMCP were higher in both groups after treatment than before treatment, and ARP and AMCP were higher in sitz bath group 2 than in sitz bath group 1 after treatment, which indicates that the treatment of complex anal fistula with a phased Chinese herbal sitz bath approach based on the theory of Fuzheng Quxie can help improve postoperative anal function and prevent the occurrence of postoperative fecal incontinence.

To recap, based on the theory of Fuzheng Quxie, the effectiveness and superiority of a phased Chinese herbal sitz bath for the treatment of complex anal fistula were remarkable, and this approach improved wound healing and anal function, which may be related to the regulation of relevant growth factor concentrations and anorectal dynamics indicators.

#### **DATA AVAILABILITY STATEMENT**

The data used and/or analyzed during the current study are available from the corresponding author.

#### CONFLICT OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

#### **AUTHOR CONTRIBUTIONS**

WD, WC, and WY designed the study and performed the experiments; WD and WC collected the data; WY analyzed the data; and WD, WC, and WY prepared the manuscript. All authors read and approved the final manuscript. WD and WC contributed equally to this work.

#### SCIENTIFIC RESEARCH PROJECT

Project Name: Clinical study on the treatment of complex anal fistula based on the phased Chinese herbal sitz bath based on "Fuzheng Quxie" theory (project number 2021MS258).

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