

Effect of *Longgu* on prognostic survival and nutritional status of critically ill patients with incontinence-associated dermatitis

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Abstract: Incontinence-associated dermatitis (IAD) is a progressive disease based on the occurrence of incontinence. *Longgu* is a very classic Chinese medicine, which can promote blood coagulation and reduce vascular permeability. In this study, we analyzed the therapeutic effect of *Longgu* on IAD. We divided 102 patients with IAD into a control group using routine treatment and an experimental group using *Longgu* treatment to compare their wound healing time and clinical outcomes. In addition, the levels of inflammatory response and nutrient proteins were examined before and after treatment in both groups. Finally, a 6-month follow-up investigation was conducted to record the mortality rate and IAD recurrence rate of the patients. The results showed that the experimental group had a shorter wound healing time and better efficacy ($P < 0.05$). Inflammatory factors were lower and nutritional proteins were higher in the experimental group than in the control group after treatment ($P < 0.05$). In addition, the prognostic overall survival rate of the experimental group was higher than that of the control group ($P < 0.05$). This shows that *Longgu* is an excellent IAD treatment program.

Keywords: Incontinence-associated dermatitis; Inflammatory responses; *Longgu*; Nutritional status; Safety

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INTRODUCTION

Incontinence is a very common complication in neurological or metabolic system diseases and it is believed in the clinic that the occurrence of incontinence mainly depends on the patient's overall health and nutritional status (Gacci *et al.*, 2022). Incontinence-associated dermatitis (IAD) mainly refers to skin inflammatory diseases caused by long-term exposure of the skin to urine and feces, often occurring in areas such as the perineum and sacrococcygeal region and is clinically manifested as erythema, rash, maceration, erosion and other types of skin damage (Banharak *et al.*, 2021). Clinical statistics suggest that the incidence of IAD is approximately 5.6 percent and can reach more than 55 percent in critically ill patients (Beele *et al.*, 2018). This is because critically ill patients usually do not have normal digestive and metabolic functions, the nutritional status of the body is extremely poor and they generally lose the ability to move independently (Jiang *et al.*, 2023). IAD is an insidious and underestimated hospital-acquired complication, which not only increases the risk of complications such as infection and pressure ulcers, but also prolongs the length of hospital stay, increasing distress and economic burden (Pather *et al.*, 2021). Antimicrobial dressings are a common treatment for IAD, which can absorb exudate and sweat to form a gel, maintain skin dryness, reduce local friction of the affected skin and isolate bacteria, with a certain effect on the treatment of IAD. However, the efficacy still needs to be further improved (Qiao & Banharak, 2023).

Longgu, a very classic and valuable traditional Chinese medicine (TCM), is a fossil of large mammals (Wang *et al.*, 2020). For the central nervous system, *Longgu* has sedative, hypnotic and anticonvulsant effects and can inhibit the excitability of skeletal muscles. For the blood system, *Longgu* contains a lot of calcium ions, which can promote blood coagulation and reduce vascular permeability (Cao *et al.*, 2023). At present, the use of *Longgu* has been proven to greatly promote the healing process for wound repair (Jia *et al.*, 2023), but its influence on IAD is still rarely reported. Meanwhile, as *Longgu* is rich in various minerals and trace elements, it can effectively promote the metabolic circulation of nutrients in the human body and improve physical health to a certain extent (Chen *et al.*, 2022). In other words, the potential pharmacological effects of *Longgu* may not only have a therapeutic effect on IAD, but may also improve the nutritional status of patients. However, there are no studies available to confirm this idea.

Therefore, this study will provide new references and guidance for future treatment of IAD by observing the therapeutic effect of *Longgu* on IAD and its influence on patients' nutritional status.

MATERIALS AND METHODS

Study design and setting

The subjects were 102 IAD patients admitted to The Ninth

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#Both authors have the same contribution, and therefore they are co-first authors.

Hospital of Xi'an from October 2022 to October 2023. Using a table of random numbers, they were assigned to a control group and an experimental group, with 51 cases each, for routine treatment and *Longgu* based on routine treatment, respectively.

Inclusion and exclusion criteria

Inclusion criteria: patients (45-90 years old) hospitalized in the intensive care unit, who accorded with the diagnostic criteria for IAD (Coyer & Campbell, 2018) and gave informed consent, nutrition risk screening (NRS2002) (Cortes-Aguilar *et al.*, 2024) survey results showed a moderate or severe malnutrition risk rating, were included. Exclusion criteria: The presence of pressure sores in the sacrococcygeal region before treatment; pouch-like prolapse of the anus or perianal abscess; systemic diseases; history of drug allergies; doctor-patient communication obstacles; history of skin grafting and photosensitivity; treatment time < 7 days, death, or discharge; treatment discontinuation upon the request of patients or their families; stage III and above pressure ulcers; diabetic patients with poor glycemic control, ineffective diarrhea control, or indwelling catheter-associated urinary overflow incontinence; advanced cancer, severe malnutrition that cannot be corrected, or severe edema.

Methods

For patients with IAD, healthcare providers must follow the following standardized operating procedures: (1) Place an air mattress (pressure-distributing type) under the patient to reduce the risk of localized skin pressure; place a disposable incontinence care pad (compliant with the YY/T 0694-2008 standard) under the patient's buttocks to isolate excretions. (2) Conduct rounds every 30–60 minutes to observe the moisture level of the incontinence care pad and replace it promptly (immediately replace when the moist area exceeds 20%). During replacement, use warm water at $40\pm 2^{\circ}\text{C}$ to rinse unidirectionally from the urethral opening toward the anus, removing residual excretions from the perianal and perineal areas, and avoid back-and-forth wiping to prevent skin damage. (3) Select a disposable ostomy bag suitable for the patient's body type (the base plate size must cover a 3–5 cm area around the anus). Cut an opening in the center of the base plate with a diameter 2 cm larger than the anal margin. Remove half of the adhesive protective paper from the base plate, align the center of the ostomy bag opening with the anus, and gently press and secure it along the skin around the anus. Remove the remaining protective paper. Gently spread the perianal skin folds with the index finger and thumb, and press the adhesive surface of the base plate in a spiral pattern from the inside out, centered on the anus (apply pressure so that the patient does not experience significant pain). Ensure that the adhesive is fully adhered to the skin (no bubbles or wrinkles) to create a sealed environment. (4) Apply zinc oxide ointment (Shanghai Yunjia Huangpu Pharmaceutical Co., Ltd., H31021231) evenly over an area extending 5 cm

outward from the edge of the skin lesion (avoid contact with broken skin), with a thickness of approximately 0.2 mm. After application, gently massage the skin around the lesion in a circular motion using the fingertips (apply pressure to a level tolerable by the patient), for 10 minutes each time, to promote drug absorption. (5) Take the Kanghui foam dressing (Danish Kanglebao Company, specifications: $12.5\text{cm} \times 12.5\text{cm}$, batch number: 7753782), and smooth it out and adhere it to the wound from the center outward, ensuring that the edges of the dressing extend 2-3cm beyond the wound. Monitor the dressing for exudate leakage. If exudate penetrates beyond the outer two-thirds of the dressing or if contamination or displacement occurs, replace the dressing every 5 days (standard replacement cycle). In the experimental group, in addition to the above basic care measures, *Longgu* topical application was added: *Longgu* (provided by the Chinese medicine pharmacy of Xi'an Chest Hospital) was ground using a ball mill to a particle size ≤ 100 mesh (passing through an 80-mesh sieve), then mixed into a uniform powder. Three times daily (morning, noon, and evening), an appropriate amount of *Longgu* powder was evenly applied to the perianal skin lesion wound. Both groups underwent continuous intervention for 7 days.

Efficacy evaluation

After treatment, the efficacy of the patients was evaluated by referring to the IAD severity Instrument (IADS; 0-56 points) (Atli & Kaplan Serin, 2024). Cured: After treatment, the affected skin returned to normal and painless, with a reduction of $\geq 90\%$ in IADS. Markedly effective: The symptoms were obviously relieved and the IADS score was decreased by 70% but less than 90%. Effective: The symptoms were improved and the IADS score was decreased by 50% but less than 70%. Ineffective: The skin of the affected area did not improve significantly and the total score of IADS was decreased by $< 50\%$, or the condition worsened. Total effective rate = (cured + markedly effective + effective)/total cases $\times 100\%$. Excellent rate = (cured + markedly effective)/total cases $\times 100\%$.

Prognostic follow-up

Prognostic follow-up of all subjects was performed at 6 months, which included the survival of the patients and the recurrence of IAD.

Endpoints

Patient skin lesion healing, pain relief time, clinical efficacy and adverse reactions during treatment were counted. Fasting venous blood was collected before and after treatment and the serum was separated and divided into two parts. One was used to detect interleukin- $1\beta/6$ (IL- $1\beta/6$) and tumor necrosis factor- α (TNF- α) using enzyme-linked immunosorbent assay and the other was used to measure albumin (ALB), transferrin (TRF), hemoglobin (Hb) and total protein (TP) using an automated

biochemistry analyzer. Finally, the prognostic survival and IAD recurrence rates of the patients were counted.

Statistical analysis

SPSS software 22.0 (IBM, Armonk, NY, USA) was used for statistical analysis. Count data were recorded in the form of [n(%)] and chi-square tests were used for comparison between groups. The measurement data were recorded in the form of ($\bar{x} \pm s$) and the between-group and within-group comparisons used independent sample t-tests and paired t-tests, respectively. Survival and recurrence rates were calculated using the Kaplan-Meier method and comparisons were made using the log-rank test. $p < 0.05$ was considered a statistically significant difference.

RESULTS

The two groups were similar in clinical baseline data

The two groups showed comparability, given the absence of statistical significance in age, sex, IADS and other baseline data ($P > 0.05$) (Table 1).

The skin healing process was shortened in the experimental group

Statistics showed that the healing time and pain relief time of the experimental group were $(3.67 \pm 0.52)d$ and $(1.59 \pm 0.50)d$, respectively, both of which were significantly shorter compared with the control group ($P < 0.05$), suggesting a faster healing process in the experimental group (Fig. 1).

The experimental group showed higher clinical efficacy than the control group

According to statistics, the total effective rate in the experimental group was 88.24%, which was not significantly different from that in the control group ($P > 0.05$); however, a higher rate of treatment was determined in the experimental group (66.67%) versus the control group ($P < 0.05$), indicating better treatment efficacy in the experimental group (Fig. 2).

The inflammatory reaction was milder in the experimental group than in the control group

No statistical inter-group difference was found in the detection results of inflammatory factors before treatment ($P > 0.05$). Both groups showed a reduction in IL-1 β , IL-6 and TNF- α after treatment, especially in the experimental group ($P < 0.05$), indicating less severe inflammation in the experimental group after treatment (Fig. 3).

The nutritional protein levels were higher in the experimental group compared with the control group

The nutritional protein levels were similar in the two groups before treatment ($P > 0.05$). After treatment, the nutritional proteins of the control group did not change ($P > 0.05$); however, ALB, TRF, Hb and TP of the experimental group all increased versus the control group

($P < 0.05$), suggesting better nutritional status of the experimental group (Fig. 4).

The two groups were comparable in safety

Finally, we conducted a statistical analysis of adverse reactions and found that the incidence in the experimental and control groups was 7.84% and 11.76%, respectively, with no statistical inter-group significance ($P > 0.05$), indicating a consistent treatment safety profile (Table 2).

The prognosis of the experimental group was better than that of the control group

We successfully followed up all patients in the control group as well as 50 patients in the experimental group. Comparison of the prognostic survival rates between the two groups showed that the experimental group had a higher survival rate than the control group ($P < 0.05$). However, there was no significant difference in the comparison of prognostic IAD recurrence rate between the two groups ($P > 0.05$) (Fig. 5).

DISCUSSION

IAD, as a very common complication in critically ill patients, seriously affects the treatment progress of patients (Kottner *et al.*, 2024). Clinical studies have confirmed that malnutrition is one of the important triggers of IAD and the occurrence of IAD accelerates the loss of nutrients, forming a vicious cycle that ultimately leads to poor prognosis for patients (Barakat-Johnson *et al.*, 2021). How to achieve more effective and safe IAD treatment has become an important link in improving medical service treatment and patient prognosis.

In this study, we found that the use of *Longgu* not only helps to better treat IAD, but also improves the nutritional status of patients, indicating its great potential in future clinical treatment of IAD. First, through inter-group comparison of the skin healing process, we found that the experimental group had shorter healing time and pain relief time compared to the control group, indicating that *Longgu* can promote wound healing in IAD patients. In the comparison of clinical efficacy, although there was no significant inter-group difference in the total effective rate, the experimental group showed higher treatment effectiveness, indicating that *Longgu* can effectively improve the clinical treatment effect of IAD.

Skin dressings are currently the treatment of choice for IAD and the mechanism of treatment is to promoting the maturation of new tissue cells in skin lesions without damaging the skin lesions (J. Wang *et al.*, 2023). We believe that the accelerated recovery of patients after the use of *Longgu* is mainly related to the pharmacological effect of the drug and the combination with Comfeel foam dressings.

Table 1: Clinical baseline information.

		Control (n=51)	Experimental (n=51)	χ^2 (t)	P
Sex	male	28 (54.90)	31 (60.78)	0.362	0.548
	female	23 (45.10)	20 (39.22)		
Age		60.16±5.94	62.06±6.81	1.503	0.136
Duration of IAD (d)		7.20±1.65	7.33±1.52	0.437	0.663
Area of IAD (cm ²)		8.29±1.59	8.01±1.21	0.983	0.328
Types of incontinence	fecal incontinence	30 (58.82)	28 (54.90)	0.446	0.800
	urinary incontinence	13 (25.49)	16 (31.37)		
	both				
IADS		40.27±4.89	41.45±3.23	1.433	0.155

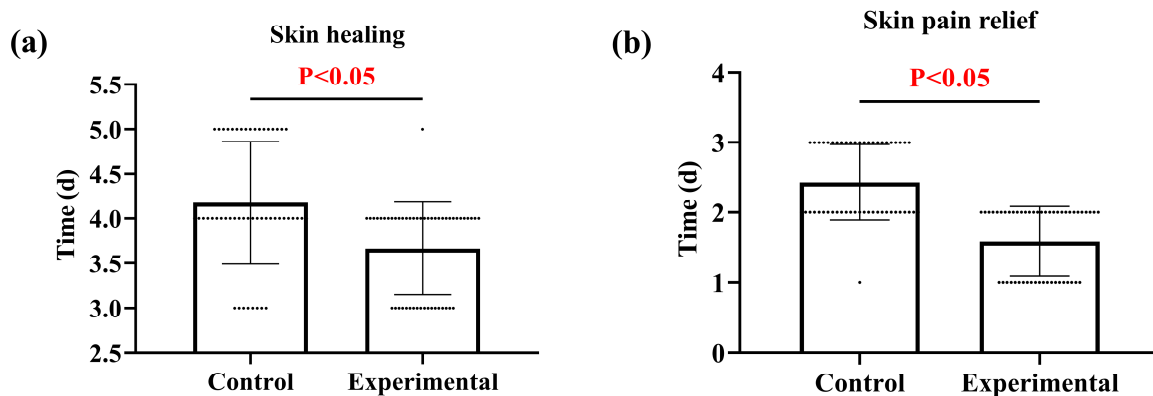


Fig. 1: Comparison of skin healing processes. (a) Skin healing times, and (b) skin pain relief time.

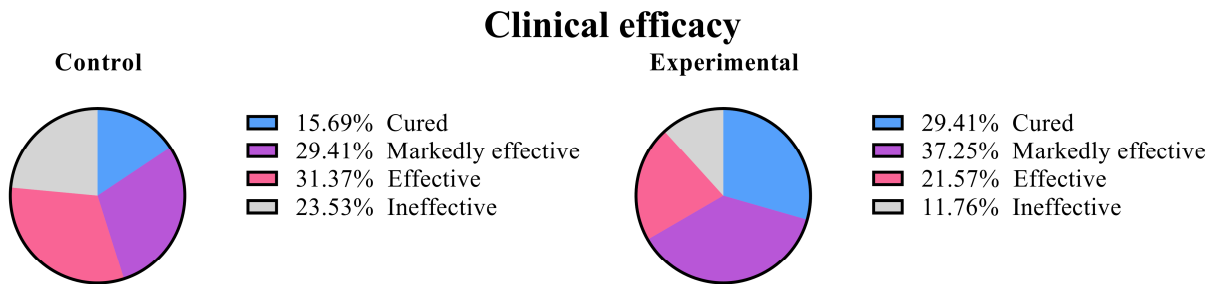


Fig. 2: Comparison of clinical efficacy.

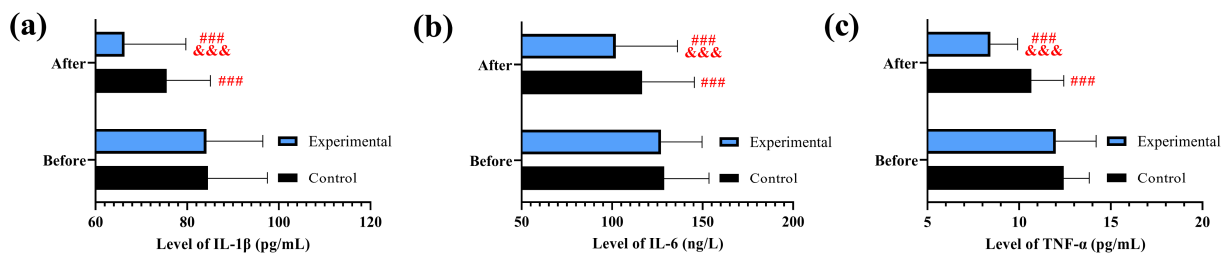


Fig. 3: Comparison of inflammatory factors. (a) IL-1 β , (b) IL-6, and (c) TNF- α . vs before treatment $###P<0.001$, vs control group $###P<0.001$. Interleukin-1 β /6 (IL-1 β /6), tumor necrosis factor- α (TNF- α).

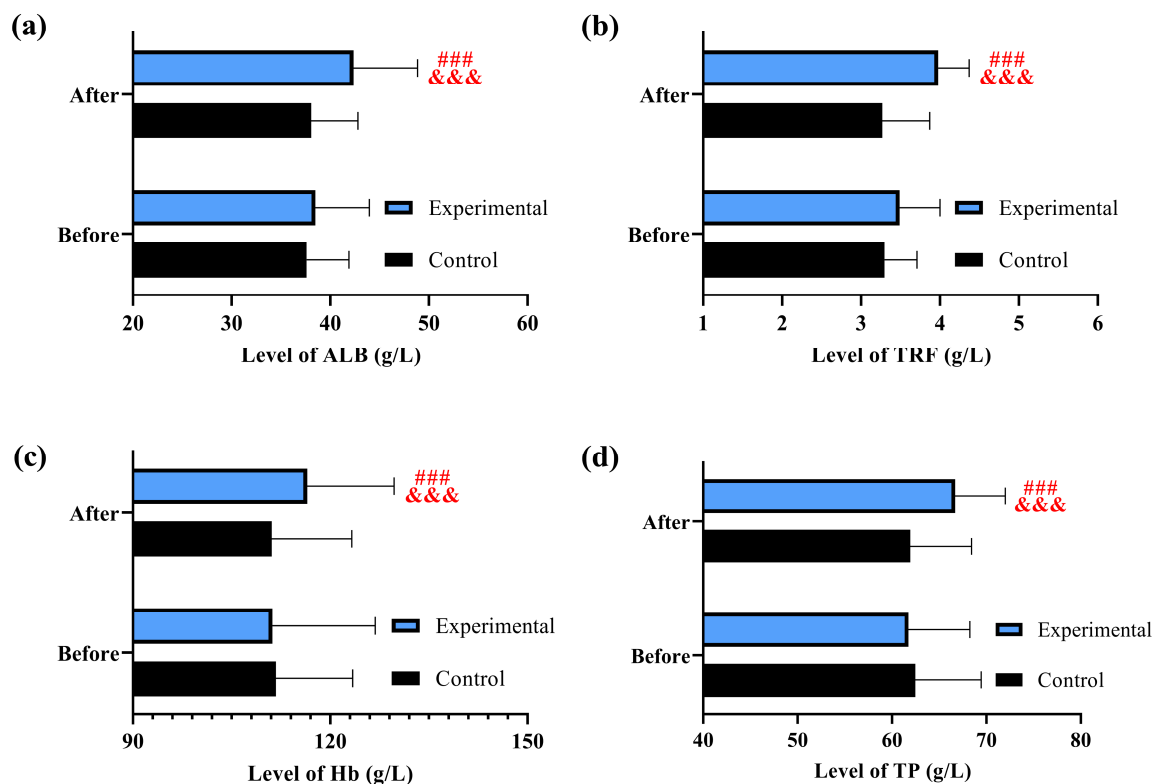


Fig. 4: Comparison of nutrient proteins. (a) ALB, (b) TRF, (c) Hb, and (d) TP. vs before treatment $^{###}P<0.001$, vs control group $^{\&\&\&}P<0.001$. Albumin (ALB), transferrin (TRF), hemoglobin (Hb), and total protein (TP).

Table 2: Comparison of safety.

Groups	Burning skin	Flaking	Stinging	Total incidence of adverse effects
Control (n=51)	2 (3.92)	1 (1.96)	3 (5.88)	6 (11.76)
Experimental (n=51)	1 (1.96)	1 (1.96)	2 (3.92)	4 (7.84)
χ^2				0.444
P				0.505

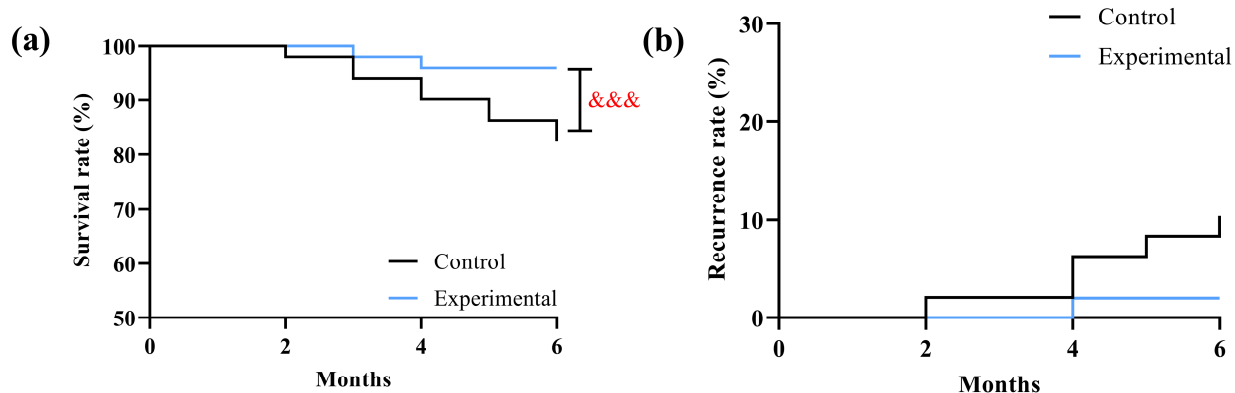


Fig. 5: Comparison of prognosis. (a) Prognostic survival curves for both groups, (b) Prognostic IAD recurrence curves for both groups. vs control group $^{\&\&\&}P<0.001$.

(1) It has been confirmed by TCM-related research that the *Longgu* mainly enters the heart, liver and kidney meridians, while the oyster partially enters the liver, gallbladder and kidney meridians, exerting the effects of benefiting qi and nourishing blood, calming the heart and tranquilizing the mind, restoring liver yin-yang balance, promoting astriction and stemming desertion and relieving hyperacidity and pain (Y. Wang, R. Guan, *et al.*, 2023). Replenishing qi, dredging collaterals and tranquilizing liver and yang can activate qi and blood biochemistry and sufficient qi and blood will contribute to the regeneration of blood vessels and tissues in the affected area. The blood circulates as Qi circulates and sufficient qi and blood in the affected area are conducive to removing blood stasis and dredging collaterals on the wound, promoting blood circulation and absorption of local inflammatory exudates, accelerating skin healing in the affected area and enhancing therapeutic effects (Wan *et al.*, 2021).

(2) The combination of *Longgu* and Comfeel foam dressing can form a foam pad of a certain thickness, which can reduce the degree of skin injury and have a better protective effect on the wound surface under the mechanism of improving skin oxygen partial pressure and local skin oxygen supply and blood supply, thus further inhibiting inflammatory exudation (Y. Wang, P. Li, *et al.*, 2023; Yang *et al.*, 2024). When we compare the inflammatory response between the two groups, we also observed lower IL-1 β , IL-6 and TNF- α in the experimental group after treatment, which can also support our view.

In terms of nutritional status, the nutritional protein levels increased in the experimental group but barely changed in the control group after treatment, indicating that the use of *Longgu* also helps to enhance the nutritional status of IAD patients. The reason is that the main components of *Longgu* are calcium carbonate, magnesium oxide, etc., among which calcium, phosphorus, iron and other nutrients are all necessary elements to maintain human health (Xia *et al.*, 2021). In the rehabilitation treatment of diseases such as stroke, *Longgu* is often used as an adjuvant medicine to improve the overall health of patients (Li *et al.*, 2023). It is precisely because of the promotion of *Longgu* on the nutritional status of patients that the immunity and metabolic function of patients can be improved to a certain extent, which is not only conducive to the treatment of IAD, but also lays a more reliable foundation for the rehabilitation of patients with basic diseases (Jia *et al.*, 2023). Finally, there was no significant inter-group difference in adverse reactions, which indicates that *Longgu* has an extremely high clinical safety profile, indicating its high potential for clinical application in the future.

Finally, the prognostic follow-up results showed that there was no significant difference in the prognostic IAD recurrence rate between the two groups, but the prognostic

survival rate of the experimental group was higher than that of the control group, which also indicated that the use of *Longgu* was more helpful in improving the prognostic health of IAD patients. We believe that the reason for this is that *Longgu* not only inhibits the inflammatory infiltration of IAD patients' wounds, but also strengthens the nutritional status of the patients, thus laying a more reliable foundation for the prognosis of the patients' health (Wang *et al.*, 2020).

However, due to the limited number of cases included in this study and the short follow-up time, the research results may be somewhat contingent. It is also necessary to evaluate the comprehensive impact of *Longgu* on IAD by analyzing more objective evaluation indicators. Finally, in vitro trials should be carried out to further analyze the specific mechanism of *Longgu* in promoting wound healing, so as to provide more comprehensive reference opinions for clinical practice.

CONCLUSION

Longgu is recommended for clinical use as it can provide IAD patients with a more reliable guarantee for their prognosis and health by effectively accelerating wound healing, enhancing the healing effect and comprehensively improving patients' nutritional status.

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Not applicable.

Authors' contributions

Xiaojuan Guo and Qianfeng He conceived and designed the project, and wrote the paper. Hui Li and Xingfeng Yu generated the data. Yan Chen and Qinhu Zhang analyzed the data. Wei Jiang modified the manuscript. All authors gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Data availability statement

The datasets generated during and/or analysed during the current study are available from the corresponding author on reasonable request.

Ethical approval

The Ninth Hospital of Xi'an's Ethics Committee has approved the research (No. 20220303005) and all the subjects have signed informed consent. This study was conducted in strict compliance with the Declaration of Helsinki.

Conflict of interest

Authors have no conflict of interest to declare.

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