Efficacy of endoscopic submucosal dissection in the treatment of early gastric cancer in the elderly and its effect on recent prognosis

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Introduction. To investigate the efficacy of endoscopic mucosal dissection in the treatment of early gastric cancer in the elderly and its effect on patients' recent prognosis.

Methods. One hundred cases of elderly patients with early gastric cancer admitted to the Department of Surgical Oncology of our hospital between January 2020 and May 2022 were selected and grouped according to the actual surgical modality adopted (55 cases treated with endoscopic mucosal dissection were set up as the observation group, and 45 cases treated with complete laparoscopic radical gastric cancer treatment were set up as the control group), and the two groups were compared with respect to the clinical efficacy, surgery-related indexes, inflammatory reaction, pain level, complications and recent prognosis.

Results. The postoperative disease control rate of the observation group (was 98.18%, 54/55) was higher than that of the control group (was 88.89%,40/45), but the difference was not significant (Z=0.960,χ^2=2.321, all P>0.05). The operation time, postoperative exhaust time and postoperative hospital stay of the observation group were shorter than that of the control group (P＜0.05), but its complete tumour resection rate was lower than that of the control group (P＜0.05). The differences in serum interleukin-6 (IL-6), interleukin-12 (IL-12) and tumour necrosis factor-α (TNF-α) levels between the two groups before surgery were not obvious (P > 0.05), and the levels of IL-6, IL-12 and TNF-α in the two groups after surgery decreased compared with those before (P < 0.05), and the levels of IL-6, IL-12 and TNF-α in the observation group were significantly lower than those of the control group (P < 0.05). The

visual analogue score (VAS) of the observation group was significantly lower than that of the control group at all postoperative points ($P < 0.05$), and the incidence of perioperative complications was also lower than that of the control group ($P < 0.05$). At 2-year follow-up, 3 cases of recurrence were found in the observation group, accounting for 5.45%, and no recurrence was seen in the control group, but there was no significant difference in the recurrence rate between the two groups ($P > 0.05$). The median follow-up was 27.4 months in the observation group and 26.8 months in the control group, and the cumulative survival rate in the observation group (98.18%, 54/55) was higher than that in the control group (93.33%, 42/45), but the difference was not statistically significant (log-rank χ^2=0.516,P=0.473＞0.05). Conclusion.The use of endoscopic mucosal dissection for the treatment of early gastric cancer in the elderly can improve the efficacy, promote postoperative recovery, reduce the postoperative inflammatory response and pain level, reduce perioperative complications, and have a more favourable near-term prognosis.

Keywords. Early gastric cancer; elderly patients; endoscopic mucosal dissection; total laparoscopic radical gastrectomy for gastric cancer; prognosis

INTRODUCTION

Gastric cancer occupies a prominent position in the global statistics of tumour incidence and death, and the International Agency for Research on Cancer (IARC) estimates that in 2020, there will be as many as 1,089,000 new cases of gastric cancer worldwide, and more than 769,000 deaths due to gastric cancer [1]. And in China, the situation is equally serious. According to the data of the National Cancer Centre, in 2020, there will be about 779,000 new cases of gastric cancer and 598,000 deaths in China [2]. The condition of Chinese gastric cancer patients is generally more serious, and most of them are in the middle and late stages of gastric cancer when diagnosed, accounting for more than 80% of the cases. Despite the existence of surgically resectable gastric cancer cases, the 5-year survival rate of such patients is only 46%, which is significantly lower compared with 81% and 71.1% in Korea and Japan during the same period [3]. The reason for this phenomenon is largely related to the

low rate of early detection of gastric cancer patients in China. Early gastric cancer refers to gastric cancer with lesions limited to the gastric mucosal layer or submucosal layer, regardless of whether lymph node metastasis occurs. In China, patients with TNM stage I account for only 28%, which is much lower than the 58.7% and 62% in Japan and Korea [4]. This also means that most of the patients have already entered the middle and late stages when they are detected, which greatly increases the difficulty of treatment and mortality. Previous studies have confirmed that the 5-year survival rate of patients with early gastric cancer is significantly higher than that of patients with intermediate and advanced stages [5], so the key to improving the survival rate of gastric cancer patients lies in early detection and timely treatment.

In recent years, with the increasing popularity and accuracy of gastric cancer screening, the detection rate of early gastric cancer has been increasing, especially with the increasing aging, the function of the body of the elderly and their immune function decreases, which can seriously damage their gastric mucosa cells and increase the risk of early gastric cancer [6]. Currently, the treatment modalities for early gastric cancer include traditional open surgery, laparoscopic surgery, endoscopic mucosal stripping, endoscopic total resection, and dual-lens combined surgery. Complete laparoscopic radical gastrectomy for gastric cancer can effectively resect local lesion tissues and has the characteristics of less trauma, less intraoperative bleeding and lower risk of postoperative infection, but this procedure has more postoperative complications and patients' postoperative recovery is slow, which is difficult to be tolerated by some elderly patients with early gastric cancer [7]. Endoscopic mucosal dissection has certain advantages in the treatment of early gastric cancer, which can achieve the whole resection of local lesions and reduce the occurrence of heterochronous cancer. Moreover, this procedure can preserve the basic structure of the stomach, which helps to reduce postoperative complications, improve postoperative quality of life, and the survival time of patients is comparable to that of traditional procedures [8]. However, endoscopic mucosal stripping can cause bleeding, perforation, resulting in stenosis, etc., and there is a risk of recurrence [9], and its

efficacy, safety, and impact on patients' prognosis in the treatment of early gastric cancer in the elderly still need to be further clarified. In view of this, this study aims to compare and observe the application effect of endoscopic mucosal dissection in the treatment of early gastric cancer in the elderly and its impact on the recent prognosis of patients, with a view to providing a basis for the clinical treatment of early gastric cancer in the elderly.

1 MATERIALS AND METHODS

1.1 Basic information

1 100 cases of elderly patients with early gastric cancer admitted to the Department of Surgical Oncology of our hospital between January 2020 and June 2022 were selected for the study. Inclusion criteria: (1) age ≥60 years; (2) meeting the diagnostic criteria for gastric cancer [10] and TNM stage I; (3) patients' expected survival period of more than 1 month; (4) complete relevant data (including demographic data, clinical data, and relevant examination indexes, etc.). Exclusion criteria: (1) age <60 years; (2) with severe organ insufficiency; (3) combined with acute and chronic infectious diseases; (4) combined with other malignant tumours. The patients were grouped according to the actual surgical procedures (55 cases were treated with endoscopic mucosal dissection and were set up as the observation group, of which 30 cases were male and 25 cases were female, aged 62-79 (69.82±7.20) years old, with the maximum diameter of the tumour ranging from 1.50 to 2.10 (1.79±0.16) cm, clinical typing: 33 cases of type Ia, 22 cases of type Ib, and the depth of infiltration: 35 cases of mucosal layer, 20 cases of sub-mucosal layer. Depth of infiltration: 35 cases in the mucosal layer, 20 cases in the submucosal layer. There were 45 cases of gastric cancer treated by total laparoscopic radical gastrectomy (set up as control group), of which 24 cases were male and 21 cases were female, aged 64-82 (69.75±7.32) years old, with the maximum diameter of the tumour ranging from 1.45 to 2.08 (1.81±0.14) cm, and the clinical typing: 28 cases of type Ia, 17 cases of type Ib, and the depth of infiltration: 32 cases of the mucous membrane layer, 13 cases of the submucous

membrane layer. The data of the two groups did not show significant differences and were comparable (P>0.05) (Table 1). The study was reported to the Medical Ethics Committee of the hospital for review and approval.

Table 1 Comparison of clinical data between the two groups

groups	Sex (m/f)	Age (years)	Maximum diameter of tumour（cm）	clinical typing		Infiltration depth	
				Ia	Ib	mucous membrane layer	submucosa
Observation group (n=55)	30/25	69.82±7.20	1.79±0.16	33	22	35	20
Control group (n=45)	24/21	69.75±7.32	1.81±0.14	28	17	32	13
χ^2/t	0.015	0.048	0.657	0.051		0.625	
P	0.904	0.962	0.513	0.821		0.429	

1.2 Surgical methods Fifty-five cases in the observation group were treated with endoscopic mucosal stripping, and after receiving intravenous anaesthesia in the lying position, the patients were introduced to the gastroscope through the oral cavity to penetrate deep into the stomach for routine endoscopic examination. Under the gastroscope, the doctor observed the gastric lesions meticulously to determine the location, size and depth of the lesions. Next, the lesion was precisely marked using an electric knife and injected with 2ml of saline mixture to augment the lesion for subsequent operations. Subsequently, the doctor used a needle knife to incise the mucosa around the lesion along the marked edge, and then used an insulated scalpel to separate the lesion part from the muscle layer. During the peeling process, the doctor gradually separated the lesion from the normal submucosal layer underneath it according to the gastroscopic field of view, until the lesion was completely removed and sent for pathological examination. After completing the dissection, doctors

performed haemostasis on all visible blood vessels on the traumatic surface, and finally closed the incision meticulously to ensure that the patient's recovery was smooth. Forty-five cases in the control group received total laparoscopic radical gastric cancer treatment: after receiving general anaesthesia, the patients lay supine on the operating table, and the surgical area was strictly disinfected and prepared with towels. Through umbilical puncture, CO2 pneumoperitoneum was established, and the pressure was maintained between 12 and 15 mmHg. Subsequently, according to the surgical needs, incisions were made under the left costal margin, under the right costal margin, under the right and left mid-abdomen, and under the umbilical lower margin, and puncture trocars were inserted to explore the abdominal cavity and determine the scope of surgery. Depending on the patient's lesion, the surgeon may choose to perform laparoscopic distal gastrectomy, proximal gastrectomy or total gastrectomy. Postoperative specimens were fixed in neutral formaldehyde buffer and sent for pathological examination. A D1-wide lymph node dissection was performed, and gastrointestinal reconstruction was completed laparoscopically. At the end of surgery, a drain was left in the patient for further observation and care.

1.3 Observation indicators Compare the clinical efficacy, surgery-related indexes, inflammatory response, pain level, complications and recent prognosis of the two groups. (1) Efficacy. They were classified as complete remission (abbreviation: CR, complete disappearance of the tumour confirmed by postoperative examination and lasting for more than 1 month), partial remission (abbreviation: PR, postoperative testing of the tumour showed that the reduction of the product of the maximal diameter (maximal diameter×maximal vertical diameter) was more than 50%), stable disease (abbreviation: SD, the reduction of the above product was less than 50% or the increase of the above product was less than 25% after the operation), and progression (abbreviation: PD, the increase of the above product was less than 25% after the operation). (abbreviation: SD, postoperative reduction of the above product of less than 50% or increase of less than 25%), disease progression (abbreviation: PD, postoperative increase of the above product of more than 25%). The postoperative

disease control rate was calculated (number of achieved CR cases + number of achieved PR cases + number of achieved SD cases/total number of cases × 100%) [11]. (2) Surgery-related indexes. Record the operation time, postoperative exhaust time and postoperative hospital stay of the two groups, and calculate their complete tumour resection rate. (3) Inflammatory factors. Five ml of fasting peripheral venous blood was collected before and after surgery, and the serum was separated and sent for examination after centrifugal processing (3000 r/min, centrifugation for 15 min), and the levels of serum interleukin-6 (IL-6), interleukin-12 (IL-12), and tumour necrosis factor-alpha (TNF-alpha) were determined by enzyme-linked immunosorbent assay. (4) Pain level. Visual analogue scoring (VAS) was used to assess the pain level of patients in the two groups in 1d, 3d, 5d and 7d after surgery as follows: a 10 cm horizontal line was drawn on top of the paper, with 0 at one end of the horizontal line indicating no pain, 10 at the other end indicating severe pain, and the middle portion indicating different degrees of pain. The patient was asked to draw a mark on the horizontal line to indicate the degree of pain according to his/her self-perception [12]. (5) Complications. Record the occurrence of perioperative-related complications in the two groups and compare their complication rates. (6) Prognosis. Follow-up was carried out through outpatient clinics or by telephone, and the follow-up ended on 30 May 2024, with tumour recurrence or death as the follow-up endpoint. Survival and recurrence rate were recorded and compared between the two groups (recurrence was defined as the presence of tumour within 2 cm of the original lesion or margin found on examination and confirmed by imaging).

1.4 statistical processing　SPSS26.0 statistical software was used to process the data. Measurement data were expressed as（$\bar{x}\pm s$）, and independent sample t-test was used for comparison between groups, and paired sample t-test was used for comparison before and after treatment within groups; counting data were tested by χ^2 test, and rank-sum test was used for hierarchical data.Survival curves were plotted by the kaplan-Meier method. $P<0.05$ was regarded as the statistically significant difference in comparison of each variable.

2 RESULTS

2.1 Clinical efficacy The postoperative disease control rate of the observation group (was 98.18%, 54/55) was higher than that of the control group (was 88.89%,40/45), but the difference was not significant (Z=0.960,χ2=2.321, both P>0.05). See Table 2.

Table 2 Comparison of clinical efficacy between the two groups [n (%)]

groups	CR	PR	SD	PD	Disease control rate
Observation group (n=55)	30（54.55）	14（25.45）	10（18.18）	1（1.82）	54（98.18）
Control group (n=45)	22（48.89）	10（22.22）	8（17.78）	5（11.11）	40（88.89）
Z/χ^2		0.960			2.321
P		0.337			0.128

2.2 Surgery-related indexes The operation time, postoperative exhaustion and postoperative hospital stay of the observation group were shorter than that of the control group (P < 0.05), but its complete tumour resection rate was lower than that of the control group (P < 0.05). See Table 3.

Table 3 Comparison of surgery-related indicators between the two groups

groups	Surgical time（$\bar{x}$±s，min）	Postoperative venting time（$\bar{x}$±s，min）	Length of hospitalisation（$\bar{x}$±s，d）	Complete tumour resection rate[n(%)]
Observation group (n=55)	172.56±15.39	2.18±0.20	8.76±1.11	44（80.00）
Control group (n=45)	194.78±15.20	2.97±0.44	9.90±1.68	44（97.78）
t/χ^2	7.223	11.906	4.065	7.407
P	＜0.001	＜0.001	＜0.001	＜0.001

2.3 Inflammatory factor indexes Preoperative differences in serum IL-6, IL-12, and TNF-α levels between the two groups were not obvious (P > 0.05), and postoperative levels of IL-6, IL-12, and TNF-α in the two groups were decreased compared with the preoperative period (P < 0.05), and the levels of IL-6, IL-12, and TNF-α in the observation group were significantly lower than those in the control group (P < 0.05). See Table 4.

Table 4 Comparison of inflammatory factor indicators between the two groups（$\bar{x}$±s，%）

groups	IL-6（ng/L）		IL-12（ng/L）		TNF-α（g/L）	
	preoperative	postoperative	preoperative	postoperative	preoperative	postoperative
Observation group (n=55)	80.45±10.96	38.72±5.93	30.55±5.42	4.86±1.15	8.67±1.95	1.58±0.32
Control group (n=45)	81.37±10.48	52.08±6.79	31.14±5.36	9.95±2.07	8.72±2.04	3.09±0.54
t	0.426	10.499	0.544	15.548	0.125	17.356
P	0.671	＜0.001	0.588	＜0.001	0.901	＜0.001

2.4 VAS scores The VAS scores at all time points of postoperative in the observation group were significantly lower than those in the control group (P < 0.05), see Table 5.

Table 5 Comparison of VAS scores at each time point of postoperative between the two groups（$\bar{x}$±s，分）

groups	postoperative1d	postoperative3d	postoperative5d	postoperative7d
Observation group (n=55)	4.25±1.08	2.36±0.89	1.38±0.65	0.88±0.20
Control group (n=45)	6.34±1.20	3.90±1.02	2.45±0.72	1.04±0.37
t	9.157	8.060	7.802	2.755
P	＜0.001	＜0.001	＜0.001	0.007

2.5 Complications The perioperative complication rate of the observation group was significantly lower than that of the control group (P < 0.05). See Table 6.

Table 6 Comparison of perioperative complication rates between the two groups [n (%)]

groups	reflux oesophagitis	intestinal obstruction	anastomotic fistula	perforated	rate of occurrence
Observation group (n=55)	4（7.27）	2（3.64）	2（3.64）	1（1.82）	9（16.36）
Control group (n=45)	7（15.56）	4（8.89）	3（6.67）	2（4.44）	16（35.56）
χ^2					4.862
P					0.028

2.6 Prognosis At 2 years of follow-up, 3 cases of recurrence were found in the observation group, accounting for 5.45%, and no recurrence was seen in the control group, but there was no significant difference in the recurrence rate between the two groups (P > 0.05). The median follow-up was 27.4 months in the observation group and 26.8 months in the control group, and the cumulative survival rate of the observation group (98.18%, 54/55) was higher than that of the control group (93.33%, 42/45), but the difference was not statistically significant (log-rank χ2=0.516,P=0.473 ＞0.05). See Figure 1.

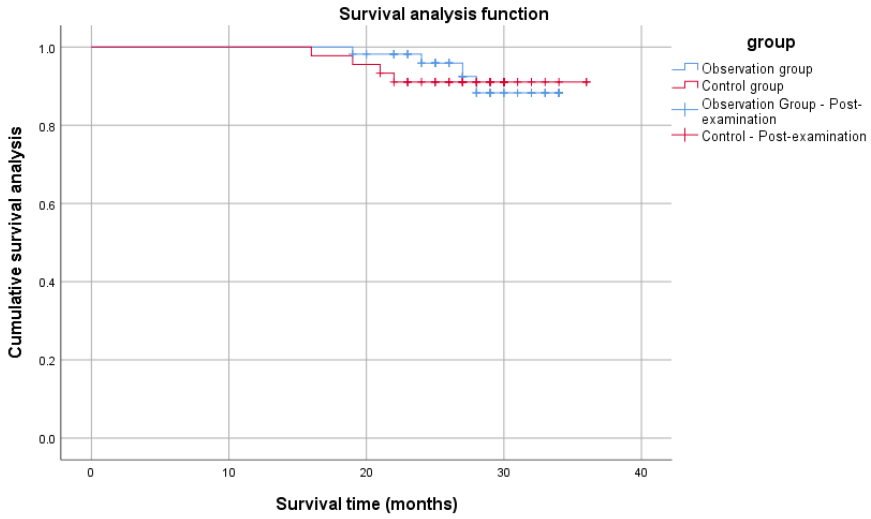

Figure 1 Survival curves of the two groups of patients

3 DISCUSSION

In recent years, the advantages of gastrointestinal endoscopy in the treatment of early gastric cancer without lymph node metastasis have gradually emerged and have been widely recognised. Compared with traditional surgery, endoscopic treatment does not require gastrointestinal reconstruction, complications and sequelae are significantly reduced, and the postoperative survival quality of patients has been significantly improved [13]. Endoscopic resection has become the treatment of choice for patients with early gastric cancer without the risk of lymph node metastasis, with endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) being the two main approaches.EMR removes the diseased mucosa by means of a circling device, which is suitable for the absence of ulcerative changes and the small diameter of the mucosa to be removed. However, EMR has been gradually replaced by ESD in recent years due to its relatively low block and complete resection rates [14].ESD is a more advanced technique developed on the basis of EMR, which employs circumferential excision of the mucosa and submucosal dissection with an electrosurgical knife to remove diseased tissues more precisely.ESD not only improves the block and complete resection rates, but also reduces the risk of recurrence and has become the standard endoscopic approach for the treatment of early gastric cancer.ESD has shown greater stability in responding to gastric lesions and is less disturbed by lesion size and ulceration [15]. In terms of surgical outcomes, ESD has been previously reported to have a high block resection and complete resection rate of 92.4% and 82.1%, respectively [16], which is comparable to surgery. In addition, ESD has significant advantages in terms of postoperative recovery, such as shorter postoperative hospital stay, lower costs, fewer long-term complications, and better quality of life for patients. However, it should be noted that ESD is mainly suitable for differentiated intramucosal cancers without ulcers, and the size of the lesion should be controlled within a certain range. In addition, ESD has shown some therapeutic efficacy in differentiated intramucosal cancers with ulcers and high-grade intraepithelial neoplasia of the gastric mucosa. However, ESD is no longer suitable

for early gastric cancer in which the tumour has already invaded the submucosa. Despite the advantages of ESD in the treatment of gastric cancer, its curative resection rate still needs to be improved. It was found that the curative resection rate of ESD was about 79.5% [17]. One of the important reasons is the limitation of preoperative ultrasound endoscopy in locating the T-stage of tumour, which may lead to the discovery that the tumour has invaded the submucosal layer in some patients during postoperative pathological examination, thus affecting the surgical outcome. Therefore, in the future, the accuracy and comprehensiveness of preoperative diagnosis need to be strengthened along with the improvement of ESD surgical skills to ensure that patients can obtain better treatment results.

In this study, it was found that the disease control rate in the observation group was as high as 98.18%, which was higher than the 88.89% in the control group, but the difference between the disease control rates of the two groups was not statistically significant, which may be related to the small sample size included in this study. It is now generally accepted that regardless of the form of surgery, a certain degree of trauma is inevitable, and this trauma is closely linked to changes in postoperative serum inflammatory factors. Among these, IL-6 is a key pro-inflammatory factor that plays a central role in the immune response and triggers the body to release more inflammatory factors.IL-12 is a class of inflammatory factors produced by immune cells, with roles such as activating and modulating immune cells and transducing inflammatory signals.TNF-α also plays an important role in anti-infective, anti-tumour, and immunomodulatory aspects, and surgical trauma increases its release, thereby increasing the risk of infection [18-19]. Therefore, how to effectively inhibit the postoperative inflammatory response is crucial for the treatment of elderly patients with early gastric cancer. In this study, it was found that the operation time, postoperative exsufflation and postoperative hospitalisation time of the observation group were shorter than those of the control group, suggesting that the use of endoscopic submucosal dissection for the treatment of early gastric cancer in the elderly can significantly shorten the operation time, postoperative exsufflation and

postoperative hospitalisation time, which is beneficial to the postoperative recovery, and the postoperative inflammatory response can be effectively suppressed. The postoperative serum IL-6, IL-12, TNF-α levels and VAS scores at all time points were significantly lower than those of the control group, and the incidence of perioperative complications was also significantly lower than that of the control group, which was consistent with previous reports. The reasons for this may be: (1) Early gastric cancer lesions do not break through the mucosal base and usually do not have lymph node metastasis, endoscopic submucosal dissection not only can accurately resect the primary tumour lesion, but also can completely preserve the anatomical structure and physiological function of the patient's stomach [20], so it can significantly reduce the postoperative pain, and has a facilitating effect on postoperative recovery in the elderly patients with EGC. postoperative recovery. (2) Endoscopic submucosal dissection is centred on gastrointestinal polypectomy, which can effectively resect lesions with a diameter of more than 2 cm. This procedure is less traumatic than radical gastrectomy for gastric cancer, and there is no need for gastric partial resection and gastrointestinal tract reconstruction during the operation, so it has the advantages of minimal intraoperative blood loss, low trauma, and a low incidence of complications, and its therapeutic efficacy is precise and reliable. The procedure is performed endoscopically, using high-frequency electrosurgical instruments, which can accurately and completely remove the tumour, avoiding the residual tumour caused by multiple cuts. At the same time, endoscopic submucosal dissection can protect the normal tissues around the lesion, reduce postoperative inflammatory reaction, and reduce the risk of adhesion of abdominal organs and other risks [21]. (3) Laparoscopic radical gastrectomy for gastric cancer has a long surgical operation time, and intraoperatively it is necessary to anastomose the residual stomach with the small intestine, and then make the flow of food into the distal end of the anastomosis through the gastric tube, so it will prolong the time of postoperative venting and even the time of tube removal, which affects the process of postoperative recovery. However, this study also found that the complete resection rate of the tumour in the

observation group was lower than that in the control group, which was attributed to the fact that laparoscopic radical gastrectomy for gastric cancer could achieve complete resection of the lesion laparoscopically, and at the same time carry out the perigastric lymph node dissection [22], so that the complete resection rate as well as the curative resection rate were higher. This study also found that the median follow-up was 27.4 months in the observation group and 26.8 months in the control group, and the cumulative survival rate of the observation group (98.18%) was higher than that of the control group (93.33%), but there was no significant difference between them, suggesting that the two different surgical modalities can achieve a more satisfactory prognosis, but the impact on the long-term prognosis of the patients still needs to be further studied.

CONCLUSION

the use of endoscopic mucosal stripping for the treatment of early gastric cancer in the elderly can improve the therapeutic efficacy, promote postoperative recovery, reduce the degree of postoperative inflammatory response and pain, reduce perioperative complications, and have a better prognosis in the near future. However, it should be noted that endoscopic mucosal dissection for the treatment of early gastric cancer in the elderly is relatively complex, with a long learning curve and high requirements for the operator, so clinical attention should be paid to training doctors and trying to improve their operation skills, which will in turn improve the efficacy of the surgical treatment of early gastric cancer in the elderly and improve their prognosis.

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