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Efficacy and safety of anastomotic leak testing in gastric cancer: a randomized controlled trial

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Abstract

Background Anastomosis-related complications such as bleeding, leakage, and strictures, continue to be serious complications of gastric cancer surgery. Presently, these complications have yet to be reliably prevented. Here we design a comprehensive leak testing procedure which combines gastroscopy, air, and methylene blue (GAM) leak testing. We aimed to evaluated the efficacy and safety of the GAM procedure in patients with gastric cancer.

Methods Patients aged 18–85 years without an unresectable factor as confirmed via CT were enrolled in a prospective randomized clinical trial at a tertiary referral teaching hospital and were randomly assigned to two groups: intraoperative leak testing group (IOLT) and no intraoperative leak testing group (NIOLT). The primary endpoint was the incidence of postoperative anastomosis-related complications in the two groups.

Results 148 patients were initially randomly assigned to the IOLT group ($n = 74$) and to the NIOLT group ($n = 74$) between September 2018 and September 2022. After exclusions, 70 remained in the IOLT group and 68 in the NIOLT group. In the IOLT group, 5 patients (7.1%) were found to have anastomotic defects intraoperatively, which included anastomotic discontinuity, bleeding, and strictures. The NIOLT group had a higher incidence of postoperative anastomotic leakage compared to the IOLT group: 4 patients (5.8%) vs 0 patients (0%), respectively. No GAM-related complications were observed.

Conclusion The GAM procedure is an intraoperative leak test that can be performed safely and efficiently after a laparoscopic total gastrectomy. GAM anastomotic leak testing may effectively prevent technical defect-related anastomotic complications in patients with gastric cancer who undergo a gastrectomy.

Trial registration: Clinical Trials.gov Identifier: NCT04292496.

Keywords Anastomotic leakage · Gastric cancer · Leakage testing · Total gastrectomy · Gastroscopy

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Gastric cancer is the fifth most frequently diagnosed cancer and the fourth leading cause of cancer-related deaths [1]. In particular, the incidence of cancers originating from the proximal part of the stomach and cardia is increasing [2]. The primary treatment for gastric cancer is surgery [3], though anastomotic leakage (AL) is a serious complication after gastrectomy [4]. The incidence of AL after gastrectomy is 2.1–14.6%, and is associated with increased medical cost, length of hospital stay, postoperative morbidity, mortality, and recurrence rate [5–7]. Anastomotic leakage occurs mainly due to the technique being used, though the cause is complex with a variety of factors [8, 9]. Despite improvements in perioperative treatment of anastomotic leaks, the management continues to remain challenging and an optimal treatment protocol needs to be determined [10, 11].

Currently, detection of anastomotic continuity is done through air or methylene blue testing, with or without gastroscopy. Previous studies show conflicting results with the use of IOLT—some suggest reduction in postoperative anastomotic leakage [12–14], while others suggest no change from NIOLT [15, 16]. Furthermore, IOLT may cause trauma within the anastomosis, and methylene blue may contaminate the area, leading to adverse reactions or necrosis [17]. Thus, the potential of IOLT for risk reduction remains a topic of debate in the literature.

The precise techniques used in IOLT is widely variable. Previously reported techniques include (1) gastroscopy combined with air leak testing [18] and (2) air or methylene blue injection via nasogastric tube [19, 20]. We introduce a new IOLT technique combining gastroscopy with air and methylene blue leak testing (GAM). We hypothesized that this combined procedure will improve the efficacy of IOLT, and reduce the risk of postoperative anastomotic complications. To test this hypothesis, we conducted a single-center randomized clinical trial, comparing the incidence of postoperative anastomotic complications in patients with gastric cancer who underwent intraoperative leakage testing with GAM vs. those who did not undergo intraoperative leakage testing. The safety and efficacy of the GAM procedure were also evaluated through investigation of surgery duration, length of hospital stay, overall cost, and other surgical complications between the two groups.

Patients and methods

Study design

This study is an investigator-initiated, single center, randomized controlled trial from Nanchong Central Hospital. The study was approved by the Ethical Committee of Nanchong Central Hospital and conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all patients.

Sample size

The sample size was based on the assumption that incidence of anastomotic leakage after gastrectomy is less than 2.1% in the IOLT group and no GAM-related complications were observed at the end of 3 months. Using PASS15.0 (NCSS, Kaysville, Utah, USA) statistical software, we calculated that approximately 73 patients would be required in each group to achieve a power of 0.80 and a significant level of 0.05 to assess the difference between the two groups.

Patients

The trial enrolled patients aged 18–85 with gastric cancer who qualified for total gastrectomy. All patients had an Eastern Cooperative Oncology Group performance status score of 0 or 1; an American Society of Anesthesiologists class of I–III; and resectable gastric carcinoma according to the eighth edition of the TNM (clinical stages I–III) [21]. The exclusion criteria consisted of possible distant metastasis detected in the preoperative studies, past history of gastric resection, gastric cancer-related complications, other malignancy diagnosed within the previous 5 years, previous chemotherapy or radiation therapy for any malignancies, presence of obvious contraindications to surgery (e.g., liver and/or kidney function abnormalities), and any participation in another clinical trial within the past 6 months.

Objectives and endpoints

The primary endpoint was the incidence of postoperative anastomosis-related complications, in patients with gastric cancer who underwent gastrectomy with IOLT (using GAM) and without IOLT (NIOLT). The secondary endpoints were the average duration of the GAM procedure, surgical duration, length of hospital stay, overall cost, and other surgical complications in the two groups.

Randomization and masking

The investigators were responsible for the randomization. After the subject meets the inclusion and exclusion criteria and signs the informed consent form, the participators were randomly assigned to IOLT or NIOLT group via a central internet-based program running a computer-generated randomization sequence. District randomization method was used for randomization. Four adjacent patients in the same month of admission were taken as a block, and randomly divided into the trial group and the control group at a ratio of 1:1. The interval length was 4, and there were six permutation combinations. The permutation combination block numbers selected according to the random number table entered the IOLT or NIOLT group. The allocation result was communicated to the surgeons by the circulating nurses only after the completion of the anastomosis.

Surgical quality control, procedures, and follow-up

All surgeons taking part in the trial were required to have experience performing more than 100 gastrectomies for gastric cancer. All patients underwent a total gastrectomy with lymphadenectomy, conducted in accordance with the 2018 Japanese gastric cancer treatment guidelines (5th edition) [22]. Due to the difference of surgeon's habits and location of the tumor, reconstruction was done through Roux-en-Y esophagojejunostomy, either using linear stapler or round stapler and there was no significant difference between the two groups ($p > 0.05$). After the anastomosis is completed, proximal and distal anastomotic perfusion and anastomotic tension was carefully checked by observing the color of the small intestine, the pulsation of the marginal artery, and the tightness of the mesentery.

The GAM procedure used in the IOLT group consisted of (1) gastroscopy to observe the integrity of the anastomosis, (2) immersion of the anastomosis in 500–1000 mL warm saline and temporary blockage of the distal end, (3) inflation of the bowel of the anastomosis with air, and (4) injection of 60 mL methylene blue through the gastroscope. A white gauze pad was wrapped around the anastomosis to observe if methylene blue leaked out. Leakage testing was done using the Olympus GIF-170 gastroscope (Olympus America, Melville, NY), which has an 8.6-mm outer diameter.

Anastomotic discontinuity was diagnosed when air bubbles and/or methylene blue was observed at the staple line. This section was then strengthened with full-thickness simple suture and reinforced with Lembert sutures. The GAM procedure was repeated to verify the successful repair of the anastomosis before the surgery was completed. Anastomosis stricture was diagnosed if the gastroscopy could not go through the anastomosis. After surgery, patients were regularly followed using the following protocol to collect data [23, 24]: (1) daily measurements of the highest body temperature, heart rate, urine output, and respiratory rate until the day prior to discharge, (2) daily physical examinations to check for symptoms of peritonitis, intestinal obstruction, worsening surgical incision sites, and other surgical complications, (3) daily checks for drainage fluid (nature and amount, also sampled and cultured), (4) daily review of blood routine, biochemistry, CRP, and liver and kidney functions. One week after surgery, all patients underwent an upper gastrointestinal radiography to evaluate the integrity of the anastomosis. If extravasation of the contrast agent from the anastomosis was detected, a diagnosis of postoperative anastomotic leakage was made. Complications that occurred within 90 days after the surgery were considered to be related to the operation and recorded for this study [25]. Surgical complications were classified using the Clavien–Dindo classification [26].

Statistical analysis

Categorical variables are presented as numbers and percentages. Continuous variables are presented as means and standard deviations if normal distribution is observed. Continuous variables are presented as median (range or IQR) if normal distribution is not observed. The Student's t test was used to compare means; all outcomes were performed using conventional 2-tailed superiority hypothesis tests with $\alpha = 0.05$ and with 2-sided 95% CIs using IBM® SPSS® Statistics software (version 20, IBM Corporation, Armonk, NY, USA).

Results

Patients

From September 2018 to September 2022, 148 patients with gastric cancer or esophagogastric junction cancer were recruited. Patients were randomly assigned to the IOLT group ($n = 74$) and NIOLT group ($n = 74$). After randomization, 10 patients (IOLT $n = 4$; NIOLT $n = 6$) who did not undergo gastrectomy were excluded: five patients had distant metastases (IOLT $n = 2$; NIOLT $n = 3$), two patients deviated from the protocol (IOLT, $n = 1$; NIOLT $n = 1$), and three patients underwent surgical procedures other than a gastrectomy, such as palliative surgery (IOLT $n = 1$; NIOLT $n = 2$). After exclusions, 138 patients remained (IOLT $n = 70$; NIOLT $n = 68$; Fig. 1). The two study groups have balanced baseline clinical characteristics as shown in Table 1.

Intraoperative characteristics

In the IOLT group, 5 out of 70 patients (7.1%) who underwent a laparoscopic total gastrectomy had a positive GAM procedure test. Leakage was found in the anterior wall of the esophagojejunostomy in two patients, which was repaired with laparoscopic sutures. Anastomotic stricture was found in one patient, which was repaired with a repeat anastomosis. A bleeding artery in the esophagojejunostomy was found in two patients, which was controlled with laparoscopic sutures. The average duration of the GAM procedure was 4.90 ± 1.85 min. The average total operation duration in the IOLT group was 28 min longer than the NIOLT group ($p = 0.02$; Table 2).

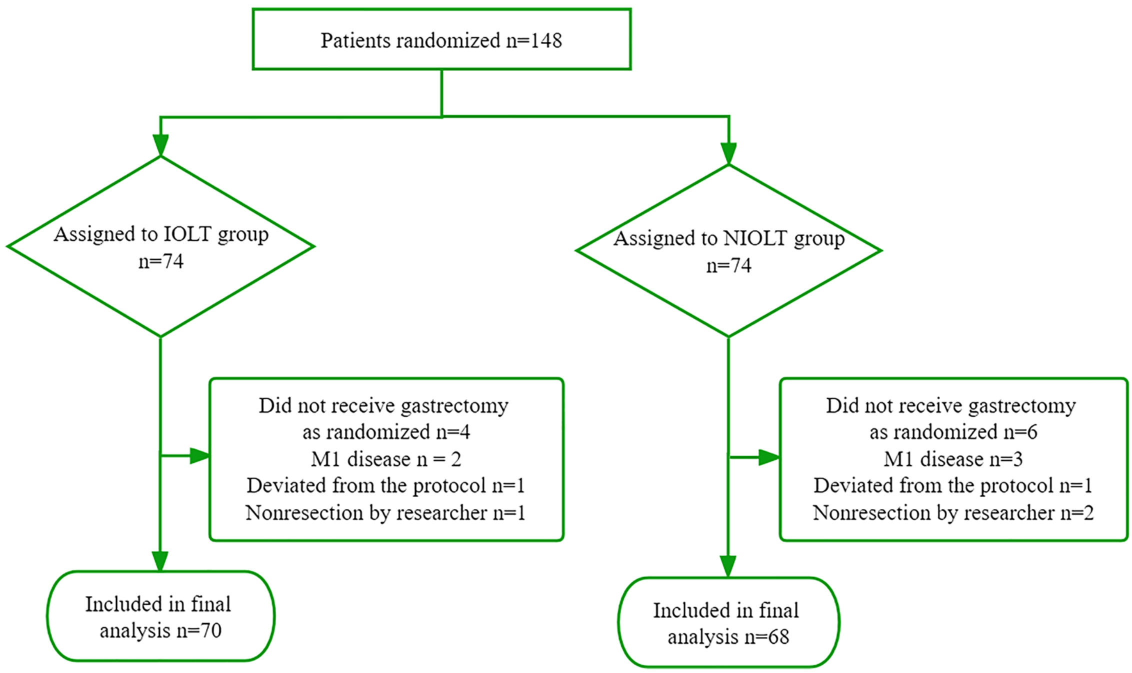

Fig. 1 Trial profile. Nonresection by researcher: patient underwent surgery other than gastrectomy; M1 disease found after opening of abdomen; organ metastases found

Surgical outcomes

After intraoperative repair of detected anastomotic discontinuities, the IOLT group had no patients with postoperative leakage. In the NIOLT group, four patients (5.8%) had postoperative anastomotic complications. One patient experienced bleeding requiring urgent endoscopic hemostasis, one patient had leakage, and two patient had anastomotic strictures. 1 week after surgery, all patients underwent an upper gastrointestinal radiography, which found anastomotic strictures in two patients and anastomotic leakage in one patient in the NIOLT group, and none in the IOLT group. Evidently, the IOLT group experienced less postoperative anastomotic complications compared to the NIOLT group ($p=0.04$, Table 2). However, according to the Clavien–Dindo classification, the incidence of the overall postoperative complications, did not significantly differ between the groups ($p=0.51$, Table 3).

Postoperative clinical characteristics

The length of hospital stay was 12.35 ± 1.6 days in the IOLT group and 12.6 ± 2.1 days in the NIOLT group ($p=0.34$). Patients with postoperative leaks had extended stays, with the longest hospitalization time being 31 days in the NIOLT group. The overall cost of hospitalization was higher in the NIOLT group compared to the IOLT group (11,025.04 ± 1146.05 vs. 9947.05 ± 1036.42 US dollars, respectively, $p=0.51$), with the highest cost over 14,500 US dollars. The difference in cost was not statistically significant (Table 4).

Discussion

Anastomotic leakage is a common complication after radical resection for gastric cancer. It influences prognosis and is a significant risk factor for postoperative mortality [27].Various prevention strategies have been tested for anastomotic leakage. Advancements in surgical techniques, improvements in anatomical knowledge, and heightened awareness of risk factors and treatment options have all undoubtedly contributed to the decrease in incidence of, and mortality from, anastomotic leakage [28].

After a comprehensive literature review [18–20, 29], we designed the GAM procedure and assessed the safety and efficacy of it. This procedure requires both air and methylene blue to be injected through the gastroscope, which allowed inspection via gastroscopy to occur first. First, gastroscopy was used to obtain a clear and direct observation of the anastomotic staple line. Second, the air leak test was done to check for any defects in the anastomosis, with air bubbles being evidence for a defect. The injection of methylene blue was held off until the last step to preserve a clear view of the anastomosis. With a white gauze pad wrapped around

Table 1 Patient clinical characteristics

	IOLT (*n* = 70)	NIOLT (*n* = 68)	*p* value
Sex (male/female)	51/19	55/13	0.267
Age (years)	62.1 ± 9.3	61.7 ± 9.2	0.565
BMI (kg/m^2)	22.4 ± 2.8	22.3 ± 2.7	0.191
History of abdominal surgery (yes/no)	9/61	11/57	0.631
COPD (yes/no)	11/59	12/56	0.582
Hypertension (yes/no)	9/61	7/61	0.641
Diabetes (yes/no)	6/64	6/62	0.958
Anemia (yes/no)	29/41	30/38	0.751
Esophagogastric junction cancer	31 (44.2%)	28 (41.1%)	0.714
Tumor markers			
CA72-4 (positive/negative)	20/50	24/44	0.400
CA19-9 (positive/negative)	18/52	19/49	0.769
CEA (positive/negative)	21/49	23/45	0.632
Roux-en-Y esophagojejunostomy (linear stapler/round stapler)	32/38	31/37	0.988
Pathological T status			0.913
T1a	3 (4.2%)	4 (5.8%)	
T1b	2 (2.8%)	4 (5.8%)	
T2	11 (15.7%)	10 (14.7%)	
T3	16 (22.8%)	7 (10.2%)	
T4a	30 (42.8%)	33 (48.5%)	
T4b	8 (11.4%)	10 (14.7%)	
Pathological N status			0.691
N0	26 (37.1%)	28 (41.1%)	
N1	15 (21.4%)	16 (23.5%)	
N2	14 (20.0%)	8 (11.7%)	
N3	15 (21.4%)	16 (23.5%)	

Data for continuous variables are shown as mean ± standard deviation

BMI Body Mass Index, *COPD* Chronic Obstructive Pulmonary Disease, *CEA* carcinoembryonic antigen, *IOLT I*ntraoperative Leakage Testing, *NIOLT* No Intraoperative Leakage Testing

Table 2 Postoperative results

	IOLT (*n* = 70)	NIOLT (*n* = 68)	*p* value
Anastomosis-related complications	0 (0%)	4 (5.8%)	**0.04**
Anastomotic leakage	0 (0%)	1 (1.4%)	
Intraluminal bleeding	0 (0%)	1 (1.4%)	
Anastomotic stricture	0 (0%)	2 (2.9%)	
Lymph node dissection	27.4 ± 11.9	24.9 ± 10.6	0.16
Lymph node metastases	5.5 ± 7.9	5.0 ± 6.2	0.65
Maximum tumor diameter (cm)	4.3 ± 2.3	4.7 ± 2.3	0.27
Proximal margin length (cm)	3.1 ± 2.1	3.2 ± 2.5	0.78
Distal margin length (cm)	7.1 ± 3.9	6.1 ± 3.7	0.10
Length of hospital stay (days)	12.35 ± 1.6	12.6 ± 2.1	0.34
Average operative duration	301.7 ± 76.2	273.6 ± 80.1	0.02
Hospitalization cost (US dollars)	9947.05 ± 1036.42	11,025.04 ± 1146.05	0.51

Data for continuous variables are shown as mean ± standard deviation

IOLT Intraoperative Leakage Testing, *NIOLT* No Intraoperative Leakage Testing

Table 3 Postoperative overall complications

	IOLT ($n=70$)	NIOLT ($n=68$)	p value
Clavien–Dindo classification (n, %)			0.51
Grade I	30 (42.8%)	27 (39.7%)	0.71
Grade II	17 (24.2%)	15 (22.0%)	0.75
Grade III	2 (2.8%)	2 (2.9%)	0.97
Grade IV	0 (0%)	0 (0%)	N/A
Grade V	0 (0%)	0 (0%)	N/A
Details (n, %)			
Wound infection	3 (4.3%)	2 (2.9%)	0.67
Intra-abdominal effusion/abscess	10 (14.2%)	8 (11.7%)	0.66
Pancreatic fistula	3 (4.3%)	2 (2.9%)	0.67
Pneumonia	8 (11.4%)	9 (13.2%)	0.74
Hypoproteinemia	18 (25.7%)	15 (22.0%)	0.62
Ileus/motility disorder	2 (2.8%)	1 (1.4%)	0.58
Intraluminal bleeding	0 (0%)	1 (1.4%)	0.31
Anastomotic leakage	0 (0%)	1 (1.4%)	0.31
Anastomotic stricture	0 (0%)	2 (2.9%)	0.15
Pleural effusion	5 (7.1%)	3 (4.4%)	0.49

Data for continuous variables are shown as mean ± standard deviation

IOLT Intraoperative Leakage Testing, *NIOLT* No Intraoperative Leakage Testing

Table 4 Comparison of hospital stay and hospital costs

	Anastomosis-related complications occurred ($n=4$)	No anastomosis-related complications occurred ($n=134$)	p value
Length of hospital stay (days)	22.6 ± 1.14	12.7 ± 2.36	0.012
Hospitalization cost (US dollar)	13,284.02 ± 1181.03	10,132.15 ± 1067.16	0.000

Data for continuous variables are shown as mean ± standard deviation

the anastomosis, injection of methylene blue would dye the gauze pad blue if any defects existed in the anastomosis.

The primary findings from this study are as follows: (1) anastomotic discontinuities using the GAM procedure was detected in 7.1% of the IOLT group, (2) postoperative leakage incidence was lower in the IOLT group than the NIOLT group (0% vs. 5.8%, $p=0.04$), with no complications associated with anastomotic leakage testing, (3) the average duration of the GAM procedure was 4.90 ± 1.85 min, and (4) the average operation duration in the IOLT group was 28 min longer than the NIOLT group. Our study shows that the GAM procedure is safe and effective at preventing postoperative anastomosis-related complications in patients with gastric cancer. Several studies have demonstrated the value of anastomotic leakage testing through intraoperative endoscopy in colorectal and bariatric surgery. Li and Wexner et al. reported that routine intraoperative endoscopy in laparoscopic colorectal surgery aids in the prevention of anastomotic failure [30]. In laparoscopic Roux-en-Y gastric bypass and sleeve gastrectomy, intraoperative endoscopy has been introduced as a surgical strategy to prevent leakage and stenosis [31, 32]. Reports of intraoperative endoscopy in gastric cancer surgery come from localization studies in laparoscopic gastrectomy and laparoscopic endoscopic cooperative surgery [33, 34]. Few papers have discussed anastomotic leak testing after gastrectomy for gastric cancer. Lieto et al. reported endoscopic intraoperative anastomotic testing to be a safe and reliable method to assess the integrity of gastric and colonic anastomoses [18]. However, there lacks any large-scale, prospective research to confirm the safety of this technology. We conducted a randomized controlled study with 138 patients who underwent total gastrectomy reconstructed by laparoscopic Roux-en-Y esophagojejunostomy. To maximize homogeneity and to avoid bias, this study adopted a strict inclusion criteria. Patients receiving chemotherapy were excluded from the study.

In our study, early anastomotic complications included leakage, stricture, and bleeding. Postoperative anastomotic complications were avoided in the IOLT group, where discontinuity was repaired by suture ligation. One study has suggested that intraoperative methylene blue leak testing prevents postoperative anastomotic leakage [35]. However, its reliability in IOLT has not been verified. Furthermore, findings from Sethi et al. demonstrated the use of methylene blue leak testing to not prevent anastomotic leakage [16].

Anastomotic discontinuities were found in five patients (7.1%) in the IOLT group, which is similar to previous literature findings. Kanaji et al. reported that the IOLT positive rate was 3.2% for patients with gastric cancer. Air leakage testing was adopted in their study [19]. Nishikawa et al. found that the IOLT positive rate was 4.2% for patients with gastric cancer. Gastroscopy combined with air leakage testing was adopted in their study [29].

Surgeons have strategically used drain placements, drainage fluid checks (for characteristic and amount), and routine postoperative upper gastrointestinal radiography, for early detection of leaks [36]. Though these methods are helpful in identifying leaks in the early postoperative period, they do not prevent the occurrence of them. By performing the GAM procedure in our study, we were able to not only detect the anastomotic discontinuities intraoperatively, but also take preventative measures for anastomotic leakage. As anastomotic leaks are damaging and a serious issue, every preventative effort is worthwhile. Routine IOLT during operations will detect and repair anastomotic defects, enabling patients to avoid serious complications such as bleeding, leakage, and abdominal infection postoperatively [37]. One study found that treatment for serious complications accounted for 27.0% of the total hospital cost [38].

We have been able to establish the safety and efficacy of using the GAM procedure in laparoscopic total gastrectomy. None of the 68 patients in the IOLT group experienced anastomotic insufficiency or IOLT-related complications in the postoperative period. More clinical studies are required to identify the role of the GAM procedure in reducing the rate of anastomotic insufficiency in different parts of the gastrointestinal tract.

There are unique aspects in our study. Firstly, the average BMI of the patients was low, and further research is needed for patients with gastric cancer and high BMI. Secondly, according to Japanese gastric cancer treatment guidelines 2018 5th edition, patients with cT2-4 lesions could directly undergo surgery without neoadjuvant therapy [22]. At our research center, patients (including T4a/T4b) who were considered capable of complete tumor resection based on preoperative examination were given priority for surgical treatment followed by postoperative adjuvant therapy. However, patients with T4a or T4b lesion would have received preoperative in Western populations.

This study does have some limitations. First, it is a single-center study with a relatively small sample size. It also does not assess whether the GAM procedure is the simplest or most optimal method of leak detection. Specifically, the GAM procedure did not have precise control of the air inflation pressure, as high-power insufflation can lead to mechanical destruction of the staple lines and produce a falsely high air leak rate. Additional data collection with well-designed prospective multicentric studies is needed to overcome these limitations, and to confirm the safety and efficacy of the GAM procedure in gastric cancer surgery. Second, compared to other studies of minimally invasive surgery, the length of hospital stay was over 12 days in both groups, which may be a general problem in our research center.

In summary, the GAM procedure appears to be a safe and reliable procedure to evaluate the integrity of gastrointestinal anastomosis. It can be used as an important surgical strategy to avoid early anastomotic complications such as leakage and intraluminal bleeding. Routine GAM procedure is recommended for IOLT in esophagojejunostomy for gastric cancer surgery.

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Author contributions ZG and YT participated in the design of this study, and they both performed the statistical analysis. DB, XQ and YP carried out the study and collected important background information. ZG drafted the manuscript. All authors read and approved the final manuscript. YT, HL and LM carried out the concepts, design, definition of intellectual content, literature search, data acquisition, data analysis and manuscript preparation, LG and YT provided assistance for data acquisition and manuscript editing. MB and JH performed manuscript review. All authors have read and approved the content of the manuscript.

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Declarations

Disclosures Zhenguo Gao, Heng Luo, Longyin Ma, Dan Bai, Xiangzhi Qin, Matthew Bautista, Lei Gong, Yong Peng, Jiani Hu and Yunhong Tian have no conflicts of interest to disclose.

Human rights statement All procedures were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the 1964 Declaration of Helsinki and later versions.

Informed consent Informed consent for inclusion in the study was obtained from all patients.

References

1. Sung H, Ferlay J, Siegel RL, Laversanne M, Soerjomataram I, Jemal A, Bray F (2021) Global Cancer Statistics 2020: GLOBOCAN estimates of incidence and mortality worldwide for 36 Cancers in 185 Countries. CA Cancer J Clin 71:209–249

2. Rawla P, Barsouk A (2019) Epidemiology of gastric cancer: global trends, risk factors and prevention. Prz Gastroenterol 14:26–38
3. Japanese Gastric Cancer Association (2017) Japanese gastric cancer treatment guidelines 2014 (ver. 4). Gastric Cancer 20:1–19
4. Hyman N, Manchester TL, Osler T, Burns B, Cataldo PA (2007) Anastomotic leaks after intestinal anastomosis: it's later than you think. Ann Surg 245:254–258
5. Carboni F, Valle M, Federici O, Levi Sandri GB, Camperchioli I, Lapenta R, Assisi D, Garofalo A (2016) Esophagojejunal anastomosis leakage after total gastrectomy for esophagogastric junction adenocarcinoma: options of treatment. J Gastrointest Oncol 7:515–522
6. Deguchi Y, Fukagawa T, Morita S, Ohashi M, Saka M, Katai H (2012) Identification of risk factors for esophagojejunal anastomotic leakage after gastric surgery. World J Surg 36:1617–1622
7. Makuuchi R, Irino T, Tanizawa Y, Bando E, Kawamura T, Terashima M (2019) Esophagojejunal anastomotic leakage following gastrectomy for gastric cancer. Surg Today 49:187–196
8. Sparreboom CL, van Groningen JT, Lingsma HF, Wouters M, Menon AG, Kleinrensink GJ, Jeekel J, Lange JF (2018) Different risk factors for early and late colorectal anastomotic leakage in a nationwide audit. Dis Colon Rectum 61:1258–1266
9. Eriksen JR, Ovesen H, Gögenur I (2018) Short- and long-term outcomes after colorectal anastomotic leakage is affected by surgical approach at reoperation. Int J Colorectal Dis 33:1097–1105
10. Zheng YZ, Dai SQ, Shan HB, Gao XY, Zhang LJ, Cao X, Zhu JF, Wang JY (2013) Managing esophageal fistulae by endoscopic transluminal drainage in esophageal cancer patients with superior mediastinal sepsis after esophagectomy. Chin J Cancer 32:469–473
11. Lang H, Piso P, Stukenborg C, Raab R, Jähne J (2000) Management and results of proximal anastomotic leaks in a series of 1114 total gastrectomies for gastric carcinoma. Eur J Surg Oncol 26:168–171
12. Causey MW, Fitzpatrick E, Carter P (2013) Pressure tolerance of newly constructed staple lines in sleeve gastrectomy and duodenal switch. Am J Surg 205:571–574 (**discussion 574–575**)
13. Sekhar N, Torquati A, Lutfi R, Richards WO (2006) Endoscopic evaluation of the gastrojejunostomy in laparoscopic gastric bypass. A series of 340 patients without postoperative leak. Surg Endosc 20:199–201
14. Kligman MD (2007) Intraoperative endoscopic pneumatic testing for gastrojejunal anastomotic integrity during laparoscopic Roux-en-Y gastric bypass. Surg Endosc 21:1403–1405
15. Bingham J, Lallemand M, Barron M, Kuckelman J, Carter P, Blair K, Martin M (2016) Routine intraoperative leak testing for sleeve gastrectomy: is the leak test full of hot air? Am J Surg 211:943–947
16. Sethi M, Zagzag J, Patel K, Magrath M, Somoza E, Parikh MS, Saunders JK, Ude-Welcome A, Schwack BF, Kurian MS, Fielding GA, Ren-Fielding CJ (2016) Intraoperative leak testing has no correlation with leak after laparoscopic sleeve gastrectomy. Surg Endosc 30:883–891
17. Lee JH, Chang CH, Park CH, Kim JK (2014) Methylene blue dye-induced skin necrosis in immediate breast reconstruction: evaluation and management. Arch Plast Surg 41:258–263
18. Lieto E, Orditura M, Castellano P, Pinto M, Zamboli A, De Vita F, Pignatelli C, Galizia G (2011) Endoscopic intraoperative anastomotic testing may avoid early gastrointestinal anastomotic complications. A prospective study. J Gastrointest Surg 15:145–152
19. Kanaji S, Ohyama M, Yasuda T, Sendo H, Suzuki S, Kawasaki K, Tanaka K, Fujino Y, Tominaga M, Kakeji Y (2016) Can the intraoperative leak test prevent postoperative leakage of esophagojejunal anastomosis after total gastrectomy? Surg Today 46:815–820
20. Celik S, Almalı N, Aras A, Yılmaz Ö, Kızıltan R (2017) Intraoperatively mlue. Scand J Surg 106:62–67
21. O'Sullivan B, Brierley J, Byrd D, Bosman F, Kehoe S, Kossary C, Piñeros M, Van Eycken E, Weir HK, Gospodarowicz M (2017) The TNM classification of malignant tumours-towards common understanding and reasonable expectations. Lancet Oncol 18:849–851
22. Japanese Gastric Cancer Association (2021) Japanese gastric cancer treatment guidelines 2018 (5th edition). Gastric Cancer 24:1–21
23. Frouws MA, Snijders HS, Malm SH, Liefers GJ, Van de Velde CJH, Neijenhuis PA, Kroon HM (2017) Clinical relevance of a grading system for anastomotic leakage after low anterior resection: analysis from a National Cohort Database. Dis Colon Rectum 60:706–713
24. den Dulk M, Witvliet MJ, Kortram K, Neijenhuis PA, de Hingh IH, Engel AF, van de Velde CJ, de Brauw LM, Putter H, Brouwers MA, Steup WH (2013) The DULK (Dutch leakage) and modified DULK score compared: actively seek the leak. Colorectal Dis 15:e528-533
25. Ojima T, Nakamura M, Hayata K, Kitadani J, Katsuda M, Takeuchi A, Tominaga S, Nakai T, Nakamori M, Ohi M, Kusunoki M, Yamaue H (2021) Short-term outcomes of robotic gastrectomy vs laparoscopic gastrectomy for patients with gastric cancer: A Randomized Clinical Trial. JAMA Surg 156:954–963
26. Dindo D, Demartines N, Clavien PA (2004) Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240:205–213
27. Roh CK, Choi S, Seo WJ, Cho M, Kim HI, Lee SK, Lim JS, Hyung WJ (2021) Incidence and treatment outcomes of leakage after gastrectomy for gastric cancer: Experience of 14,075 patients from a large volume centre. Eur J Surg Oncol 47:2304–2312
28. Kim YI, Lee JY, Khalayleh H, Kim CG, Yoon HM, Kim SJ, Yang H, Ryu KW, Choi IJ, Kim YW (2022) Efficacy of endoscopic management for anastomotic leakage after gastrectomy in patients with gastric cancer. Surg Endosc 36:2896–2905
29. Nishikawa K, Yanaga K, Kashiwagi H, Hanyuu N, Iwabuchi S (2010) Significance of intraoperative endoscopy in total gastrectomy for gastric cancer. Surg Endosc 24:2633–2636
30. Li VK, Wexner SD, Pulido N, Wang H, Jin HY, Weiss EG, Nogeuras JJ, Sands DR (2009) Use of routine intraoperative endoscopy in elective laparoscopic colorectal surgery: can it further avoid anastomotic failure? Surg Endosc 23:2459–2465
31. Nimeri A, Maasher A, Salim E, Ibrahim M, Al Hadad M (2016) The Use of Intraoperative endoscopy may decrease postoperative stenosis in laparoscopic sleeve gastrectomy. Obes Surg 26:1398–1401
32. Al Hadad M, Dehni N, Elamin D, Ibrahim M, Ghabra S, Nimeri A (2015) Intraoperative endoscopy decreases postoperative complications in laparoscopic Roux-en-Y Gastric Bypass. Obes Surg 25:1711–1715
33. Kamiya S, Ohashi M, Ida S, Kumagai K, Nunobe S, Sano T, Hiki N (2018) Laparoscopic subtotal gastrectomy with a new marking technique, endoscopic cautery marking: preservation of the stomach in patients with upper early gastric cancer. Surg Endosc 32:4681–4687
34. Hiki N, Nunobe S, Matsuda T, Hirasawa T, Yamamoto Y, Yamaguchi T (2015) Laparoscopic endoscopic cooperative surgery. Dig Endosc 27:197–204
35. Nelson L, Moon RC, Teixeira AF, Jawad MA (2015) Methylene blue or upper GI, which is more effective for detecting leaks in gastric bypass patients? Surg Laparosc Endosc Percutan Tech 25:451–454
36. Quartararo G, Facchiano E, Scaringi S, Liscia G, Lucchese M (2014) Upper gastrointestinal series after Roux-en-Y gastric bypass for morbid obesity: effectiveness in leakage detection. A systematic review of the literature. Obes Surg 24:1096–1101

37. Tanizawa Y, Bando E, Kawamura T, Tokunaga M, Ono H, Terashima M (2010) Early postoperative anastomotic hemorrhage after gastrectomy for gastric cancer. Gastric Cancer 13:50–57
38. Goense L, van Dijk WA, Govaert JA, van Rossum PS, Ruurda JP, van Hillegersberg R (2017) Hospital costs of complications after esophagectomy for cancer. Eur J Surg Oncol 43:696–702