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*Retrospective Cohort Study*

# 3D laparoscopic-assisted *vs* open gastrectomy for carcinoma in the remnant stomach: a retrospective cohort study

Di Wu, Qi-Ying Song, Xiong-Guang Li, Tian-Yu Xie, Yi-Xun Lu, Ben-Long Zhang, Shuo Li, Xin-Xin Wang

**Abstract**

BACKGROUND

3D laparoscopic technique is gradually applied in the treatment of carcinoma in the remnant cancer, but its clinical efficacy remains controversial.

AIM

To explore its clinical efficacy by comparing the short-term and long-term results of 3D laparoscopic-assisted gastrectomy (3DLAG) with open gastrectomy (OG) for carcinoma in the remnant stomach.

METHODS

The clinical data of patients diagnosed with carcinoma in the remnant stomach(CRS) and admitted to the First Medical Center of Chinese PLA General Hospital from January 2016 to January 2021 were retrospectively collected. A total of 84 patients who met the inclusion and exclusion criteria were enrolled in this study. All their clinical data were collected in detail and a database was established. All patients were treated with 3DLAG or OG by experienced surgeons and were divided into two groups based on the different operation methods mentioned above. By using outpatient and

telephone follow-up, we were able to determine postoperative survival and tumor status. The postoperative short-term efficacy and 1-year and 3-year overall survival rates were compared between the two groups.

RESULTS

Among 84 patients with CRS, 48 patients were treated with OG and 36 patients were treated with 3DLAG. All patients successfully completed surgery. There was no statistically significant difference between the two groups in terms of age, gender, BMI, ASA score, initial disease state (benign or malignant), primary surgical anastomosis method, interval time of carcinogenesis, and tumorigenesis site. Patients in the 3DLAGC group had experienced less intraoperative blood loss (188.33±191.35 mL *vs* 305.83±303.66 mL; $P = 0.045$) and smaller incision (10.86±3.18 cm *vs* 20.06±5.17 cm; $p < 0.001$) than those in the OG group, the difference had statistical significance. 3DLAGC was a more minimally invasive operation method. Meanwhile, 3DLAGC retrieved significantly more lymph nodes than OGC (14.00±7.17 *vs* 10.73±6.82; $P = 0.036$), whereas the number of positive lymph nodes did not differ between the two groups (1.56 ±2.84 *vs* 2.35 ±5.28; p=0.413). The complication rate (8.3% *vs* 20.8%; $P = 0.207$) and ICU admission rate (5.6% *vs* 14.5%; $P = 0.372$) were equivalent between the two groups, and the difference didn't reach statistical significance. In terms of postoperative recovery, 3DLAGC group had a lower visual analogue score (VAS), shorter indwelling time of gastric tube and drainage tube, shorter time of early off-bed motivation, shorter time of postoperative initial flatus and initial soft diet intake, shorter postoperative hospital stays and total hospital stays, and there were statistically significant differences, showing better short-term efficacy. The 1-year and 3-year overall survival rates of OGC group were 83.2% (95%CI 72.4%-95.6%), 73.3% (95%CI 60.0%-89.5%) respectively. While the 1-year and the 3-year overall survival rate of 3DLAGC group were 87.3% (95%CI 76.4%-99.8%),75.6% (95%CI 59.0%-97.0%) respectively. However, the 1-year OS rate and 3-year OS rate were statistically similar between the two groups, this suggested the long-term survival results were comparable between the two groups ($P = 0.68$).

CONCLUSION

Compared with open gastrectomy, 3D laparoscopic-assisted gastrectomy for carcinoma in the remnant cancer can achieve better short-term efficacy and equivalent oncological results without increasing the clinical complications. In conditional medical centers, 3D laparoscopic-assisted gastrectomy for CRS can be promoted safely and effectively in selected patients .

**Key Words:** Carcinoma in the remnant stomach; Remnant gastric cancer; 3D laparoscopic-assisted gastrectomy; Open gastrectomy; Safe; Effective

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**Core Tip:** The application of minimally invasive surgery in carcinoma in the remnant stomach(CRS) is seriously affected by factors such as abdominal adhesion, anatomical displacement and unclear landmark caused by previous partial gastrectomy. Most of previous studies were case series or small sample studies. This study explored the therapeutic efficacy of 3D laparoscopic-assisted gastrectomy *vs* open gastrectomy for CRS. 3D laparoscopic-assisted gastectomy has shown obvious short-term advantages and equivalent long-term oncological efficacy in the treatment of carcinoma in the remnant stomach without increasing the incidence of complications. This study provides evidence-based medical support for the treatment of CRS by 3D laparoscopic-assisted gastectomy.



## INTRODUCTION

Remnant gastric cancer(RGC) is initially defined as carcinoma arising in the residual stomach after gastrectomy for benign or malignant disease. The incidence of

remnant gastric cancer is about 2%-3%, which is a relatively rare disease in the clinic[1,2,3]. However, as the long-term survival rate of patients with gastric cancer improves due to early detection and individual comprehensive therapy, the incidence of RGC is gradually increasing. As a unique type of gastric cancer, RGC had gained increasing attentions in recent years. The Japanese Gastric Cancer Association (JGCA) proposed the broad nomenclature of carcinoma in the remnant stomach (CRS), which contains new cancer, recurrent cancer, residual cancer, to replace the narrow definition of RGC[4].

At present, there is no consensus on the surgical and postoperative management of CRS. Completion gastrectomy of the remnant stomach combined with adequate lymph nodes dissection remains the mainstay treatment for resectable CRS [4,5,6]. In traditional opinion, most scholars believed that the history of upper abdominal surgery was relatively contraindicated for laparoscopic surgery, and patients with remnant gastric cancer were treated with open surgery. With the development of minimally invasive techniques and equipment, three-dimensional (3D) laparoscopy is widely used in the treatment of gastric cancer, and displays advantages over two-dimensional (2D) laparoscopy and open surgery [7,8]. The emergence of three-dimensional (3D) laparoscopy has pushed minimally invasive surgery into the stereoscopic era. 3D laparoscopy provides a three-dimensional sense of depth and layerization that allows surgeons to obtain a field of vision similar to open surgery. At the same time, compared with open surgery, 3D laparoscopic surgery has a magnified view of local surgical field and gains a better and clearer anatomical structure, thus making it easier and more precise to perform the delicate procedures such as dissection, separate tissues, stop blood and ligate vessels, especially in complicated surgery. However, there are limited reports and studies about the application of 3D laparoscopic-assisted technique in the treatment of CRS. Our study retrospectively collected the clinical data of 3D laparoscopic-assisted and open surgery in the treatment of CRS, analyzed the short-term and long-term efficacy of two groups, and provided a reference for the minimally invasive treatment of CRS.

## MATERIALS AND METHODS

### Inclusion and exclusion criteria

This retrospective cohort study was conducted in the First Medical Center of Chinese PLA General Hospital in China, and it was approved by the ethics committee of the hospital. This study set the inclusion and exclusion criteria of patients as follows.

Inclusion criteria:1.Patients underwent function-preserving gastrectomy such as proximal or distal gastrectomy due to benign or malignant gastric lesions were diagnosed as carcinoma in the remnant stomach (CRS) including new cancer, recurrent cancer, residual cancer, multifocal cancer by preoperative gastroscopy and biopsy pathology; 2.The surgical method was open or 3D laparoscopic-assisted total residual gastrectomy for remnant gastric cancer; 3. The clinical and pathological data were complete; 4. The operation was performed by experienced doctors at least associate professor; 5. Patients and their relatives were fully aware of the surgical risks and signed the surgical informed consent.

Exclusion criteria: 1. Preoperative examination showed that CRS with distant metastasis such as liver, peritoneum, ovary and other metastases could not be radically resected; 2. Patients confirmed other malignant tumors simultaneously; 3. Patients underwent palliative gastrectomy or remnant stomach-jejunal anastomosis due to acute tumor complications such as hemorrhage, obstruction and perforation; 4. Partial resection or palliative resection of the residual stomach was performed during surgery; 5. Clinical data and pathological data of patients were missing or deficient; 6. Postoperative pathology confirmed high-grade epithelial neoplasia and other precancerous lesions; 7. Patients received systemic chemotherapy or local radiotherapy within 1 mo before surgery.

### Patients

A total of 102 patients with CRS who underwent gastrectomy in the First Medical Center of Chinese PLA General Hospital from January 2016 to January 2021 were retrospectively collected. Among them, 8 patients underwent subtotal resection of the

remnant stomach, 7 patients were pathologically confirmed as precancerous lesions after surgery, and 3 patients underwent palliative surgery due to acute complications, thus a total of 18 patients were excluded from this study. Finally, a total of 84 patients with CRS were enrolled in this study and divided into two groups according to different surgical methods. Of them, 48 patients underwent open gastrectomy (OG) for CRS , whereas 36 patients underwent 3D laparoscopic-assisted gastrectomy (3DLAG) for CRS (Figure 1).

2.3. Observation indicators

The basic information of all patients who met the inclusion and exclusion criteria were collected based on the hospital records, including gender, age, body mass index (BMI), ASA score (ASA Physical Status Classification system), initial gastric disease status (benign or malignant), operation type of initial gastrectomy, interval time from surgery to occurrence of CRS, tumor site (anastomotic or non-anastomotic), *etc.* The surgical information included surgical methods (3D laparoscopic-assisted or open surgery), grade of abdominal adhesions, operation time, intraoperative blood loss *etc.* The postoperative information included gastric tube removal time, time to first soft diet intake, time to first off-bed ambulation, time to first flatus and defecation, time to remove the drainage tube, visual analogue score (VAS) of postoperation (day1, day3 and day5), intensive care unit (ICU) stay, postoperative hospital stay, total hospital stay. Postoperative pathological information included pathological type, total number of harvested lymph nodes, number of positive lymph nodes, TNM stage. Perioperative complications were registered and collected according to the Clavien-Dindo classification system.

2.4. Surgical procedures

No matter 3D laparoscopic-assisted or open surgery for CRS, the common procedures of radical gastrectomy for remnant gastric cancer are adhesiolysis, lymph node dissection, total resection of the remnant stomach and digestive tract reconstruction. It's a great challenge for surgeons to perform adhesiolysis of CRS surgery. Severe adhesion always is a major cause of unplanned organ injury or

combined resection. Laparotomy for remnant gastric cancer usually chooses the middle incision of the upper abdomen, but it is necessary to pay attention to the adhesion of the small intestine under the abdominal wall to avoid unnecessary injury. For regular laparoscopic-assisted gastrectomy of gastric cancer, 1 centimeter below the navel is always selected to be the location of the observation port. However, the location of the observation port needs to be changed according to abdominal adhesions caused by upper-abdomen operation history in order to avoid unplanned intra-abdominal organs injury. The right lower-abdomen area was recommended as the optimum site of observation port during surgery for gastric remnant cancer. The other trocars could be subsequently inserted carefully under visualization. Sometimes, you also can choose the left upper abdomen as the site of observation port and then as the main operating port. When the initial operation was distal gastrectomy, lymph nodes dissection around the celiac axis, proximal splenic artery and paracardial nodes were routinely performed, and the left gastric artery was ligated at its base if it had been reserved. When proximal gastrectomy was performed before, it is necessary to open the esophageal hiatus of the diaphragm and fully dissect the lower segment of the esophagus in order to obtain sufficient cutting edge and facilitate follow-up anastomosis. Meanwhile, the lymph nodes dissection around the celiac axis, infra-pyloric and supra-pyloric areas were routinely performed. Roux-en-Y anastomosis was the regular method of digestive tract reconstruction using circular stapler.

2.5. Follow-up

Postoperative follow-up was performed by outpatient and telephone to investigate the postoperative survival data and tumor conditions of the patients. The overall survival was defined as the time from radical operation of remnant gastric cancer to death due to any cause or last time of follow-up. The follow-up time was up to December 2021.

2.6. Statistical analyses

All observation indicators were included and a database of patients with CRS was established. All data were processed and analyzed using IBM SPSS Statistics 25 and R

(Version.4.2.2) software. Continuous variables were analyzed using the t-test or Mann-Whitney U test; the latter was used for variables that did not meet the criteria for positivity and homogeneity. Categorical variables were compared using the chi-square test or Fisher's exact probability test. Overall survival was estimated using the Kaplan-Meier method, and curves were compared using the log-rank test. P-value < 0.05 was considered statistically significant.

## RESULTS

### Patients' characteristics

The demographic and clinicopathological characteristics and initial gastrectomy information of the 3D laparoscopic assisted gastrectomy for CRS(3DLAGC) group compared with those of the open gastrectomy for CRS(OGC) group were summarized in Table 1. In this study, there were more males than females with remnant gastric cancer with a male-to-female ratio of 7.4:1. Among the reasons for initial gastrectomy, patients with benign diseases accounted for 39.3%, mainly due to gastrointestinal ulcerative diseases, while patients who performed gastrectomy due to malignant tumors accounted for 60.7% in the initial surgery. Main digestive tract reconstruction methods for distal gastrectomy included Billroth-I anastomosis, Billroth-II anastomosis, and Roux-en-Y anastomosis, accounting for 33.3%, 50.0%, and 6.0%, respectively. The main anastomosis method of proximal gastrectomy was esophageal residual gastric tube-like anastomosis, accounting for 10.7%. No patient underwent proximal gastrectomy with double tract anastomosis in this study. The interval time is generally considered to be the time from primary gastrectomy to the occurrence of adenocarcinoma in the remnant stomach. Patients with benign gastric ulcer who underwent partial gastrectomy, the interval time of CRS took longer than those with malignant gastric disease (415.64 months *vs* 98.16 mo ). However, there was no statistically significant difference in the interval time between the OGC group and the 3DLAGC group (211.56±197.35 months vs 237.97±209.01 months; p=0.556). According to our study, the incidence of CRS occurring at anastomotic stoma was higher than that at

non-anastomotic stoma, and the ratio was 1.47:1. However, there were no statistically significant differences in age, gender, BMI, disease status of the initial surgery, reconstruction method of the initial surgery, interval time from the initial surgery to the occurrence of remnant gastric cancer, and location of remnant gastric cancer between two groups in this study.

Surgical outcomes and postoperative recovery

Clinical data of intraoperative and postoperative recovery in patients with CRS in the 3DLAGC group compared with the OGC group were shown in Table 2. The initial surgical operation often causes the adhesion of residual stomach, anastomotic stoma and surrounding tissues, thus affecting the exposure of anatomical level. One of the difficulties in the surgical resection of remnant gastric cancer is intra-abdominal adhesion. Abdominal adhesions grade 2 and grade 3 were found in the majority of patients in both groups, with no significant difference between the two groups ($P$ = 0.098). The mean operative time was less in the OGC group than in the 3DLAGC group (215.67 minutes vs 243.11minutes), but the difference between the two groups was not statistically significant ($P$ = 0.075). 3DLAGC group had less intraoperative blood loss (188.33±191.35 ml vs 305.83 ±303.66 ml; $P$ = 0.045); meanwhile, 3DLAGC group had shorter surgical incision (10.86±3.18 *vs* 20.06±5.17; p < 0.001), which was minimally invasive, and the difference had statistical significance. In terms of postoperative recovery, the 3DLAGC group had a lower pain score according to Visual Analogue Score (VAS) on day 1, day 3 and day 5 after surgery(p<0.001). The indwelling time of gastric tube and drainage tube, the time of early off-bed motivation, the time to first flatus, the time to first soft diet intake, postoperative hospital stay and total hospital stay in the 3DLAGC group were shorter than OGC group, and the differences had statistical significance (p< 0.001). There was no statistically significant difference in the incidence of complications ($P$ = 0.372) and ICU admission rate ($P$ = 0.207) between the two groups.

Pathology results

Table 3 depicts the pathological results for the 3DLAGC and the OGC group. There were no significant differences between the two groups in postoperative pathological type, tumor size, tumor invasion depth or lymph node metastasis. However, the 3DLAGC group exhibited a certain advantage in peri-gastric lymph node dissection. Total numbers of lymph nodes retrieved by 3DLAG were significantly higher than OG, and the difference had statistical significance (14.00±7.17 *vs* 10.73±6.82; $P$ = 0.036).

Survival results

Figure2 depicted the survival results of the two groups. The median follow-up duration of of OGC group was 34 mo, while 27 mo for 3DLAGC.The 1-year and 3-year overall survival rate of the OGC group were 83.2% (95%CI 72.4%-95.6%), 73.3% (95%CI 60.0%-89.5%) respectively. While the 1-year and the 3-year overall survival rate of the 3DLAGC group were 87.3% (95%CI 76.4%-99.8%),75.6% (95%CI 59.0%-97.0%) respectively. However, these overall survival rates did not differ significantly between the two groups (P=0.68).

## DISCUSSION

Remnant gastric cancer (RGC), first described by Balfour in 1922, is defined as a carcinoma occurring in the remnant stomach after partial gastrectomy for peptic ulcer disease[9]. Since then, remnant gastric cancer had been gradually known as a unique disease. In 1998, the concept of carcinoma in the remnant stomach (CRS) was initially proposed and continuously used by the Japanese Gastric Cancer Association (JGCA) [10]. It was widely accepted that the adenocarcinoma occurring in the remnant stomach after gastrectomy was called CRS, regardless of whether the initial disease was benign or malignant as well as the interval time.

As a subtype of gastric cancer with unique characteristics, the incidence of CRS showed a male advantage with a male-to-female incidence ratio of 3.1:1 [11]. In our study, CRS was also more common in males, but the incidence ratio of male-to-female was 7.4:1, which was higher than the ratio reported in previous literatures. Several studys clearly indicated that the remnant stomach after gastrectomy had high risk of

developing CRS, and the anastomosis had higher prevalence to develop stump carcinomas in a shorter time interval than other site of remnant stomach [12-14]. It has also been shown that CRS tended to arise from the sites of anastomosis in patients treated with Billroth II reconstruction, in contrast to non-anastomotic sites in patients treated with Billroth I reconstruction[5,15,16]. In our study, carcinoma in the remnant stomach occurred at the anastomotic site accounted for about 59.5%, of which operated with Billroth-I reconstruction accounted for 32% while Billroth-II anastomosis accounted for 52%, which was consistent with the epidemiological characteristics of previous studies.

Intra-abdominal adhesions and anatomical displacement presented significant challenges for surgeons in both open gastrectomy and laparoscopic gastrectomy for remnant gastric cancer [17,18,19]. Extensive and intensive intra-abdominal adhesions due to the previous surgery significantly may prolong the operation time, increase intraoperative blood loss, even lead to unplanned collateral damage to the surrounding tissues and organs. In our study, the degree of abdominal adhesions were macroscopically inspected and scored using Knightly's grading system for assessment of the intensity and Linsky's grading system for assessment of the extent of adhesions[20]. Almost 13.1% of patients had abdominal adhesion with grade 4, which may lead to unplanned damage to peripheral organ. While majorities of patients with CRS, approximately 56%, had abdominal adhesion below grade 3, where the abdominal adhesion mainly existed in was the previous operation area. However, there was no statistical difference in abdominal adhesions between the 3DLAGC group and the OGC group ($P$ = 0.098). The first successful application of laparoscopic surgery in the treatment of remnant gastric cancer was reported by Yamada H *et al* in 2005 [17]. Other reports had recently shown the ever increasing feasibility and safety of laparoscopic assisted gastrectomy for remnant gastric cancer, in some cases even proving superior to traditional open surgery[18,19]. However, Professor Sang-Yong Son suggested that though laparoscopic completion total gastrectomy was technically feasible, it didn't show a definite clinical advantage over laparotomy in the treatment of remnant

gastric cancer [21]. With the application of 3D laparoscopy in the treatment of CRS, it had shown many advantages in the separation of abdominal adhesion. An outstanding advantage of laparoscopic surgery was that the establishment of carbon dioxide pneumoperitoneum could make the connective tissue space appear clearly and made it possible to identify the correct dissection layer[22]. In addition, 3D laparoscopy overcomed the disadvantages of traditional laparoscopy, such as lack of sense of space and distance, presenting a stereoscopic vision closer to open surgery[23]. However, compared with open surgery, the enlarged surgical field of 3D laparoscopy displayed the anatomical structure more clearly, which was more conducive to delicate operation, easier to find the correct anatomical level, resulted in less surgical bleeding and adverse consequences. It also avoided unnecessary damage to surrounding tissues or organs due to adhesiolysis and decreased the probability of unplanned combined devisceration.

Our study found that 3DLAGC group showed obvious advantages in short-term postoperative outcomes. We attributed those advantages to the magnification effect, three-dimensional sense and spatial depth of the surgical field of 3D imaging technology. Because 3D laparoscopic surgery made it easier to achieve accurate anatomy, bare-bone important vessels and nerves, dissect perigastric lymph nodes and identify anatomical section correctly [24,25]. 3DLAGC group had less intestinal traction and flipping, less damage to surrounding tissues during adhesiolysis, less trauma and less inflammatory response. Enhanced recovery after surgery (ERAS) protocols have been effective in improving postoperative recovery after major abdominal surgeries[26,27]. All patients with CRS enrolled in this study underwent preoperative education and evaluation, intraoperative stretch socks for thrombosis prevention, intraoperative warmth, postoperative multi-mode analgesia, encouragement of early ambulation, and postoperative enteral and parenteral nutrition support, which were in line with ERAS protocols. But minimally invasive surgery was the cornerstone of ERAS. Take cosiderations of the difficulty in accomplishing necessary compliance to all protocol items, we hold the opinion that the patient got into the

management of ERAS as long as adopting some of the ERAS protocols.Through minimally invasive surgical methods, patients can remove the gastric tube and drainage tube early after surgery, thus reducing nausea, vomiting and other gastrointestinal reactions caused by gastric tube stimulation and reduce pain and discomfort caused by abdominal drainage tube. The early removal of gastric tube and drainage tube is beneficial to the early off-bed activity of patients, promoting the recovery of gastrointestinal function, facilitating the early eating of patients and accelerating the rehabilitation process of patients. In terms of lymph node dissection, the total number of dissected lymph nodes was more in the 3DLAGC group than OGC group, and the difference was statistically significant, which may be related to the visual magnification and flexibility in tight spaces. While the staging system of CRS was not yet to be established, it generally follow the TNM staging of primary gastric cancer. The amount of positive lymph nodes (pN) was key to determine the N staging, but inadequate lymph nodes harvested in patients with CRS might influence the predicting value of pN. Some research demonstrated the lymph node (LN) ratio (LNR) had significant prognostic value for patients with CRS[28]. When the retrieved lymph node (LN) count was less than 15, the LNR was superior to pN as an important and independent prognostic index of CRS[29]. In spite of the obvious postoperative short-time advantages shown by 3DLAGC, the long-term survival results were similar between the 3DLAGC group and OGC group with the 1-year OS rate and 3-year OS rate were comparable between the two groups.

Several limitations in our study warranted mention. Our study was a retrospective study, which indicated the potential for selection bias. What's more, the number of patients enrolled was relatively small. Prospective randomized controlled trials with large scales and multiple centers are needed in the future. Despite these limitations, our study illuminated the feasibility and efficacy of 3D laparoscopic-assisted gastrectomy for CRS and showed certain advantages over open gastrectomy in short-term postoperative outcomes.

## CONCLUSION

In summary, nowadays patients with gastric cancer can obtain long-term survival due to the application of comprehensive treatments, thus causing the incidence of CRS is bound to increase. Compared with open gastrectomy, 3D laparoscopic-assisted gastrectomy for CRS can achieve better short-term efficacy and equivalent oncological results without increasing the clinical complications. In conditional medical centers, 3D laparoscopic-assisted gastrectomy for CRS can be applied and promoted in selected patients.

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