

World Journal of *Gastroenterology*

World J Gastroenterol 2021 May 14; 27(18): 2054-2250



EVIDENCE REVIEW

- 2054 Role of microbial dysbiosis in the pathogenesis of esophageal mucosal disease: A paradigm shift from acid to bacteria?

D'Souza SM, Houston K, Keenan L, Yoo BS, Parekh PJ, Johnson DA

REVIEW

- 2073 Immune disorders and rheumatologic manifestations of viral hepatitis

Maslennikov R, Ivashkin V, Efremova I, Shirokova E

MINIREVIEWS

- 2090 Neurological manifestations of hepatitis E virus infection: An overview

Jha AK, Kumar G, Dayal VM, Ranjan A, Suchismita A

- 2105 Stroma-targeting strategies in pancreatic cancer: Past lessons, challenges and prospects

Polani F, Grierson PM, Lim KH

- 2122 Magnetic resonance imaging-based artificial intelligence model in rectal cancer

Wang PP, Deng CL, Wu B

- 2131 Remaining issues of recommended management in current guidelines for asymptomatic common bile duct stones

Saito H, Kadono Y, Shono T, Kamikawa K, Urata A, Nasu J, Imamura H, Matsushita I, Tada S

ORIGINAL ARTICLE**Basic Study**

- 2141 Alleviation of acute pancreatitis-associated lung injury by inhibiting the p38 mitogen-activated protein kinase pathway in pulmonary microvascular endothelial cells

Zhang XX, Wang HY, Yang XF, Lin ZQ, Shi N, Chen CJ, Yao LB, Yang XM, Guo J, Xia Q, Xue P

- 2160 Partially hydrolyzed guar gum attenuates non-alcoholic fatty liver disease in mice through the gut-liver axis

Takayama S, Katada K, Takagi T, Iida T, Ueda T, Mizushima K, Higashimura Y, Morita M, Okayama T, Kamada K, Uchiyama K, Handa O, Ishikawa T, Yasukawa Z, Okubo T, Itoh Y, Naito Y

Retrospective Cohort Study

- 2177 Factors influencing the failure of interferon-free therapy for chronic hepatitis C: Data from the Polish EpiTer-2 cohort study

Janczewska E, Kolek MF, Lorenc B, Klapaczynski J, Tudrujek-Zdunek M, Sitko M, Mazur W, Zarębska-Michaluk D, Buczyńska I, Dybowska D, Czauż-Andrzejuk A, Berak H, Krygier R, Jaroszewicz J, Citko J, Piekarska A, Dobracka B, Socha Ł, Deroń Z, Laurans Ł, Białkowska-Warzecha J, Tronina O, Adamek B, Tomaszewicz K, Simon K, Pawłowska M, Halota W, Flisiak R

Retrospective Study

- 2193 Totally laparoscopic total gastrectomy using the modified overlap method and conventional open total gastrectomy: A comparative study

Ko CS, Choi NR, Kim BS, Yook JH, Kim MJ, Kim BS

- 2205 Radiofrequency ablation *vs* surgical resection in elderly patients with hepatocellular carcinoma in Milan criteria

Conticchio M, Inchingolo R, Delvecchio A, Laera L, Ratti F, Gelli M, Anelli F, Laurent A, Vitali G, Magistri P, Assirati G, Felli E, Wakabayashi T, Pessaux P, Piardi T, di Benedetto F, de'Angelis N, Briceño J, Rampoldi A, Adam R, Cherqui D, Aldrighetti LA, Memeo R

Clinical Trials Study

- 2219 Responses to faecal microbiota transplantation in female and male patients with irritable bowel syndrome

El-Salhy M, Casen C, Valeur J, Hausken T, Hatlebakk JG

Observational Study

- 2238 Standard *vs* magnifying narrow-band imaging endoscopy for diagnosis of *Helicobacter pylori* infection and gastric precancerous conditions

Cho JH, Jeon SR, Jin SY, Park S

ABOUT COVER

Editorial Board Member of *World Journal of Gastroenterology*, Ferenc Sipos, MD, PhD, Senior Lecturer, Head of Department, Department of Internal Medicine and Haematology, Semmelweis University, Szentkirályi Street 46, Budapest H-1088, Hungary. sipos.ferenc@med.semmelweis-univ.hu

AIMS AND SCOPE

The primary aim of *World Journal of Gastroenterology* (WJG, *World J Gastroenterol*) is to provide scholars and readers from various fields of gastroenterology and hepatology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online. WJG mainly publishes articles reporting research results and findings obtained in the field of gastroenterology and hepatology and covering a wide range of topics including gastroenterology, hepatology, gastrointestinal endoscopy, gastrointestinal surgery, gastrointestinal oncology, and pediatric gastroenterology.

INDEXING/ABSTRACTING

The WJG is now indexed in Current Contents®/Clinical Medicine, Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports®, Index Medicus, MEDLINE, PubMed, PubMed Central, and Scopus. The 2020 edition of Journal Citation Report® cites the 2019 impact factor (IF) for WJG as 3.665; IF without journal self cites: 3.534; 5-year IF: 4.048; Ranking: 35 among 88 journals in gastroenterology and hepatology; and Quartile category: Q2. The WJG's CiteScore for 2019 is 7.1 and Scopus CiteScore rank 2019: Gastroenterology is 17/137.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Ji-Hong Lin, Production Department Director: Yun-Xiaojuan Wu, Editorial Office Director: Ze-Mao Gong.

NAME OF JOURNAL

World Journal of Gastroenterology

ISSN

ISSN 1007-9327 (print) ISSN 2219-2840 (online)

LAUNCH DATE

October 1, 1995

FREQUENCY

Weekly

EDITORS-IN-CHIEF

Andrzej S Tarnawski, Subrata Ghosh

EDITORIAL BOARD MEMBERS

<http://www.wjgnet.com/1007-9327/editorialboard.htm>

PUBLICATION DATE

May 14, 2021

COPYRIGHT

© 2021 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Retrospective Study

Totally laparoscopic total gastrectomy using the modified overlap method and conventional open total gastrectomy: A comparative study

Chang Seok Ko, Nam Ryong Choi, Byung Sik Kim, Jeong Hwan Yook, Min-Ju Kim, Beom Su Kim

ORCID number: Chang Seok Ko 0000-0002-4155-4312; Nam Ryong Choi 0000-0002-7120-660X; Byung Sik Kim 0000-0001-9579-9211; Jeong Hwan Yook 0000-0002-7987-5808; Min-Ju Kim 0000-0003-4600-5352; Beom Su Kim 0000-0002-3656-2086.

Author contributions: Ko CS, Choi NR, Kim BS, Yook JH and Kim BS performed the literature search, conception and design, drafting of the article; Kim MJ performed the analysis and interpretation; all authors were involved in the critical revision and final approval of the article.

Institutional review board

statement: This study was approved by the Institutional Review Board of the Asan Medical Center (approval No. 2019-0702).

Informed consent statement:

Patients were not required to give informed consent for the study because the clinical data were obtained retrospectively after each patient agreed to treatment by written consent.

Conflict-of-interest statement: We have no financial relationships to disclose.

Data sharing statement: No

Chang Seok Ko, Nam Ryong Choi, Byung Sik Kim, Jeong Hwan Yook, Beom Su Kim, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, Seoul 05505, South Korea

Min-Ju Kim, Department of Clinical Epidemiology and Biostatistics, Asan Medical Center, University of Ulsan College of Medicine, Seoul 05505, South Korea

Corresponding author: Beom Su Kim, MD, PhD, Professor, Surgeon, Department of Surgery, Asan Medical Center, University of Ulsan College of Medicine, 88, Olympic-ro 43-gil, Songpa-gu, Seoul 05505, South Korea. bskim0251@naver.com

Abstract

BACKGROUND

Although several methods of totally laparoscopic total gastrectomy (TLTG) have been reported. The best anastomosis technique for LTG has not been established.

AIM

To investigate the effectiveness and surgical outcomes of TLTG using the modified overlap method compared with open total gastrectomy (OTG) using the circular stapled method.

METHODS

We performed 151 and 131 surgeries using TLTG with the modified overlap method and OTG for gastric cancer between March 2012 and December 2018. Surgical and oncological outcomes were compared between groups using propensity score matching. In addition, we analyzed the risk factors associated with postoperative complications.

RESULTS

Patients who underwent TLTG were discharged earlier than those who underwent OTG [TLTG (9.62 ± 5.32) vs OTG (13.51 ± 10.67), $P < 0.05$]. Time to first flatus and soft diet were significantly shorter in TLTG group. The pain scores at all postoperative periods and administration of opioids were significantly lower in the TLTG group than in the OTG group. No significant difference in early, late and esophagojejunostomy (EJ)-related complications or 5-year recurrence free and overall survival between groups. Multivariate analysis demonstrated that body

additional data are available.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Invited manuscript

Specialty type: Gastroenterology and hepatology

Country/Territory of origin: South Korea

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): B, B
Grade C (Good): C, C, C, C
Grade D (Fair): D, D
Grade E (Poor): 0

Received: January 27, 2021

Peer-review started: January 27, 2021

First decision: March 7, 2021

Revised: March 21, 2021

Accepted: April 20, 2021

Article in press: April 20, 2021

Published online: May 14, 2021

P-Reviewer: Balducci G, Garbarino GM, Laracca GG, Zhou XP

S-Editor: Gao CC

L-Editor: A

P-Editor: Liu JH



mass index [odds ratio (OR), 1.824; 95% confidence interval (CI): 1.029-3.234, $P = 0.040$] and American Society of Anaesthesiologists (ASA) score (OR, 3.154; 95%CI: 1.084-9.174, $P = 0.035$) were independent risk factors of early complications. Additionally, age was associated with ≥ 3 Clavien-Dindo classification and EJ-related complications.

CONCLUSION

Although TLTG with the modified overlap method showed similar complication rate and oncological outcome with OTG, it yields lower pain score, earlier bowel recovery, and discharge. Surgeons should perform total gastrectomy cautiously and delicately in patients with obesity, high ASA scores, and older ages.

Key Words: Laparoscopic surgery; Gastrectomy; Anastomosis; Stomach neoplasms; Totally laparoscopic total gastrectomy

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: The aim of the present study was to investigate the effectiveness and surgical outcomes of totally laparoscopic total gastrectomy (TLTG) using the modified overlap method compared with open total gastrectomy (OTG) using the circular stapled method. Although TLTG with the modified overlap method demonstrated similar complication rate and oncological outcome with OTG, it resulted in lower pain scores, and earlier bowel recovery and hospital discharge.

Citation: Ko CS, Choi NR, Kim BS, Yook JH, Kim MJ, Kim BS. Totally laparoscopic total gastrectomy using the modified overlap method and conventional open total gastrectomy: A comparative study. *World J Gastroenterol* 2021; 27(18): 2193-2204

URL: <https://www.wjnet.com/1007-9327/full/v27/i18/2193.htm>

DOI: <https://dx.doi.org/10.3748/wjg.v27.i18.2193>

INTRODUCTION

Laparoscopic total gastrectomy (LTG) is becoming increasingly used to treat upper or middle third gastric cancer because it shows earlier recovery and is considered less invasive[1-3]. Of the entire procedure of LTG, esophagojejunal reconstruction is the most crucial process. This is because the failure of esophagojejunostomy (EJ) such as leakage and stricture could induce the patients to suffer[4]. When performing EJ, EJ using linear stapler method is widely adopted due to its simplicity in comparison to the circular stapled method, such as overlap and functional method[5-9]. Nonetheless, the linear stapled method has a fundamental problem that it requires larger space to dissect around the distal esophagus than does the circular stapled method because the linear stapler needs to be inserted in the abdominal hiatus.

Recently, we developed a modified overlap method for totally LTG (TLTG) for overcoming these disadvantages of linear stapled method[10]. This method is performed with an intracorporeal side to side esophagojejunal anastomosis using a 45-mm linear stapler at 45° from the longitudinal direction of the esophagus (Figure 1). This procedure requires less dissection around abdominal esophagus; therefore, it can create a secure esophagojejunal anastomosis with reduced tension as circular stapled method.

Several studies have investigated the surgical outcomes of the TLTG compared with open total gastrectomy (OTG), including EJ-related complications[11,12]. However, to the best of our knowledge, there are few studies which compared TLTG with the overlap method and OTG with circular stapled method including oncological outcome.

The aim of the present study was to investigate the technical feasibility and oncological outcome of TLTG with the modified overlap method when compared with OTG with circular stapled method in the treatment of upper or middle third gastric cancer.

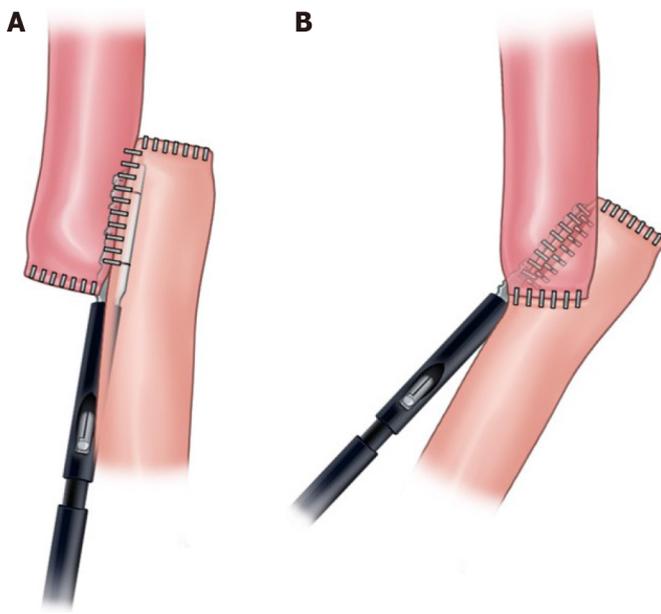


Figure 1 Two types of intracorporeal esophagojejunostomy methods. A: The conventional overlap method; B: The modified overlap method.

MATERIALS AND METHODS

Patients

This study was approved by the institutional review board of the Asan Medical Center. We reviewed the retrospectively collected and analyzed data of 462 patients who underwent curative TLTG ($n = 178$) and OTG ($n = 284$) as a treatment for upper or middle third gastric cancer between March 2012 and December 2018 at Asan Medical Center. We excluded all patients who received neoadjuvant chemotherapy, were diagnosed with esophagogastric junction cancer, underwent resection additional organs except for gall bladder, and did not have a gastric cancer diagnosis. Finally, 151 and 131 patients who underwent TLTG and OTG, respectively, were enrolled. All TLTG procedures were performed as TLTG with the modified overlap method. We evaluated TNM (tumor-node-metastasis) stage using the American Joint Committee on Cancer (AJCC), 7th edition[13]. Clinical characteristics and pathologic data were compared between TLTG and OTG groups. Additionally, we evaluated surgical outcomes, including EJ-related complications, and oncologic outcomes, including recurrence free survival (RFS) and overall survival (OS). Early and late complications were defined as events occurring within or after 30 d postoperatively, respectively. EJ complications, including bleeding, leakage and stricture, were diagnosed *via* upper gastrointestinal series, esophagogastroduodenoscopy, computed tomography, and clinical signs. These complications were reviewed and classified based on the Clavien-Dindo classification system (CDC)[14]. Patients were matched using propensity score matching (PSM) analysis and surgical and oncologic outcomes were evaluated.

Surgical technique of anastomosis

We performed TLTG with modified overlap method and OTG with circular stapled method, which was similar to our previous studies[3,10]. Both procedures were performed by a single experienced surgeon who conducts approximately 300 cases of gastrectomy annually.

Statistical analysis

In the un-matched group, numerical variables were presented as the mean \pm SD using the Student's *t*-test or Kruskal-Wallis test. Categorical variables was performed using the Chi-square test. Univariate and multivariate analyses were performed for the entire patient cohort (un-matched group) using logistic regression. Variables were included in the multivariate analysis if their univariate significance was < 0.1 .

To reduce the impact of treatment selection bias and potential confounding factors in this observational study, we performed rigorous adjustments for significant differences in the baseline characteristics of patients using the logistic regression models with generalized estimating equations (GEE) with a propensity score matched

set. When that technique was used, the propensity scores were estimated without considering the outcomes using multiple logistic regression analysis. A full non-parsimonious model was developed that included all the variables shown in [Table 1](#). Model discrimination was assessed using the C statistic and model calibration was evaluated using Hosmer-Lemeshow statistics. Overall, the model was well calibrated (Hosmer-Lemeshow test; $P = 0.368$) with reasonable discrimination (C statistic = 0.858). We matched the two groups (1:1 ratio) using a 'greedy nearest-neighbour' algorithm method. The Matching balance was measured based on the standardized mean differences. A > 10% difference in the absolute value was considered significantly imbalanced.

In the matched group, numerical variables were reported as the means \pm SD using the paired *t*-test. Categorical variables were performed using McNemar's test or Marginal homogeneity test. To evaluate the association between type of surgery, and complication and survival (and recurrence), the propensity score adjusted model was applied. Finally, the logistic regression model with GEE was applied using propensity score-based matching. The Cox proportional hazards model was applied using propensity score-based matching with robust standard errors. All reported *P* values are two-sided; values < 0.05 were considered statistically significant. Data manipulation and statistical analyses were performed using SAS® Version 9.4 (SAS Institute Inc., Cary, NC, United States).

RESULTS

Clinicopathological characteristics

The clinical variables are summarized in [Table 1](#). There was a significant difference in body mass index (BMI), tumor size, and pathologic tumor stage before PSM between groups (all $P < 0.05$); however, these differences disappeared after PSM. There were no statistically significant differences in all baseline variables included in the model between groups.

Surgical outcomes and postoperative complications in PSM

All surgical outcomes and postoperative complications are shown in [Table 2](#). There was no significant difference in operation time between groups ($P = 0.351$). Patients who underwent TLTG had significantly lower pain scores on all postoperative days than patients who underwent OTG. Moreover, patients in the TLTG group required significantly less analgesic and opioid administration than in the OTG group. The TLTG group reported earlier time to first flatus (3.62 ± 0.84 d vs 4.15 ± 0.87 d, $P = 0.002$) and soft diet (4.62 ± 2.67 d vs 7.47 ± 7.92 d, $P = 0.001$). Furthermore, patients who underwent TLTG stayed statistically significantly fewer days at the hospital after surgery than patients who underwent OTG (9.62 ± 5.32 d vs 13.51 ± 10.67 d; $P < 0.001$). No significant differences in postoperative complications were noted between the two groups ($P = 0.161$).

Postoperative complications, including EJ-related complications, are summarized in [Table 3](#). There were no significant differences in the early and late postoperative overall complications between groups ($P = 0.317$ and $P = 0.257$, respectively). In addition, there was no difference in the incidence of patients with ≥ 3 CDC complications in the early and late postoperative periods between groups ($P = 0.428$ and $P > 0.999$, respectively). There was no significant differences in EJ-related complications. [Table 4](#) shows the details of EJ-related complications. Five cases of EJ leakage were observed, and two cases of EJ bleeding were found. Four patients with CDC 3 complications required interventions such as endoscopic management and pigtail drainage, whereas 2 patients with CDC 2 complications fully recovered by conservative treatment. One postoperative mortality occurred due to EJ bleeding.

Oncologic outcomes of PSM

There were no significant differences in the number of retrieved lymph nodes between groups ($P = 0.713$). The 5-year RFS and OS are shown in [Figure 2](#). There were no significant differences in pathologic tumor stage between groups after PSM. The 5-year RFS rates of patients who underwent TLTG and OTG were 87.7% and 92.3%, respectively; however, these differences were not significant ($P = 0.653$). The 5-year OS rates of patients who underwent TLTG and OTG were 74.6% and 80.4%, respectively ($P = 0.476$).

Table 1 Patient clinical characteristics

Variable	Total set (n = 282)		P value	SD	PSM set (1:1) (n = 122)		P value	SD
	TLTG (n = 151)	OTG (n = 131)			TLTG (n = 61)	OTG (n = 61)		
Age (yr)	60.74 ± 11.55	59.11 ± 11.02	0.231	0.144	58.30 ± 11.26	58.70 ± 10.65	0.841	0.037
Gender			0.257	0.136			0.847	0.035
Male	94 (62.25)	90 (68.70)			40 (65.57)	41 (67.21)		
Female	57 (37.75)	41 (31.30)			21 (34.43)	20 (32.79)		
BMI (kg/m ²)	24.57 ± 3.25	23.69 ± 3.21	0.023	0.273	24.01 ± 2.98	23.98 ± 2.73	0.957	0.010
ASA score			0.859	0.044			0.885	0.073
I	30 (19.87)	26 (19.85)			13 (21.31)	14 (22.95)		
II	114 (75.50)	97 (74.05)			46 (75.41)	44 (72.13)		
III	7 (4.64)	8 (6.11)			2 (3.28)	3 (4.92)		
Number of comorbidities			0.068	0.222			0.655	0.083
0-2	137 (90.73)	126 (96.18)			59 (75.41)	44 (72.13)		
> 2	14 (9.27)	5 (3.82)			2 (3.28)	3 (4.92)		
Combined operation			0.176	0.161			> 0.999	0
No	136 (90.07)	111 (84.73)			55 (90.16)	55 (90.16)		
Yes	15 (9.93)	20 (15.27)			6 (9.84)	6 (9.84)		
History of abdominal surgery			0.061	0.254			0.846	0.103
No	120 (79.47)	102 (77.86)			50 (81.97)	48 (78.69)		
Minor surgery	24 (15.89)	14 (10.69)			6 (9.84)	6 (9.84)		
Major surgery	7 (4.64)	15 (11.45)			5 (8.20)	7 (11.48)		
Tumor size (mm, median)	31 (22, 46)	64 (36, 85)	< 0.001	0.841	39 (27, 62)	50 (28, 68)	0.865	0.028
Pathologic tumor stage			< 0.001	1.012			0.824	0.085
I	109 (72.19)	38 (29.01)			31 (50.82)	33 (54.10)		
II	28 (18.54)	41 (31.30)			19 (31.15)	19 (31.15)		
III	14 (9.27)	52 (39.69)			11 (18.03)	9 (14.75)		

Values are expressed as mean ± SD or n (%). PSM: Propensity score matching; BMI: Body mass index; ASA score: American Society of Anesthesiologists Physical Status Classification; TLTG: Totally laparoscopic gastrectomy; OTG: Open total gastrectomy.

Risk factors for postoperative complications

Tables 5 and 6 demonstrate the risk factors for postoperative complications after TLTG and OTG. BMI and American Society of Anaesthesiologists (ASA) scores were significantly associated with the occurrence of early complications in the univariate analysis. In addition, ASA score and age were significantly associated with the incidence of ≥ 3 CDC and EJ-related complications, respectively. Multivariate analysis demonstrated that BMI [odds ratio (OR), 1.824; 95% confidence interval (CI): 1.029-3.234, $P = 0.040$] and ASA score (OR, 3.154; 95%CI: 1.084-9.174, $P = 0.035$) were independent risk factors of early complications. Furthermore, multivariate analysis revealed that age was associated with ≥ 3 CDC and EJ-related complications.

DISCUSSION

To the best of our knowledge, this is the first study to compare feasibility and oncological outcomes between patients who underwent TLTG with the modified overlap method and OTG. This study demonstrated that TLTG with the modified overlap method is a technically safe procedure based on acceptable postoperative

Table 2 Early surgical outcomes and pathologic data in patients undergoing the totally laparoscopic gastrectomy with the modified overlap method and open total gastrectomy

Variable	Total set (n = 282)		P value	PSM set (1:1) (n = 122)		P value
	TLTG (n = 151)	OTG (n = 131)		TLTG (n = 61)	OTG (n = 61)	
Operative time (min)	147.68 ± 29.64	145.24 ± 35.48	0.282	147.11 ± 25.48	143.46 ± 38.09	0.351
Time to first flatus (d)	3.73 ± 0.90	4.14 ± 0.81	< 0.001	3.62 ± 0.84	4.15 ± 0.87	0.002
Time to soft diet (d)	4.99 ± 3.78	7.24 ± 6.29	< 0.001	4.62 ± 2.67	7.47 ± 7.92	0.001
Perioperative transfusion (n)			< 0.001			0.035
No	145 (96.03)	107 (81.68)		59 (96.72)	52 (85.25)	
Yes	6 (3.97)	24 (18.32)		2 (3.28)	9 (14.75)	
Hospital day after surgery (d)	9.96 ± 6.36	13.06 ± 11.09	< 0.001	9.62 ± 5.32	13.51 ± 10.67	< 0.001
Pick of pain score (VAS)	4 (3.92)	5 (2.51)	0.494	3 (3.16)	1 (1.05)	0.317
Pain score at postoperative day	3.19 ± 1.04	3.83 ± 1.14	< 0.001	3.23 ± 1.09	4.07 ± 1.35	< 0.001
Pain score at postoperative day 1	2.98 ± 1.07	3.76 ± 1.13	< 0.001	2.97 ± 0.87	3.77 ± 1.07	< 0.001
Pain score at postoperative day 3	2.68 ± 1.17	3.10 ± 1.28	< 0.001	2.75 ± 1.31	3.16 ± 1.27	< 0.001
Pain score at postoperative day 5	1.93 ± 1.13	2.61 ± 1.49	< 0.001	1.82 ± 1.13	2.64 ± 1.21	< 0.001
Administration of analgesics (n)	9.74 ± 8.92	16.22 ± 18.06	< 0.001	10.61 ± 11.07	16.92 ± 13.72	< 0.001
Administration of opioid (n)	2.89 ± 5.49	5.43 ± 11.51	< 0.001	3.21 ± 6.98	4.48 ± 5.15	0.031
Retrieved LN	39.53 ± 15.59	41.03 ± 15.31	0.265	38.67 ± 13.82	38.13 ± 14.52	0.713

Values are expressed as mean ± SD or n (%) or median (range). PSM: Propensity score matching; LN: Lymph node; PRM: Proximal resection margin; TLTG: Totally laparoscopic gastrectomy; OTG: Open total gastrectomy.

complications, including EJ-related complications.

The overlap method is a widely used EJ reconstruction method in TLTG, it which can lessen the tension in the anastomosis and reduce mesentery division. This secures additional jejunum length for anastomosis[15,16]. This method involves a linear stapler for anastomosis; therefore, the area around the abdominal esophagus requires sufficient dissection. Furthermore, and space in the hiatus and length of the esophagus in which the stapler will be placed should be secured. This may lead to tension in the esophagus after anastomosis and hiatal hernia caused by excessive hiatus dissection. We have devised a novel method to minimize these risks, named the modified overlap method. We use a linear stapler; however, compared with the existing side-to-side anastomosis, less esophageal dissection is required. Further, anastomosis is completed obliquely at 45°; therefore, the resulting anastomosis is similar to when a circular stapler is used because end to side anastomosis is possible. This study proved the TLTG with this modified overlap method showed no significant difference in EJ complications when compared with OTG.

A previous comparative study of LTG and OTG reported similar EJ anastomotic complications; however, a previous large multicenter cohort study in Japan has shown that open surgery is safer for EJ reconstruction[11,12,17]. This indicates that controversy remains regarding the superior method for EJ anastomosis between OTG and LTG. Furthermore, international treatment guidelines, including the Korean gastric cancer treatment and Japanese gastric cancer treatment guidelines, do not yet recognize LTG as a standard treatment[18,19]. Nonetheless, our data indicate that a randomized clinical trial assessing the surgical and oncological outcomes using the modified overlap method should be conducted to confirm its safety and efficacy.

In this study, we overcame operative time and lymphadenectomy issues using the TLTG with the modified overlap method. First, laparoscopic gastrectomy surgery is longer than open gastrectomy[2,20,21]. However, the institution in which this study was conducted is a high-volume center where more than a thousand laparoscopic gastrectomies are performed annually. The lead surgeon in this study performs > 300 gastric cancer operations per year. All surgical team members in this institution are skilled and experienced; therefore, we predicted a reduced operative time while maintaining acceptable surgical and oncological outcomes. However, it may be

Table 3 Postoperative complications

Variable	Total set (n = 282)		P value	PSM set (1:1) (n = 122)		P value
	TLTG (n = 151)	OTG (n = 131)		TLTG (n = 61)	OTG (n = 61)	
Early complications						
No	119 (78.81)	99 (75.57)	0.518	48 (78.69)	43 (70.49)	0.317
Yes	32 (21.19)	32 (24.43)		13 (21.31)	18 (29.51)	
Late complications						
No	142 (94.04)	125 (95.42)	0.607	56 (91.80)	59 (96.72)	0.257
Yes	9 (5.96)	6 (4.58)		5 (8.20)	2 (3.28)	
CDC						
0-2	138 (91.39)	116 (88.55)	0.426	56 (91.80)	54 (88.52)	0.564
≥ 3	13 (8.61)	15 (11.45)		5 (8.20)	7 (11.48)	
EJ related complications						
No	148 (98.01)	123 (93.89)	0.090	59 (96.72)	56 (91.80)	0.270
Yes	3 (1.99)	8 (6.11)		2 (3.28)	5 (8.20)	

Values are expressed as mean ± SD or n (%). PSM: Propensity score matching; TLTG: Totally laparoscopic gastrectomy; OTG: Open total gastrectomy; CDC: Clavien-Dindo classification; EJ: Esophagojejunostomy.

Table 4 Characteristics of the patients with esophagojejunostomy-related complications

Case	Sex	Age	Primary operation	TNMstage	Early or late	Type of complication	CDC	Treatment	Hospital day
1	F	79	TLTG	III	Early	Bleeding	5	Operation	8
2	M	65	TLTG	II	Early	Leakage	3A	Intervention	20
3	M	74	OTG	I	Early	Leakage	2	Conservative	14
4	M	74	OTG	I	Early	Bleeding	3A	Intervention	72
5	M	60	OTG	I	Early	Leakage	3A	Intervention	48
6	M	66	OTG	I	Early	Leakage	2	Conservative	25
7	M	63	OTG	I	Early	Leakage	3A	Intervention	32

TNM: Tumor-node-metastasis; CDC: Clavien-Dindo classification; F: Female; M: Male; TLTG: Totally laparoscopic gastrectomy; OTG: Open total gastrectomy.

difficult to apply the results of this study to low-volume centers or inexperienced surgeons.

Second, lymph node dissection is an important procedure in gastric cancer surgery because the oncologic outcome is dependent on a proper lymphadenectomy[22]. The AJCC recommends that ≥ 30 lymph nodes be removed for lymphadenectomy in gastric cancer[23]. In this study, there was no statistically significant difference in the number of retrieved lymph nodes between groups; ≥ 30 lymph nodes were removed in both groups. In addition, this study showed that the 5-year overall and RFS after PSM analysis did not differ between groups.

In general, the risk factors associated with surgical complications in laparoscopic gastrectomy are comorbidity, surgeon experience, age, malnutrition, gender, and chronic liver disease[24-26]. Most studies have included and analyzed patients who underwent total and distal gastrectomies. Fewer studies have analyzed total gastrectomy alone. Kosuga *et al*[25] and Martin *et al*[26] have classified total gastrectomy as a risk factor for complications (OR 1.63 and 3.13, respectively). This indicates that it is important to evaluate risk factors relative to limited total gastrectomy. Li *et al*[27] have shown that old age combined with splenectomy is a risk factor for overall complications after total gastrectomy. In this study, preoperative BMI and ASA scores were risk factors associated with early complications. Further, old age

Table 5 Univariate analysis of risk factors for overall early, Clavien-Dindo classification ≥ 3 , and esophagojejunostomy-related complications

Variables	Early complications		CDC ≥ 3 complications		EJ-related complications	
	OR (95%CI)	P value	OR (95%CI)	P value	OR (95%CI)	P value
Type of surgery		0.518		0.428		0.090
TLTG	1		1		1	
OTG	1.202 (0.688-2.100)		1.373 (0.628-3.002)		3.209 (0.833-12.356)	
Age		0.289		0.051		0.035
< 60	1		1		1	
≥ 60	1.358 (0.772-2.390)		2.347 (0.997-5.525)		9.220 (1.164-73.022)	
BMI		0.045		0.380		0.402
< 25	1		1		1	
≥ 25	1.773 (1.012-3.109)		1.419 (0.649-3.101)		1.678 (0.500-5.633)	
ASA score		0.030		0.036		
1-2	1		1			
3	3.224 (1.122-9.265)		3.682 (1.088-12.456)			
Number of comorbidities		0.342				0.752
0-2	1				1	
> 2	1.631 (0.594-4.480)				1.406 (0.170-11.599)	
Combined operation		0.685		0.381		0.735
No	1		1		1	
Yes	0.833 (0.346-2.008)		0.515 (0.117-2.272)		0.697 (0.086-5.618)	
History of abdominal surgery		0.130		0.323		
No	1		1		1	
Yes	1.640 (0.864-3.111)		1.554 (0.648-3.726)		1.408 (0.362-5.478)	0.622
Tumor size		0.521		0.442		0.053
< 5 cm	1		1		1	
≥ 5 cm	0.830 (0.470-1.466)	0.521	0.727 (0.323-1.638)		3.786 (0.983-14.585)	
Operation time		0.225		0.605		0.805
< 150 min	1		1		1	
≥ 150 min	1.414 (0.808-2.477)		1.230 (0.562-2.692)		1.165 (0.347-3.912)	
Retrieved lymph node		0.714		0.662		0.246
< 30	1		1		1	
≥ 30	0.888 (0.471-1.676)		1.235 (0.480-3.181)		3.416 (0.429-27.170)	
Pathologic tumor stage		0.418		0.864		0.875
I	1		1		1	
II	0.666 (0.328-1.351)		1.246 (0.497-3.126)		0.701 (0.138-3.568)	
III	0.704 (0.346-1.431)		0.950 (0.348-2.592)		1.119 (0.27-4.617)	

Values are expressed as mean \pm SD or *n* (%). TLTG: Totally laparoscopic total gastrectomy; OTG: Open total gastrectomy; CDC: Clavien-Dindo classification; EJ: Esophagojejunostomy; CI: Confidence interval; OR: Odds ratio.

was a risk factor associated with EJ complications. Patients over 60-year-old with a BMI over 25 and ASA scores of ≥ 3 were more likely to have surgical complications; therefore, caution is required during surgery and careful perioperative management is necessary.

Table 6 Multivariate analysis of risk factors for early, Clavien-Dindo classification ≥ 3 , and esophagojejunostomy-related complications

Variables	Early complications		CDC ≥ 3 complications		EJ related complications	
	OR (95%CI)	P value	OR (95%CI)	P value	OR (95%CI)	P value
Type of surgery						
TLTG	1		1		1	
OTG	1.275 (0.719-2.262)	0.405	1.431 (0.650-3.153)	0.373	3.546 (0.908-13.854)	0.069
Age						
< 60			1		1	
≥ 60			2.391 (1.013-5.641)	0.047	9.925 (1.245-79.107)	0.030
BMI						
< 25	1					
≥ 25	1.824 (1.029-3.234)	0.040				
ASA score						
1-2	1					
3	3.154 (1.084-9.174)	0.035				

Values are expressed as mean \pm SD or *n* (%). TLTG: Totally laparoscopic total gastrectomy; OTG: Open total gastrectomy; CDC: Clavien-Dindo classification; EJ: Esophagojejunostomy; CI: Confidence interval; OR: Odds ratio; BMI: Body mass index; ASA score: American Society of Anesthesiologists Physical Status Classification.

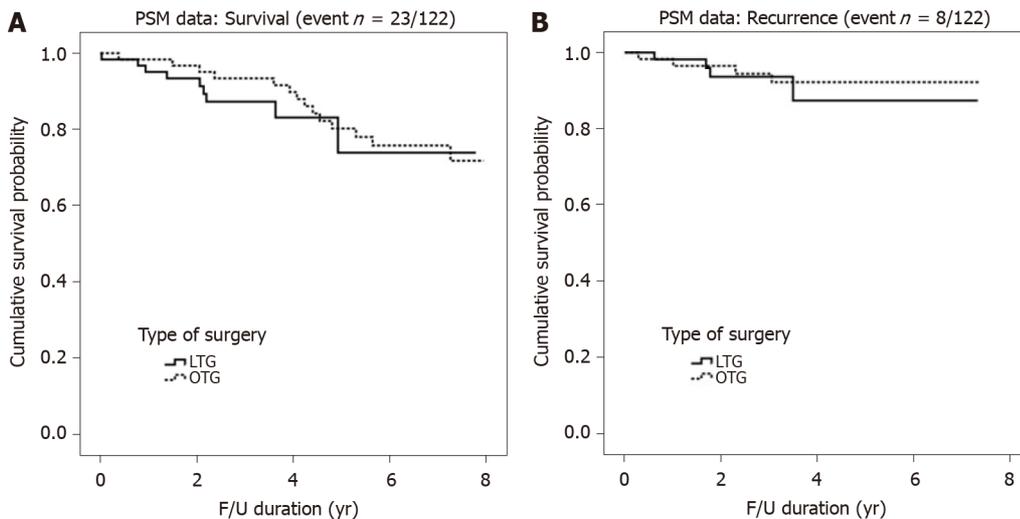


Figure 2 Survival curves for matched patients. A: Overall survival; B: Recurrence free survival. PSM: Propensity score matching; TLTG: Laparoscopic total gastrectomy; OTG: Open total gastrectomy; F/U: Follow up.

This study has some limitations. First, it is a retrospective study performed by a single experienced surgeon at a high-volume center. Therefore, our method might not be appropriate for relatively inexperienced surgeons or small-volume institutes. Second, the number of enrolled patients is relatively small; therefore, subgroup analysis, such as distinguishing between early gastric cancer and advanced gastric cancer or grouping by stage, was not possible.

CONCLUSION

In conclusion, we confirmed that TLTG with the modified overlap method had several advantages over OTG. These included a lower pain score, earlier bowel recovery, and discharge based on acceptable postoperative complications and oncological outcomes.

ARTICLE HIGHLIGHTS

Research background

Although several methods of totally laparoscopic total gastrectomy (TLTG) have been reported, the best anastomosis technique of TLTG has not been conclusively established. Recently, we developed a modified overlap method for TLTG for overcoming these disadvantages of linear stapled method. This procedure requires less dissection around abdominal esophagus; therefore, it can create a secure esophagojejunal anastomosis with reduced tension as circular stapled method.

Research motivation

Whether is a more optimal anastomotic method of esophagojejunostomy in TLTG and open total gastrectomy (OTG) remains unclear. Especially, there was no report about comparing between TLTG with overlap method and OTG.

Research objectives

The aim of this study was to investigate the effectiveness and surgical outcomes including recurrence and survival of TLTG using the modified overlap method compared with OTG using the circular stapled method.

Research methods

We performed 151 TLTG with modified overlap method and 131 OTG for gastric cancer between March 2012 and December 2018 at Asan Medical Center. We evaluated surgical and oncological outcomes between the two groups using propensity score matching. In addition, we analyzed risk factors associated with postoperative complications for improvement of postoperative management of gastric cancer surgery.

Research results

The patients who underwent TLTG were discharged earlier than those who underwent OTG. Time to first flatus and soft diet were significantly shorter in TLTG group. Pain score at all postoperative period and administration of opioid were significantly lower after the TLTG. No statistically significant difference was found between the two groups in terms of early, late and esophagojejunostomy-related complications. Significant differences were observed not with respect to 5-year recurrence free survival and overall survival.

Research conclusions

TLTG with modified overlap method have favorable surgical and oncological outcomes compared with OTG. Furthermore, the surgeon should perform total gastrectomy cautiously and delicately especially with the patients with obese, high American Society of Anaesthesiologists score and old age.

Research perspectives

Based on our results, we confirmed that the TLTG with modified overlap method has several advantages over OTG. However, this study has certain limitations. It is a retrospective study performed by a single experienced surgeon at a high-volume center, and the number of enrolled patients is relatively small.

REFERENCES

- 1 **Chen K**, Pan Y, Zhai ST, Yu WH, Pan JH, Zhu YP, Chen QL, Wang XF. Totally laparoscopic vs open total gastrectomy for gastric cancer: A case-matched study about short-term outcomes. *Medicine (Baltimore)* 2017; **96**: e8061 [PMID: 28930841 DOI: 10.1097/MD.0000000000008061]
- 2 **Haverkamp L**, Weijs TJ, van der Sluis PC, van der Tweel I, Ruurda JP, van Hillegersberg R. Laparoscopic total gastrectomy vs open total gastrectomy for cancer: a systematic review and meta-analysis. *Surg Endosc* 2013; **27**: 1509-1520 [PMID: 23263644 DOI: 10.1007/s00464-012-2661-1]
- 3 **Kim HS**, Kim BS, Lee IS, Lee S, Yook JH. Comparison of totally laparoscopic total gastrectomy and open total gastrectomy for gastric cancer. *J Laparoendosc Adv Surg Tech A* 2013; **23**: 323-331 [PMID: 23379920 DOI: 10.1089/lap.2012.0389]
- 4 **Gong W**, Li J. Combat with esophagojejunal anastomotic leakage after total gastrectomy for gastric cancer: A critical review of the literature. *Int J Surg* 2017; **47**: 18-24 [PMID: 28935529 DOI: 10.1016/j.ijssu.2017.09.019]
- 5 **Ebihara Y**, Okushiba S, Kawarada Y, Kitashiro S, Katoh H. Outcome of functional end-to-end

- esophagojejunostomy in totally laparoscopic total gastrectomy. *Langenbecks Arch Surg* 2013; **398**: 475-479 [PMID: 23354359 DOI: 10.1007/s00423-013-1051-z]
- 6 **Ito H**, Inoue H, Odaka N, Satodate H, Onimaru M, Ikeda H, Takayanagi D, Nakahara K, Kudo SE. Evaluation of the safety and efficacy of esophagojejunostomy after totally laparoscopic total gastrectomy using a trans-orally inserted anvil: a single-center comparative study. *Surg Endosc* 2014; **28**: 1929-1935 [PMID: 24488351 DOI: 10.1007/s00464-014-3417-x]
 - 7 **Jeong O**, Jung MR, Kim GY, Kim HS, Ryu SY, Park YK. Comparison of short-term surgical outcomes between laparoscopic and open total gastrectomy for gastric carcinoma: case-control study using propensity score matching method. *J Am Coll Surg* 2013; **216**: 184-191 [PMID: 23211117 DOI: 10.1016/j.jamcollsurg.2012.10.014]
 - 8 **Okabe H**, Obama K, Tanaka E, Nomura A, Kawamura J, Nagayama S, Itami A, Watanabe G, Kanaya S, Sakai Y. Intracorporeal esophagojejunal anastomosis after laparoscopic total gastrectomy for patients with gastric cancer. *Surg Endosc* 2009; **23**: 2167-2171 [PMID: 18553203 DOI: 10.1007/s00464-008-9987-8]
 - 9 **Shim JH**, Yoo HM, Oh SI, Nam MJ, Jeon HM, Park CH, Song KY. Various types of intracorporeal esophagojejunostomy after laparoscopic total gastrectomy for gastric cancer. *Gastric Cancer* 2013; **16**: 420-427 [PMID: 23097123 DOI: 10.1007/s10120-012-0207-9]
 - 10 **Choi M**, Ko CS, Yook JH, Kim BS. Comparative outcomes between totally laparoscopic total gastrectomy with the modified overlap method for early gastric cancer and advanced gastric cancer: review of 149 consecutive cases. *Wideochir Inne Tech Maloinwazyjne* 2020; **15**: 437-445 [PMID: 32904610 DOI: 10.5114/wiitm.2020.96098]
 - 11 **Inokuchi M**, Otsuki S, Fujimori Y, Sato Y, Nakagawa M, Kojima K. Systematic review of anastomotic complications of esophagojejunostomy after laparoscopic total gastrectomy. *World J Gastroenterol* 2015; **21**: 9656-9665 [PMID: 26327774 DOI: 10.3748/wjg.v21.i32.9656]
 - 12 **Lee JH**, Nam BH, Ryu KW, Ryu SY, Park YK, Kim S, Kim YW. Comparison of outcomes after laparoscopy-assisted and open total gastrectomy for early gastric cancer. *Br J Surg* 2015; **102**: 1500-1505 [PMID: 26398912 DOI: 10.1002/bjs.9902]
 - 13 **Union for International Cancer Control**. What is TNM cancer staging system? [cited 17 March 2021]. In: Union for International Cancer Control (UICC) homepage [Internet]. Available from: <https://www.uicc.org/resources/tnm>
 - 14 **Dindo D**, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; **240**: 205-213 [PMID: 15273542 DOI: 10.1097/01.sla.0000133083.54934.ae]
 - 15 **Kawamura H**, Ohno Y, Ichikawa N, Yoshida T, Homma S, Takahashi M, Taketomi A. Anastomotic complications after laparoscopic total gastrectomy with esophagojejunostomy constructed by circular stapler (OrVil™) vs linear stapler (overlap method). *Surg Endosc* 2017; **31**: 5175-5182 [PMID: 28488177 DOI: 10.1007/s00464-017-5584-z]
 - 16 **Son SY**, Cui LH, Shin HJ, Byun C, Hur H, Han SU, Cho YK. Modified overlap method using knotless barbed sutures (MOBS) for intracorporeal esophagojejunostomy after totally laparoscopic gastrectomy. *Surg Endosc* 2017; **31**: 2697-2704 [PMID: 27699517 DOI: 10.1007/s00464-016-5269-z]
 - 17 **Kodera Y**, Yoshida K, Kumamaru H, Kakeji Y, Hiki N, Etoh T, Honda M, Miyata H, Yamashita Y, Seto Y, Kitano S, Konno H. Introducing laparoscopic total gastrectomy for gastric cancer in general practice: a retrospective cohort study based on a nationwide registry database in Japan. *Gastric Cancer* 2019; **22**: 202-213 [PMID: 29427039 DOI: 10.1007/s10120-018-0795-0]
 - 18 **Guideline Committee of the Korean Gastric Cancer Association (KGCA)**; Development Working Group & Review Panel. Erratum: Korean Practice Guideline for Gastric Cancer 2018: an Evidence-based, Multi-disciplinary Approach. *J Gastric Cancer* 2019; **19**: 372-373 [PMID: 31598379 DOI: 10.5230/jgc.2019.19.e32]
 - 19 **Japanese Gastric Cancer Association**. Japanese gastric cancer treatment guidelines 2018 (5th edition). *Gastric Cancer* 2021; **24**: 1-21 [PMID: 32060757 DOI: 10.1007/s10120-020-01042-y]
 - 20 **Deng Y**, Zhang Y, Guo TK. Laparoscopy-assisted vs open distal gastrectomy for early gastric cancer: A meta-analysis based on seven randomized controlled trials. *Surg Oncol* 2015; **24**: 71-77 [PMID: 25791201 DOI: 10.1016/j.suronc.2015.02.003]
 - 21 **Zeng YK**, Yang ZL, Peng JS, Lin HS, Cai L. Laparoscopy-assisted vs open distal gastrectomy for early gastric cancer: evidence from randomized and nonrandomized clinical trials. *Ann Surg* 2012; **256**: 39-52 [PMID: 22664559 DOI: 10.1097/SLA.0b013e3182583e2e]
 - 22 **Schwarz RE**, Smith DD. Clinical impact of lymphadenectomy extent in resectable gastric cancer of advanced stage. *Ann Surg Oncol* 2007; **14**: 317-328 [PMID: 17094022 DOI: 10.1245/s10434-006-9218-2]
 - 23 **Edge SB**, Byrd DR, Compton CC, Fritz AG, Greene FL, Trotti AI; American Joint Committee of Cancer. AJCC cancer staging manual. 7th ed. New York: Springer, 2010
 - 24 **Kim MC**, Kim W, Kim HH, Ryu SW, Ryu SY, Song KY, Lee HJ, Cho GS, Han SU, Hyung WJ; Korean Laparoscopic Gastrointestinal Surgery Study (KLASS) Group. Risk factors associated with complication following laparoscopy-assisted gastrectomy for gastric cancer: a large-scale korean multicenter study. *Ann Surg Oncol* 2008; **15**: 2692-2700 [PMID: 18663532 DOI: 10.1245/s10434-008-0075-z]
 - 25 **Kosuga T**, Ichikawa D, Komatsu S, Kubota T, Okamoto K, Konishi H, Shiozaki A, Fujiwara H, Otsuji E. Clinical and surgical factors associated with organ/space surgical site infection after laparoscopic gastrectomy for gastric cancer. *Surg Endosc* 2017; **31**: 1667-1674 [PMID: 27506433]

DOI: [10.1007/s00464-016-5156-7](https://doi.org/10.1007/s00464-016-5156-7)]

- 26 **Martin AN**, Das D, Turrentine FE, Bauer TW, Adams RB, Zaydfudim VM. Morbidity and Mortality After Gastrectomy: Identification of Modifiable Risk Factors. *J Gastrointest Surg* 2016; **20**: 1554-1564 [PMID: [27364726](https://pubmed.ncbi.nlm.nih.gov/27364726/) DOI: [10.1007/s11605-016-3195-y](https://doi.org/10.1007/s11605-016-3195-y)]
- 27 **Li Z**, Liu Y, Bai B, Yu D, Lian B, Zhao Q. Surgical and Long-Term Survival Outcomes After Laparoscopic and Open Total Gastrectomy for Locally Advanced Gastric Cancer: A Propensity Score-Matched Analysis. *World J Surg* 2019; **43**: 594-603 [PMID: [30229383](https://pubmed.ncbi.nlm.nih.gov/30229383/) DOI: [10.1007/s00268-018-4799-z](https://doi.org/10.1007/s00268-018-4799-z)]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

