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Shenqi injection plus probiotics improves nutritional status in patients with gastric cancer after partial gastrectomy

Yafeng Liu[1] and Mingke Jia[2]*
[1]Department of General Surgery, Yulin First Hospital, Yulin, Shaanxi, China
[2]Department of Gastroenterology, Yulin First Hospital, Yulin, Shaanxi, China

Abstract: In recent years, the incidence of gastric cancer (GC) has been on the rise, surgical procedures usually require the removal of part of gastric tissue connected with the tumor lesion, which leads to poor postoperative health and adverse prognosis in patients. Probiotics, as an active microorganism, play an important role in improving gastrointestinal function and enhancing immunity. In this study, we randomized 135 GC patients into a control group, a probiotic group, and a combination group. All the study subjects were treated with radical GC resection in our hospital. Postoperatively, the control group was given routine treatment, the probiotic group received routine treatment + probiotics and the combined group was given routine treatment+ probiotics +Shenqi injection. Through research, we found that after the use of probiotics, the postoperative rehabilitation process of GC patients was significantly shortened compared to patients treated with conventional enteral nutrition suspension, the immune function and nutritional status were validly improved, and the prognostic survival rate was increased. In addition, the CD4+, ALB, HGB, PA and TP of patients in the combination group were higher than those in the probiotic group ($P<0.05$), while CD4+/CD8+ were lower than those in the probiotic group ($P<0.05$).

Keywords: Gastric cancer, nutritional status, partial gastrectomy, probiotics, Shenqi injection.

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INTRODUCTION

Gastric cancer (GC), originating from gastric mucosal epithelial cells, remains one of the most common malignancies worldwide, with an average incidence of approximately 23 to 54 per 100,000 (Smyth *et al.*, 2020). GC is highly insidious in the early stage, which may only be manifested as paroxysmal abdominal pain and nausea that are easily ignored or mishandled by patients, resulting in more than 60% of patients reaching the middle and late stages when diagnosed (Machlowska *et al.*, 2020). This directly contributes to the generally high prognostic risk of mortality in GC patients, with a five-year survival rate of less than 30% (Guan *et al.*, 2023). In clinical practice, the treatment of GC is still mainly based on surgery combined with chemotherapy. However, due to the malignant infiltration of GC cells, it is usually necessary to remove part of the adhered stomach tissue during the surgery, which greatly affects the postoperative rehabilitation of patients (Thrift & El-Serag, 2020). As one of the most important digestive organs in the human body, the stomach is a non-renewable organ. After partial removal of gastric tissue, the digestive function of patients is generally limited, directly influencing the normal nutrient intake and absorption of the human body and reducing patients' quality of life (Sexton *et al.*, 2020). Therefore, how to provide more reliable safety guarantees for the surgery of GC patients is also the key to determining their prognosis and health.

At present, enteral nutrition suspension is often given to patients after GC surgery to improve their immunity and nutritional status, with well-established clinical efficacy (Carrillo Lozano *et al.*, 2021; Xu *et al.*, 2022). Recently, Wang Y *et al*. proposed that probiotics, as an active microorganism, have a positive effect on ameliorating diarrhea and constipation, relieving allergies, enhancing immunity and maintaining intestinal environmental stability, which is extremely sui table for the rehabilitation treatment of patients undergoing GC surgery (Wang *et al.*, 2023), but their effectiveness has not been verified. Meanwhile, with the increasing popularity of traditional Chinese medicine (TCM) rehabilitation treatment in recent years, natural compounds have attracted clinical attention due to their ability to improve postoperative health in GC patients. Of them, Shenqi injection is a common adjuvant therapy for GC in TCM, mainly composed of *Codonopsis pilosulae, Astragalus membranaceus,* sodium chloride and excipients are sodium metabisulfite and disodium edetate (Wang *et al.*, 2024). Shenqi injection has been recognized in the treatment of various digestive tract diseases in virtue of its excellent safety and table immune improvement effects (Yang *et al.*, 2021; Zhang *et al.*, 2022). For GC, Shenqi injection has also been suggested to improve the effect of chemotherapy more effectively (Xu *et al.*, 2023).

Therefore, a clinical study will be conducted at Yulin First Hospital in China to confirm the effects of recognizing Shenqi injection, probiotics and their combination on the nutritional status of patients after GC surgery, which will

**Corresponding authors:* e-mails: jmk199007067115@163.com

provide a more reliable and safe guarantee for future GC surgery.

MATERIALS AND METHODS

Study population

First, we calculated the sample size needed for this study based on the sample size formula $N=Z^2\times[P\times(1-P)]/E^2$. The confidence interval is set to 95%, the statistic (Z) = 1.96, the error value (E) = 10% and the probability value (P) = 0.5. The sample size (N) = 96. One hundred and thirty-five GC patients admitted to Yulin First Hospital (China) from February 2021 to January 2023 were selected and randomized into control, probiotic and combined groups, each with 45 cases. All the study subjects were treated with radical GC resection in our hospital. Postoperatively, the control group was given routine treatment, the probiotic group received routine treatment + probiotics and the combined group was given routine treatment+ probiotics + Shenqi injection. The Ethics Committee of Yulin First Hospital approved the research (KL20210215) and all subjects provided written informed consent.

Eligibility and exclusion criteria

Inclusion criteria: Confirmed diagnosis of GC by gastroscopy and pathological biopsy; surgical treatment of GC excision in our hospital; provision of a signed informed consent form. Exclusion criteria: Tumor cell metastasis; serious internal medicine diseases; serious heart, liver and kidney diseases; lactating or pregnant patients; digestive system diseases; mental disorders.

Methods

After admission, all patients underwent radical surgery by the same surgeon in our hospital. All patients were given antiviral, diuretic and anti-infective treatment as well as nutritional support after surgery. Control group: Enteral nutrition suspension [Nutricia Pharmaceutical (Wuxi) Co., Ltd., H20030011] was administered. The initial postoperative dose was 1000 kcal/time, once a day, which was gradually increased to 2000 kcal/ time on the 2nd to 3rd day. Probiotic group: On the basis of the control group, Live Combined Bifidobacterium (Shanghai Sine Pharmaceutical Co., Ltd., S10950032) was taken with warm water half an hour after lunch/dinner, 0.42 g/time, twice a day. Combined group: In addition to the above treatment, Shenqi injection (Livzon Pharmaceutical Group Inc., Z19990065) was given intravenously, 250 mL/time, once a day. All patients in the three groups continued to be treated for 3 weeks.

Prognostic follow-up

All patients were followed up by telephone for one year (once a month), investigating patients' survival and recurrence.

Endpoints

(1) Patients' postoperative rehabilitation process was analyzed, including the time to first postoperative anal exhaust and ambulation and the length of hospital stay (LOHS). (2) The fasting venous blood of patients before and after treatment was collected and divided into two parts. One was used to detect $CD3^+$, $CD4^+$ and $CD8^+$ of T lymphocyte subsets by flow cytometry, with the $CD4^+/CD8^+$ ratio calculated; the other was tested by a biochemical analyzer for nutritional proteins albumin (ALB), total protein (TP), hemoglobin (Hb) and prealbumin (PA). (3) Complications during the treatment were recorded and the incidence was calculated. (4) The prognostic recurrence rate and survival rate of GC patients were statistically calculated.

Ethical approval

The study protocol was approved by the Humans Ethics Committee of Yulin First Hospital (KL20210215).

STATISTICAL ANALYSIS

This study used SPSS 25.0 software for statistical analysis. Count data, expressed in [n (%)], were compared using Chi-square tests, while quantitative data were represented by (x±s) and compared using repeated measures analysis of variance and LSD tests. The survival rate was calculated using the Kaplan-Meier method and compared using the Log-rank test. $P<0.05$ indicates that the difference is statistically significant.

RESULTS

Comparison of clinical data

The inter-group comparison of patients' clinical data (table 1) showed no statistical difference in age, sex, histopathological type, etc. ($P>0.05$).

Comparison of postoperative rehabilitation process

As shown in fig. 1, the time to first postoperative anal exhaust and ambulation as well as LOHS were shorter in the probiotic group and the combined group compared to the control group ($P<0.05$); the combined group showed shorter LOHS than the probiotic group ($P<0.05$).

Comparison of immune function

As can be seen from table 2, the three groups were similar in the detection results of T lymphocyte subsets before treatment ($P>0.05$). The probiotic and combined groups exhibited higher $CD3^+$, $CD4^+$ and $CD4^+/CD8^+$ while lower $CD8^+$ than the control group after treatment ($P<0.05$). Compared with the probiotic group, the post-treatment $CD4^+$ and $CD4^+/CD8^+$ were higher in the combined group ($P<0.05$).

Comparison of nutritional proteins

As shown in table 3, the two groups did not differ much in pre-treatment levels of nutritional proteins ($P>0.05$). After treatment, ALB, HGB, PA and TP did not change in the

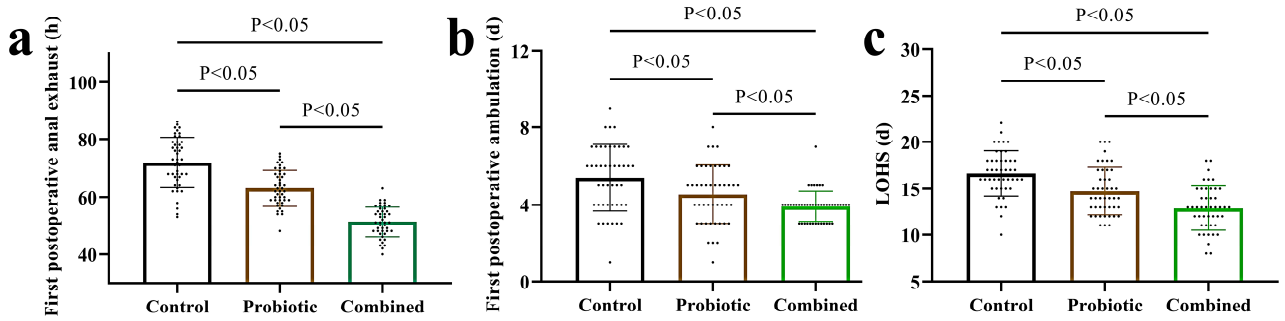

Fig. 1: Comparison of (a) time to first postoperative anal exhaust, (b) time to first postoperative ambulation and (c) LOHS. Length of hospital stay, LOHS.

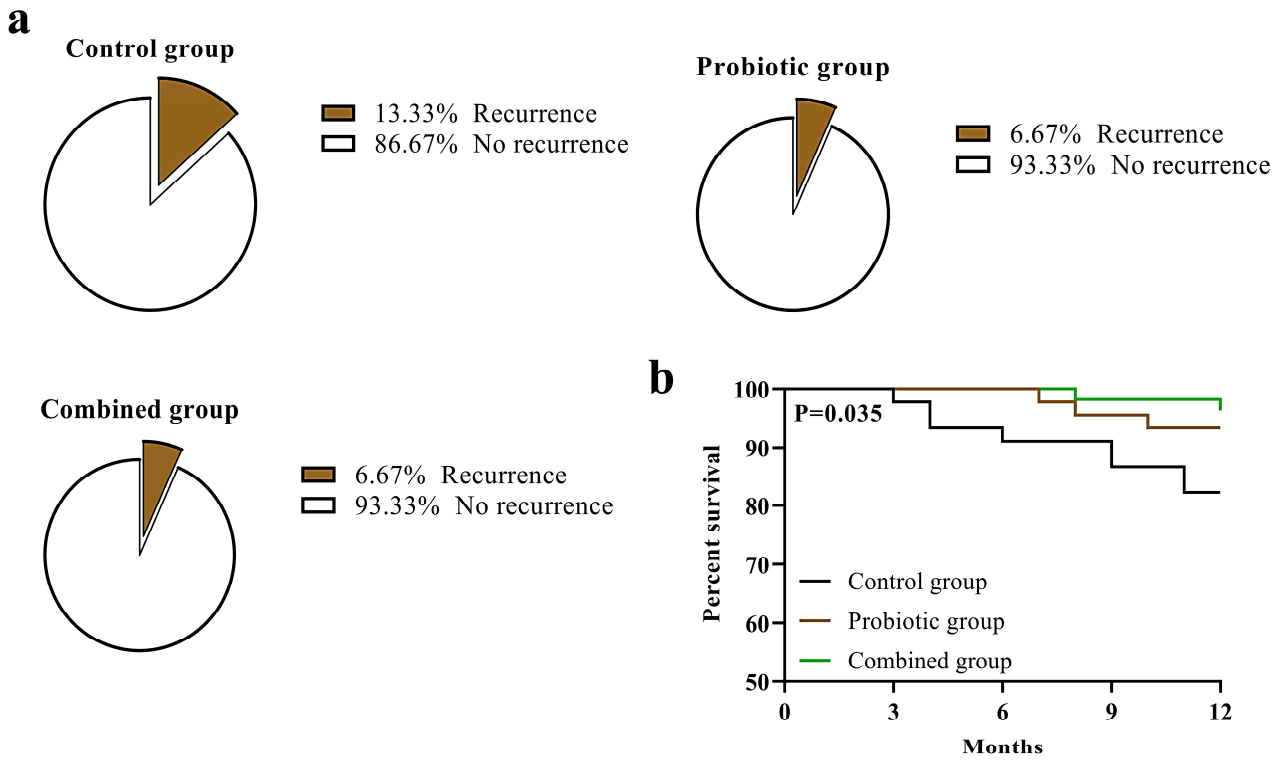

Fig. 2: Comparison of (a) prognostic recurrence rates and (b) prognostic survival rates.

control group (P>0.05); but their levels increased in the probiotic and combined groups, all of which were higher compared to the control group; moreover, higher ALB, HGB, PA and TP levels were determined in the combined group versus the probiotic group (P<0.05).

Comparison of treatment safety

As shown in table 4, the incidence of complications in the control group, the probiotic group and the combined group were 31.11%, 22.22% and 8.89%, respectively. The incidence of complications was not statistically different between the probiotic and control groups (P>0.05), the incidence of complications in the combined group was lower than that in the probiotic group and the control group (P<0.05).

Comparison of prognosis

As shown in fig. 2, the three groups showed no statistical difference in the prognostic recurrence rate (P>0.05). The probiotic and combined groups were not markedly different in the prognostic survival rate (P>0.05), the prognostic survival rate of the control group was lower than that of the combined group and the probiotic group (P<0.05).

DISCUSSION

The potential threat of GC to patients' health and life safety must be dealt with clinical attention. Although the prognostic survival rate of GC has been obviously improved since the 20th century with the advancement of the medical level, the influence of partial gastrectomy on

Table 1: Comparison of clinical data.

Groups (n=45)	Age	Sex		Body Mass Index (kg/m^2)	Duration of disease (months)	Pathological staging			Histopathological type	
		Male	Female			Stage II	Stage III	Stage IV	Adenocarcinoma	Other
Control	62.44±4.33	30 (66.67)	15 (33.33)	22.84±2.42	4.67±1.17	14 (31.11)	23 (51.11)	8 (17.78)	40 (88.89)	5 (11.11)
Probiotic	62.91±6.31	24 (53.33)	21 (46.67)	23.01±1.63	5.04±1.46	12 (26.67)	26 (57.78)	7 (15.56)	42 (93.33)	3 (6.67)
Combined	63.82±4.96	28 (62.22)	17 (37.78)	23.10±1.66	5.22±1.93	11 (24.44)	26 (57.78)	8 (17.78)	41 (91.11)	4 (8.89)
F (χ^2)	0.798	1.740		0.198	1.505	0.705			0.559	
P	0.452	0.419		0.820	0.226	0.951			0.760	

Table 2: Comparison of immune function.

Groups (n=45)	CD3+ (%)		CD4+ (%)		CD8+ (%)		CD4+/CD8+	
	Before	After	Before	After	Before	After	Before	After
Control	55.91±4.47	61.48±5.62$^{\&}$	27.55±2.18	30.48±3.20$^{\&}$	38.22±2.80	35.12±1.97$^{\&}$	0.72±0.07	0.87±0.09$^{\&}$
Probiotic	56.19±4.93	64.19±4.93$^{*\&}$	27.23±1.51	35.62±3.18$^{*\&}$	30.06±2.98	32.21±1.76$^{*\&}$	0.72±0.07	1.11±0.11$^{*\&}$
Combined	56.26±5.55	64.43±5.13$^{*\&}$	27.65±2.20	38.92±2.92$^{*\#\&}$	38.54±2.77	29.27±2.55$^{*\#\&}$	0.72±0.08	1.34±0.14$^{*\#\&}$
F	0.061	4.412	0.543	84.500	0.335	85.490	0.032	177.600
P	0.941	0.014	0.582	<0.001	0.716	<0.001	0.969	<0.001

Note: * indicates P<0.05 compared with the control group, # indicates P<0.05 compared with the probiotic group, and & indicates P<0.05 compared with the before treatment.

Table 3: Comparison of nutritional proteins.

Groups (n=45)	ALB (g/L)		HGB (g/L)		PA (mg/L)		TP (g/L)	
	Before	After	Before	After	Before	After	Before	After
Control	30.58±2.39	35.19±4.06$^{\&}$	106.64±9.62	118.78±15.96$^{\&}$	272.44±15.69	290.11±21.38$^{\&}$	61.34±4.92	67.83±5.55$^{\&}$
Probiotic	29.68±2.69	39.66±5.59$^{*\&}$	107.62±10.02	126.24±13.00$^{*\&}$	274.43±21.74	309.56±27.06$^{*\&}$	60.98±4.08	73.63±5.36$^{*\&}$
Combined	30.71±2.23	43.03±6.21$^{*\#\&}$	107.70±11.05	133.08±16.96$^{*\#\&}$	273.45±33.83	318.09±27.61$^{*\#\&}$	60.88±3.91	76.69±4.00$^{*\#\&}$
F	2.308	24.210	0.150	9.700	0.072	14.230	0.141	36.190
P	0.104	<0.001	0.861	<0.001	0.931	<0.001	0.869	<0.001

Note: * indicates P<0.05 compared with the control group, # indicates P<0.05 compared with the probiotic group, and & indicates P<0.05 compared with the before treatment.

patient prognosis and health can not be ignored (Conti *et al.*, 2023). In this study, we explored the effect of Shenqi injection plus probiotics on GC patients after surgery, which can provide a more reliable guarantee for future GC treatment.

First of all, comparing the prognosis and rehabilitation progress among the three groups of patients, it was found that the rehabilitation time of the probiotic and combined groups was significantly shortened compared to the control group, with the most significant improvement found in the combined group, suggesting that Shenqi injection plus probiotics has an excellent role in accelerating recovery after GC surgery. Research has shown that partial gastrectomy can cause intestinal flora imbalance, malabsorption and decreased nutrient intake, resulting in a series of physiological functional disorders and a decrease in immune function, which will affect the postoperative recovery of patients (Wang *et al.*, 2022). Enteral nutrition suspension is the main compound preparation for postoperative nutritional support for patients undergoing surgery. It contains many essential nutritional elements for the human body and is widely used in patients undergoing partial gastrectomy, which meets the body's nutritional needs, maintains normal flora balance, promotes patients' recovery, and effectively relieves patients' symptoms. However, due to the fact that enteral nutrition suspension mainly provides nutritional

Table 4: Comparison of treatment safety.

Groups (n=45)	Loss of appetite	Nausea	Abdominal pain	Fever	Dizziness headache	Infection	Urinary retention	Constipation	Total incidence
Control	3 (6.67)	2 (4.44)	4 (8.89)	2 (4.44)	1 (2.22)	1 (2.22)	1 (2.22)	0 (0.0)	14 (31.11)
Probiotic	2 (4.44)	1 (2.22)	3 (6.67)	0 (0.0)	2 (4.44)	0 (0.0)	1 (2.22)	1 (2.22)	10 (22.22)
Combined	1 (2.22)	1 (2.22)	1 (2.22)	0 (0.0)	1 (2.22)	0 (0.0)	0 (0.0)	0 (0.0)	4 (8.89)*#
χ^2									6.849
P									0.033

Note: * indicates P<0.05 compared with the control group and # indicates P<0.05 compared with the probiotic group.

support to patients, it cannot alleviate inflammatory cytokine responses or prevent postoperative adverse reactions. Therefore, it usually can only improve the postoperative gastrointestinal function recovery of GC patients and keep their nutrient absorption and metabolism in a table state, but cannot achieve further improvement (Rinninella *et al.*, 2020).

On this basis, the use of probiotics not only improves intestinal mucosal function by regulating the composition of gut micro biota, but also enhances immune function and facilitates recovery (Yang *et al.*, 2022). Probiotics also have anti-inflammatory effects, which can modulate patients' oxidative stress responses, improve vascular endothelial function, promote the repair of gastrointestinal injury sites and reduce the absorption of harmful substances, thereby reducing inflammatory factor responses and reducing postoperative adverse reactions (Ye *et al.*, 2023). Because of this, the probiotic group showed more significant improvement in post-treatment rehabilitation progress and T lymphocyte subsets. At the same time, Koga Y *et al*. suggested that Live Combined Bifidobacterium can inhibit and eliminate pathogenic bacteria in patients' intestines, promote nutrient absorption and digestion, reduce diamine oxidase, promote protein synthesis, and reduce the translocation of intestinal bacteria, thus improving the nutritional status of patients (Koga, 2022). This is also in line with the results of this study, which found higher nutritional protein levels in the probiotic group versus the control group after treatment. In a meta-analysis by Yang D *et al*. on probiotic-assisted treatment of GC, they also demonstrated that the use of probiotics helps to improve the inflammatory response of patients, as the intestinal flora of the human body is one of the keys to maintain the barrier function of the gastric mucosa (Yang *et al*., 2022). This shows that probiotics have an important future potential in the treatment of gastrointestinal diseases.

Shenqi injection, as a TCM, contains effective components that can protect the functions of the heart, kidneys and liver and is considered to be effective in strengthening and consolidating body resistance, tonifying deficiency, and benefiting Qi in TCM (Xi *et al.*, 2023). Pharmacological research indicates that Astragalus polysaccharide is the main component of Shenqi injection, which can enhance human immunity, protect bone marrow, strengthen the anticancer activity of T, NK, and other cells and improve humoral immunity and cellular immunity (Li *et al.*, 2015). Other effective components such as saponins is able to enhance the phagocytosis of macrophages, improve autonomic nervous function, enhance appetite and resist fatigue, thereby effectively reducing chemotherapy-associated adverse reactions and improving the body's resistance (Dong *et al.*, 2010). Therefore, using Shenqi injection to assist probiotic therapy can more effectively enhance the immune function of patients while better promoting the recovery of patients' nutritional status. At the same time, as a natural compound, the nutrients in Shenqi injection play a certain organ protection effect without causing obvious toxic and side effects. For example, Astragalus polysaccharide can enhance cardiomyocyte metabolism, reduce myocardial oxygen consumption and blood viscosity, and increase left ventricular stroke volume and ventricular ejection fraction, thereby protecting myocardial function (Wang *et al.*, 2019). We believe that this is also the reason for the lower incidence of complications in the combined group compared to the other two groups. In the study of Chen G *et al*, they also confirmed that the use of Shenqi injection can improve the safety of chemotherapy (Chen *et al.*, 2024), which can also testify the results of the current study. Not only that, in a systematic evaluation of Shenqi injection in the treatment of GC by Xu J *et al*, they also confirmed that Shenqi injection can improve the immune function of GC patients (Xu *et al*., 2023), which shows that Shenqi injection is of great significance in improving the health status of human body.

Finally, the prognostic follow-up results revealed no difference in the recurrence rate among the three groups; however, the survival rate was higher in the probiotics and combined groups versus the control group. It can be seen that probiotics and Shenqi injection have a more reliable guarantee for the prognosis and safety of GC patients. This is also because of the use of probiotics and Shenqi injection, which better promote the postoperative health of GC patients and lay the foundation for a safe prognosis. However, due to the small number of cases and short follow-up time, it is not excluded that the follow-up results are accidental, which needs supplementary research and verification as soon as possible. Besides, we need to carry out in vitro experiments as soon as possible

to further analyze the mechanism of action of probiotics and Shenqi injection on GC, so as to provide a more comprehensive clinical reference.

CONCLUSION

Shenqi injection plus probiotics can effectively promote the rehabilitation process of patients after GC resection, enhance their immunity and improve their nutritional status.

COMPETING INTERESTS

The authors report no conflict of interest.

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