Systematic Review and/or Meta-analysis

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Safety and effectiveness of totally laparoscopic total gastrectomy vs laparoscopic-assisted total gastrectomy: a meta-analysis

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Background: For gastric cancer with total gastrectomy, the usual laparoscopic surgical approaches are totally laparoscopic total gastrectomy (TLTG) and laparoscopic-assisted total gastrectomy (LATG). Due to its difficult anastomotic technique, the adoption of TLTG is limited. Therefore, surgeons prefer using LATG, which also led to TLTG being somewhat overlooked, so there is no clear conclusion today as to which surgical procedure is more favorable to the patient's recovery. This article aimed to compare the safety and short-term outcomes of the two surgical approaches.

Materials and methods: Studies comparing TLTG and LATG, published up to December 2022, were searched in PubMed, Web of Science, and Embase databases. The study outcomes, including operative time, blood loss, anastomosis time, number of retrieved lymph nodes, proximal and distal resection margins, time to first fluid and soft diet, hospitalization duration, time to first flatus, and postsurgical and anastomotic complications, were compared between these two different surgical procedures. Statistics were analyzed with RevMan 5.4 and Stata 13.1.

Results: Fifteen publications were included in this study. The total sample included 3023 cases. The meta-analysis revealed no significant difference in overall postoperative complications between the two surgical approaches ($P > 0.05$). Compared with LATG, TLTG led to reduced intraoperative blood loss ($P < 0.0001$), an increased number of lymphatic node dissections ($P < 0.0001$), and decreased hospitalization duration ($P = 0.002$). However, operative time, anastomosis time, pulmonary infection, resection margins, time to first fluid and soft diet, time to first flatus and anastomosis-related complications were no significant difference between TLTG and LATG groups ($P > 0.05$).

Conclusion: TLTG did not lead to an increase in overall postoperative complications, which is a reliable surgical approach for treatment of gastric cancer. Moreover, it may reduce harm to patients and enable them to obtain better surgical outcomes.

Keywords: complication, gastric cancer, laparoscopic, meta-analysis, outcome, total gastrectomy

Introduction

Gastric cancer remains one of the significant risk that commonly endanger human life and health worldwide, with over one million new cases and 769 000 estimated deaths by 2020. The incidence of gastric cancer is related to geography and culture, with the highest incidence observed in East Asia and Eastern Europe[1]. Complete surgical resection remains the only curative treatment for cancer[2]. Since a novel laparoscopic-assisted distal gastrectomy was reported by Kitano *et al.*[3], laparoscopic techniques for cancer treatment have been widely used for tumor resection because of its widely acknowledged advantages over open total gastrectomy, such as less blood loss, faster evacuation, shorter hospital stay, and fewer postoperative complications[4–6]. With the development of technology, totally laparoscopic total gastrectomy (TLTG) based on laparoscopic-assisted total gastrectomy (LATG) is being used as an emerging technique. This intracavitary anastomosis does not require an auxiliary incision compared to LATG. However, the diffusion of TLTG is limited because of the technical difficulties associated with

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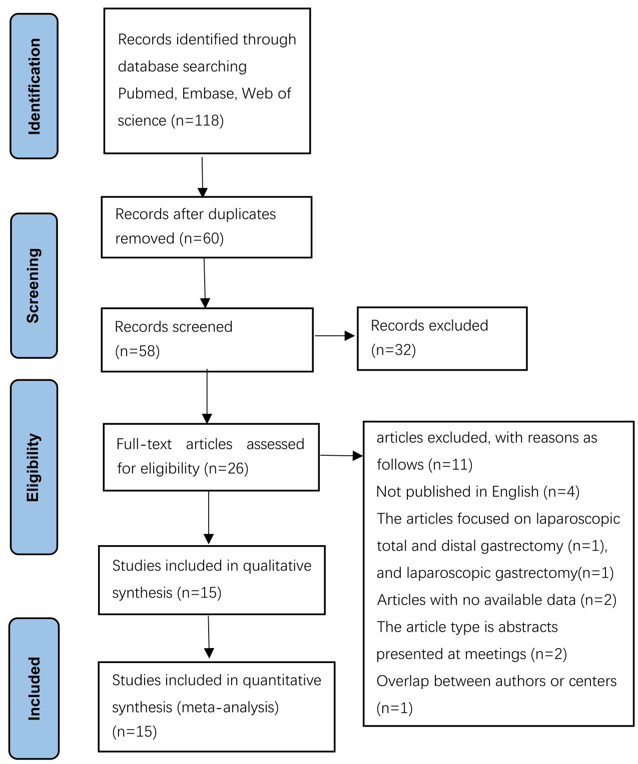

Figure 1. Flowchart for study retrieval.

esophagogastric anastomosis. In recent years, with the innovation and improvement of various esophagogastric anastomosis techniques, the operational difficulty of TLTG has been reduced, postoperative complications have been effectively prevented, and satisfactory postoperative outcomes have been achieved[7]. However, there is no definitive conclusion regarding which surgical approach is superior. Therefore, this study aimed to evaluate the safety and short-term efficacy of TLTG versus LATG.

Materials and methods

Search strategy

The study was registered on PROSPERO. The study results are reported according to the PRISMA (Preferred Reporting Items for Systematic Evaluations and Meta-Analyses) (Supplemental Digital Content 1, http://links.lww.com/JS9/B431) (Supplemental Digital Content 2, http://links.lww.com/JS9/B432) statement and AMSTAR (Assessing the methodological quality of systematic reviews) (Supplemental Digital Content 3, http://links.lww.com/JS9/B433) Guidelines[8,9]. The Embase, PubMed, and Web of Science databases were searched for primary studies published before December 2022. In addition, the language used was limited to English. To search more precisely, the terms 'totally laparoscopic' or 'intracorporeal' and 'laparoscopic-assisted' or 'extracorporeal' and 'total gastrectomy' and 'outcome*' or 'complication*' are used. The retrieved studies and their references were reviewed to ensure the accuracy of the search results.

HIGHLIGHTS

- A meta-analysis was performed on totally laparoscopic total gastrectomy (TLTG) versus laparoscopic-assisted total gastrectomy (LATG).
- This article included 15 studies with a total of 3023 samples.
- No difference between TLTG and LATG in overall postoperative complications.
- TLTG may be superior to LATG in some outcomes.
- TLTG is a reliable surgical approach for treatment of gastric cancer.

Inclusion and exclusion criteria

Studies meeting the following criteria were included in the Meta-analysis: 1. Studies comparing TLTG and LATG levels in gastric cancer. 2. Short-term outcomes, including definite study outcomes and postoperative complications. 3. The most recently published article was selected if the same author or institution published two or more articles.

Studies that met the following criteria were excluded: 1. Focused on laparoscopic distal gastric and proximal gastrectomy. 2. Articles included abstracts, case reports, review articles, and letters presented at conferences.

Data extraction

Two authors independently extracted the data according to the same criteria. When there is a disagreement, both will solve the problem by further searching the full text, consulting, and communicating with experienced authors. The compiled information included author name, study period, sample size, mean age, BMI, tumor size, tumor location, sex, lymphadenectomy, digestive tract reconstruction, esophagojejunostomy techniques, neoadjuvant therapy, geographical region, tumor stage, operative time, anastomosis time, blood loss, number of retrieved lymphatic nodes, proximal resection margin, distal resection margin, type of stapler, postsurgical hospitalization duration, time to first flatus, time to first fluid diet and soft diet, pulmonary infection, anastomotic complications, and overall postsurgical complications.

Statistical analysis

Stata 13.1 and RevMan 5.3 software were applied to analyze the data. The risk ratio (RR) was used to assess dichotomous variables, and the mean difference (MD) was calculated for continuous variables. Statistical heterogeneity was assessed using the values of I^2 and the results of χ^2tests. $I^2 < 25\%$ was considered low heterogeneity, 25–50% was considered moderate heterogeneity, and $> 50\%$ was considered high heterogeneity. Random-effects models were used for high heterogeneity ($I^2 > 50\%$ or $P < 0.100$), whereas fixed effects models were used for low-to-moderate heterogeneity. Statistical significance was recognized when the forest plot P-value was <0.05[10]. To avoid publication bias, funnel plots and Egger's and Begg's tests were used. A sensitivity analysis was performed to verify the primary outcome's stability.

Table 1

Clinical information of included studies.

References	Nation	Year	Study Period	Surgical Type	Sample Size	Mean Age	Gender (Male/Female)	BMI (Kg/m^2)	Tumor Size (cm)	Stapler Type	Lymphadenectomy	Digestive tract Reconstruction	Esophagojejunostomy Techniques	Neoadjuvant Therapy	comorbidities	Tumor stage (I/II/III/IV/pCR)
Chen[22]	China	2019	2008–2016	TLTG	26	61.8	22/4	22.5	4.60	Circular stapler	D2	Roux-en-Y	OrVil TM	2	NA	0/7/19/0/0
				LATG	26	61.3	21/5	21.6	4.71	Circular stapler	D2	Roux-en-Y	end-to-side anastomosis	5	NA	1/10/12/3/0
Park[23]	Korea	2021	2012–2018	TLTG	213	61.4	158/55	24.2	3.3	Circular stapler	D1 +	Roux-en-Y	end-to-side anastomosis	0	183	169/27/17/0/0
				LATG	111	59.8	76/35	24.1	3.2	Circular stapler	D1 +	Roux-en-Y	end-to-side anastomosis	0	75	92/12/7/0/0
Lin[24]	China	2022	2014–2018	TLTG	104	NA	71/63	NA	NA	Linear stapler	NA	Roux-en-Y	Overlap	65	NA	29/30/45/0/0
				LATG	208	NA	140/68	NA	NA	Circular stapler	NA	Roux-en-Y	end-to-side anastomosis	117	NA	59/64/85/0/0
Qiu *et al.*[25]	China	2022	2020–2020	TLTG	46	63.3	31/15	23.74	3.6	Linear stapler	D2	Roux-en-Y	SPLT	0	NA	11/15/20/0/0
				LATG	51	63.9	36/15	23.07	4.3	Circular stapler	D2	Roux-en-Y	end-to-side anastomosis	0	NA	11/17/23/0/0
Han *et al.*[26]	Korea	2020	2012–2019	TLTG	110	62	68/24	23.7	NA	Linear stapler	D1/D2/D2 +	NA	Overlap	0	NA	69/14/9/0/0
				LATG	92	59.6	68/42	23.5	NA	Circular stapler	D1/D2/D2 +	NA	end-to-side anastomosis	0	NA	98/8/4/0/0
Gong[27]	Korea	2017	2014–2016	TLTG	421	57.78	173/148	NA	3.95	Linear stapler	D1/D2	NA	FEEA	0	NA	337/62/22/0/0
				LATG	266	55.69	167/99	NA	3.72	Circular stapler	D1/D2	NA	end-to-side anastomosis	0	NA	228/27/11/0/0
Huang[28]	China	2017	2014–2016	TLTG	51	55.5	34/17	22.5	4.5	Linear stapler	D2	IJOM	Overlap	0	None	13/17/21/0/0
				LATG	102	55.9	68/34	22.6	4.7	Circular stapler	D2	Roux-en-Y	end-to-side anastomosis	0	None	18/40/44/0/0
Yamamoto[29]	Japan	2017	2006–2015	TLTG	100	64.6	59/41	22.3	NA	Linear stapler	D1 + /D2	Roux-en-Y	FEEA	0	NA	70/14/16/0/0
				LATG	9	68.3	4/5	23	NA	Circular stapler	D1 + /D2	Roux-en-Y	OrVil TM	0	NA	3/3/3/0/0
Jeong[30]	Korea	2020	2008–2018	TLTG	118	61.8	87/31	24.6	NA	Linear stapler	D1 + /D2	Roux-en-Y	Overlap	0	NA	80/23/15/0/0
				LATG	292	62.1	206/86	23.4	NA	Circular stapler	D1 + /D2	Roux-en-Y	end-to-side anastomosis	0	NA	239/38/15/0/0
Kim HB[31]	Korea	2016	2013–2015	TLTG	30	51	16/14	22.2	3	Linear stapler	D1 + β	Roux-en-Y	FEEA	0	NA	NA
				LATG	24	53	14/10	22.3	2.9	Circular stapler	D1 + β	Roux-en-Y	end-to-side anastomosis	0	NA	NA
Chen *et al.*[32]	China	2016	2006–2015	TLTG	108	59.4	73/35	23.5	4	Circular stapler	D2	Roux-en-Y	end-to-side anastomosis	0	NA	53/27/28/0/0
				LATG	145	57.3	98/47	23.1	4.3	Circular stapler	D2	Roux-en-Y	end-to-side anastomosis	0	NA	82/27/36/0/0
Lu[33]	China	2015	2011–2014	TLTG	25	59	22/3	22.5	4.8	Circular stapler	D2	Roux-en-Y	OrVil TM	0	NA	0/5/17/3/0
				LATG	25	58.4	21/4	22.9	4.6	Circular stapler	D2	Roux-en-Y	end-to-side anastomosis	0	NA	4/5/15/1/0
Ito[34]	Japan	2014	2001–2012	TLTG	117	NA	NA	NA	NA	Circular stapler	D0/D1/D2/D3	Roux-en-Y	OrVil TM	0	NA	79/24/12/2/0
				LATG	46	NA	NA	NA	NA	Circular stapler	D0/D1/D2/D3	Roux-en-Y	end-to-side anastomosis	0	NA	35/5/5/1/0
Kim[35]	Korea	2013	2010–2011	TLTG	90	58	61/29	23.2	4.4	Linear stapler	D1/D2	NA	FEEA	0	NA	NA
				LATG	23	56.8	19/6	22.2	5.5	Circular stapler	D1/D2	NA	end-to-side anastomosis	0	NA	NA
Xing[36]	China	2021	2011–2019	TLTG	21	55.3	16/5	22.4	NA	Linear stapler	D2/D2 +	Roux-en-Y	Overlap	21	NA	6/10/5/0/0
				LATG	23	62.6	19/4	23.5	NA	Linear stapler	D2/D2 +	Roux-en-Y	Overlap	23	NA	4/10/7/0/0

Table 2

Quality scores of included studies.

References	Selection (stars)	Comparability (stars)	Outcome (stars)	Total (stars)
Qiu *et al.* 2022[25]	4	2	2	8
Han *et al.* 2020[26]	4	1	2	7
Chen *et al.* 2016[32]	4	2	2	8
Gong *et al.* 2017[27]	4	1	2	7
Kim *et al.* 2016[31]	4	1	2	7
Lu *et al.* 2016[33]	4	2	2	8
Kim *et al.* 2013[35]	4	1	2	7
Yamamoto *et al.* 2017[29]	4	1	2	7
Ito *et al.* 2014[34]	4	1	1	6
Huang *et al.* 2017[28]	4	2	2	8
Chen *et al.* 2019[22]	4	1	2	7
Park *et al.* 2021[23]	4	1	2	7
Lin *et al.* 2022[24]	4	2	2	8
Xing *et al.* 2021[36]	4	2	2	8
Jeong *et al.* 2019[30]	4	1	2	7

Results

Selected studies

A total of 118 studies from the database were included in the study. After screening the titles and abstracts, 26 studies remained. After further screening the full text, the following studies were excluded: one focused on laparoscopic total and distal gastrectomy[11], and one focused on laparoscopic gastrectomy for gastric cancer[12]. Two studies with no study results that we need[13,14], four studies published in Chinese language[15–18], two academic abstracts[19,20], an article with overlapping centers[21], and 15 studies[22–36] were included in the meta-analysis (Fig. 1).

Study characteristics

The clinical characteristics of all the studies that met the criteria for the meta-analysis are shown in Table 1. Overall, 3023 patients were included in this meta-analysis. These studies were conducted in Korea (six studies), Japan (two studies), and China (seven studies).

Study quality

In the case of nonrandomized controlled trials, the NOS is often used as a measure to assess the quality of the studies. The total NOS score was 9, and papers with a score ≥ 6 were classified as high-quality studies. Scores of the 15 included studies were all greater than 6, ensuring sufficient quality of all included studies (Table 2).

Intraoperative outcomes

Regarding intraoperative outcomes, the operative time, anastomosis time, blood loss, number of retrieved lymphatic nodes, proximal resection edge, and distal resection margin edge were collected and analyzed. In the 15 studies that reported operative time[22–36], the analysis revealed no statistically significant difference between the two groups (MD = – 8.29, 95% CI: – 17.33 to 0.74, $P = 0.07$; Fig. 2). Among the 10 studies that reported intraoperative blood loss[22,24,28–34], higher bleeding volume was found in the LATG group compared to the TLTG group. (MD = – 26.31, 95% CI: – 39.48 to – 13.14, $P < 0.0001$; Fig. 3), Lymphatic node dissection was reported in 10 articles[22–25,27,28,31,32,35,36], and the number of lymph nodes removed was greater in TLTG compared to LATG (MD = 2.52, 95% CI: 1.37–3.68, $P < 0.0001$; Fig. 4). Eight studies provided data on the proximal resection margin[22,23,27,28,31–33,35] and no statistically significant difference between the two groups (MD = – 0.20, 95% CI: – 0.65, 0.25, $P = 0.38$; Fig. 5). Distal resection margin reported in four studies[27,28,31,35], no statistically significant difference between the two groups (MD = 0.32, 95% CI: – 0.28 to 0.91, $P = 0.30$; Fig. 6). Only two studies reported the anastomosis time[32,33]and the analysis showed no statistically significant difference between the two groups (MD = 4.43, 95% CI: – 15.56–24.42, $P = 0.66$; Fig. 7).

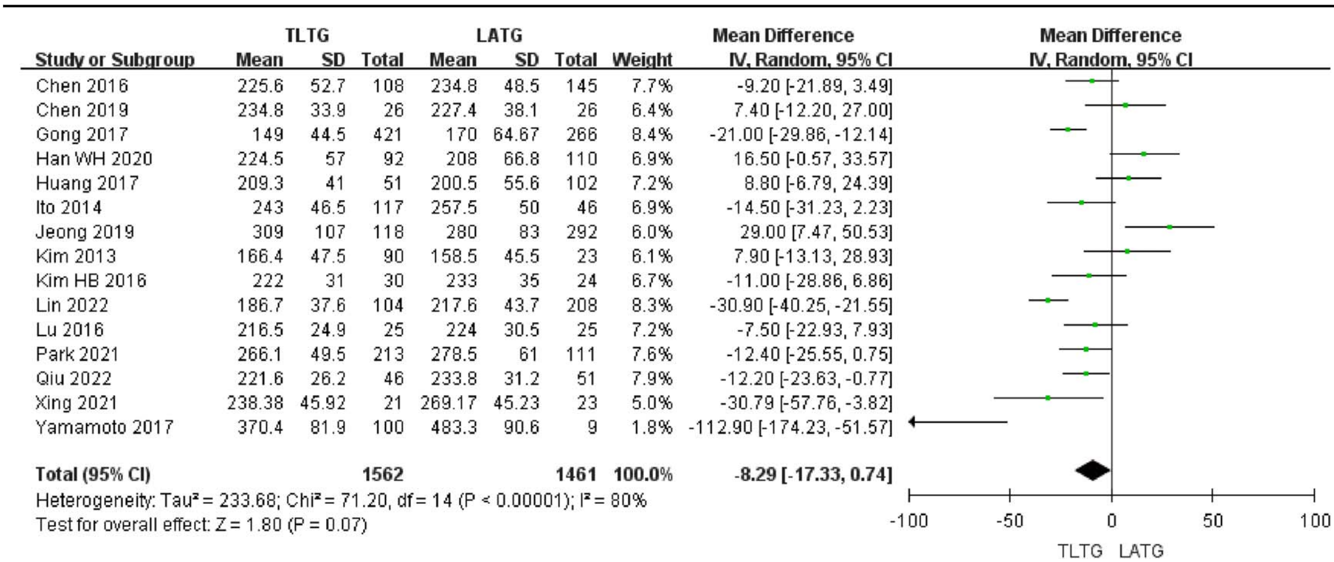

Figure 2. Meta-analysis result of operative time. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

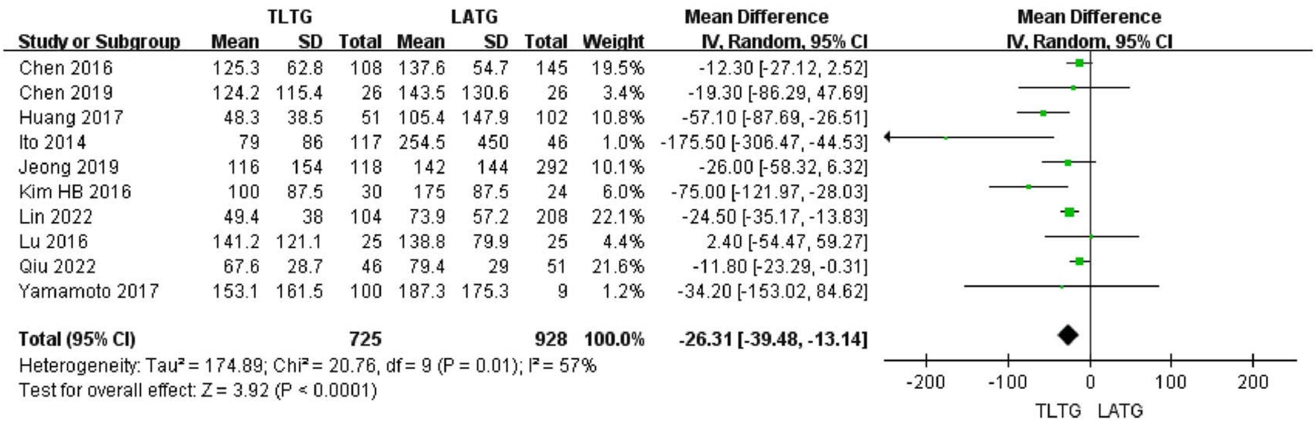

Figure 3. Meta-analysis result of intraoperative blood loss. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

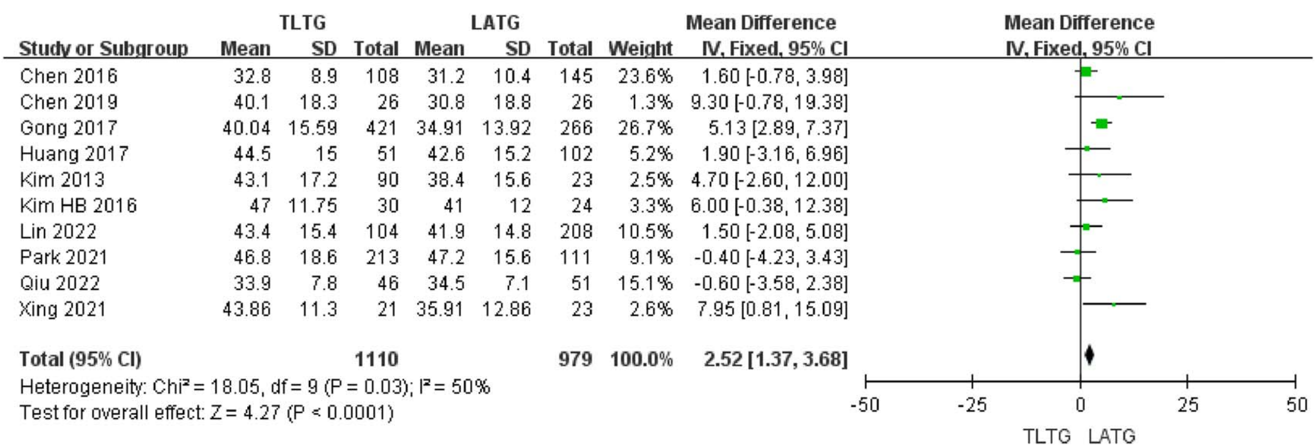

Figure 4. Meta-analysis results of the number of lymph nodes removed. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

Postsurgical outcomes

Fifteen articles reported no statistically significant difference in overall postoperative complications between the TLTG and LATG groups (RR = 0.97, 95% CI: 0.84–1.11, $P = 0.65$; Fig. 8)[22–36]. There was no statistically significant difference in anastomotic fistula (RR = 1.01, 95% CI: 0.69–1.48, $P = 0.97$; Fig. 9), anastomotic stenosis (RR = 0.63, 95% CI = 0.33–1.21, $P = 0.17$; Fig. 10), and anastomotic bleeding (RR = 0.36, 95% CI: 0.12–1.04, $P = 0.06$; Fig. 11) between the two groups. Also, nine studies provided postoperative pulmonary infection[22–26,29,32–34], and the analysis revealed no statistically significant difference between the two groups (RR = 0.83,

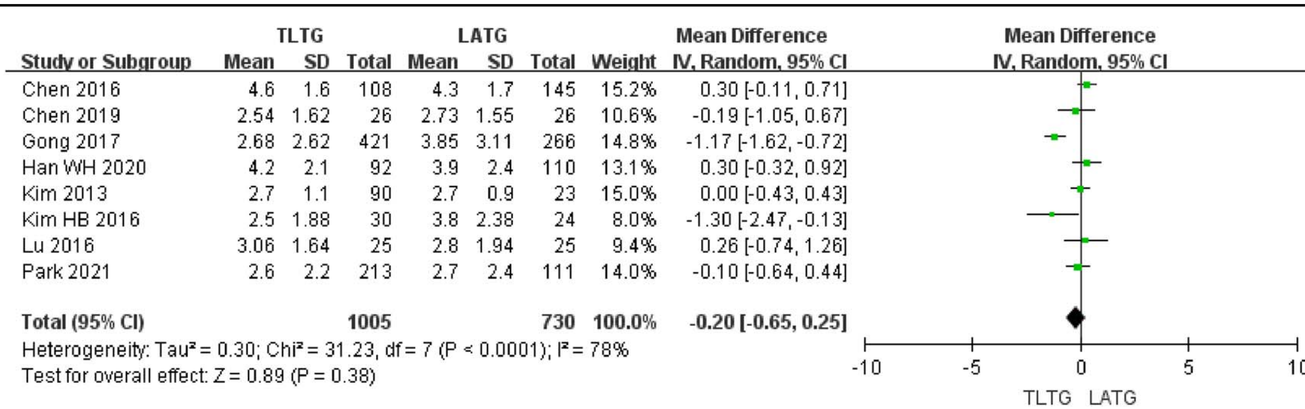

Figure 5. Meta-analysis results of the proximal resection margin. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

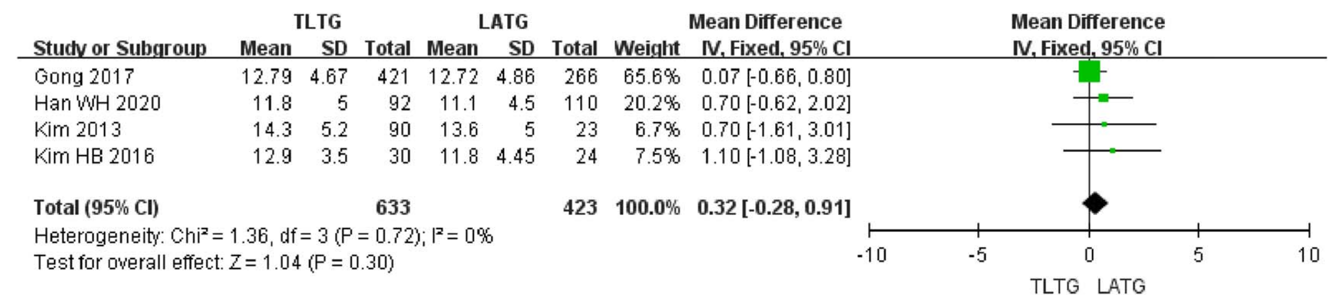

Figure 6. Meta-analysis results of the distal resection margin. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

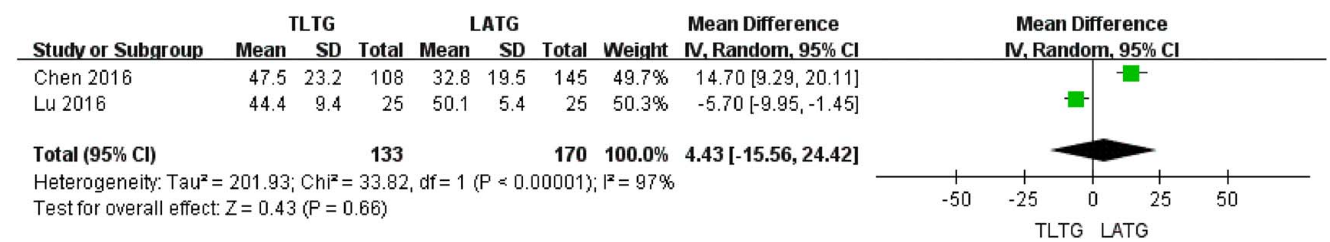

Figure 7. Meta-analysis results of the anastomosis time. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

95% CI: 0.55–1.26, $P=0.38$; Fig. 12). The postoperative hospital duration was also evaluated, time to first flatus, time to first fluid intake, and soft diet to assess postoperative recovery. In both groups, the time to postoperative hospitalization duration (MD = −0.66, 95% CI: −1.07 to −0.25, $P=0.002$; Fig. 13), time to first flatus (MD = 0.04, 95% CI: −0.14 to 0.22, $P=0.65$; Fig. 14), time to first liquid diet (MD = −0.02, 95% CI: −0.20 to 0.17, $P=0.87$; Fig. 15) and time to soft diet (MD = −0.20, 95% CI: −0.55 to 0.15, $P=0.27$; Fig. 16) were similar (Table 3).

Subgroup analyses stratified by stapler type

The studies included two types of staplers: linear stapler and circular stapler. Therefore, we can categorize the studies into two

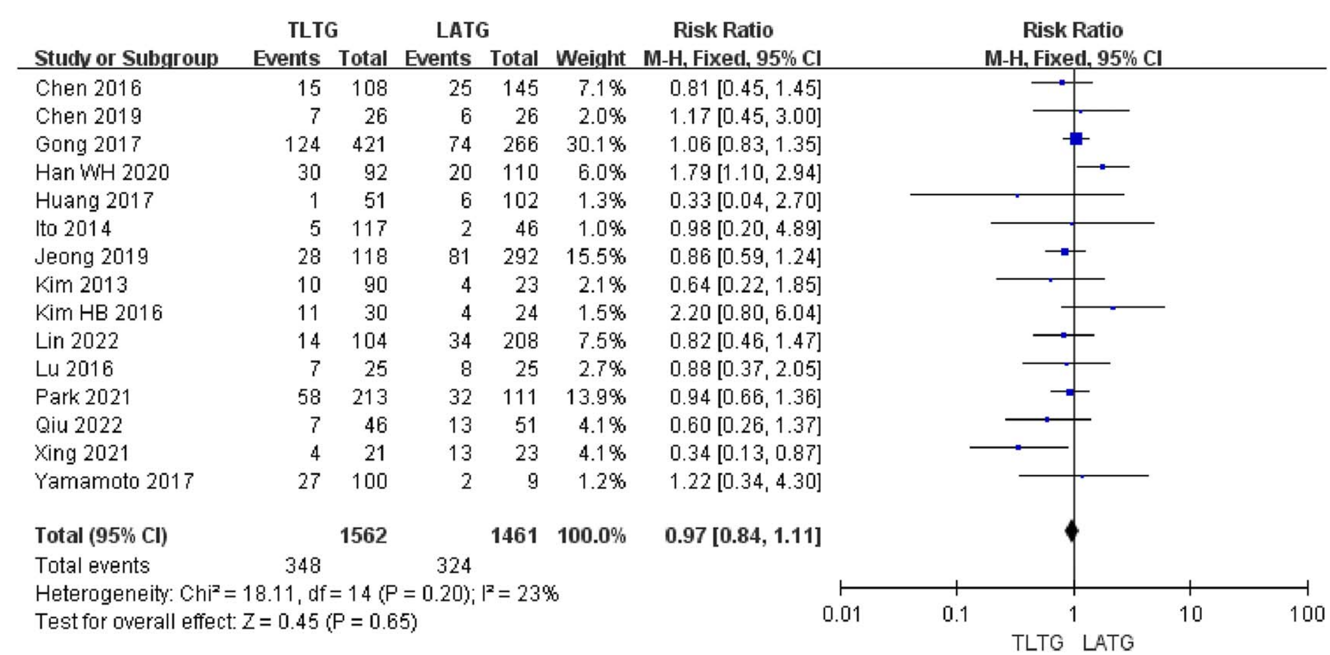

Figure 8. Meta-analysis results of the overall postoperative complications. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

Study or Subgroup	TLTG Events	TLTG Total	LATG Events	LATG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chen 2016	1	108	1	145	1.8%	1.34 [0.08, 21.23]
Chen 2019	3	26	3	26	6.3%	1.00 [0.22, 4.50]
Gong 2017	15	421	15	266	38.7%	0.63 [0.31, 1.27]
Han WH 2020	10	92	4	110	7.7%	2.99 [0.97, 9.22]
Huang 2017	1	51	4	102	5.6%	0.50 [0.06, 4.36]
Ito 2014	2	117	0	46	1.5%	1.99 [0.10, 40.71]
Jeong 2019	5	118	9	292	10.9%	1.37 [0.47, 4.02]
Kim 2013	0	90	3	23	11.6%	0.04 [0.00, 0.70]
Kim HB 2016	3	30	0	24	1.2%	5.65 [0.31, 104.25]
Lin 2022	1	104	3	208	4.2%	0.67 [0.07, 6.33]
Park 2021	9	213	2	111	5.5%	2.35 [0.52, 10.67]
Xing 2021	0	21	2	23	5.0%	0.22 [0.01, 4.30]
Total (95% CI)		**1391**		**1376**	**100.0%**	**1.01 [0.69, 1.48]**
Total events	50		46			

Heterogeneity: Chi² = 14.77, df = 11 (P = 0.19); I² = 26%
Test for overall effect: Z = 0.04 (P = 0.97)

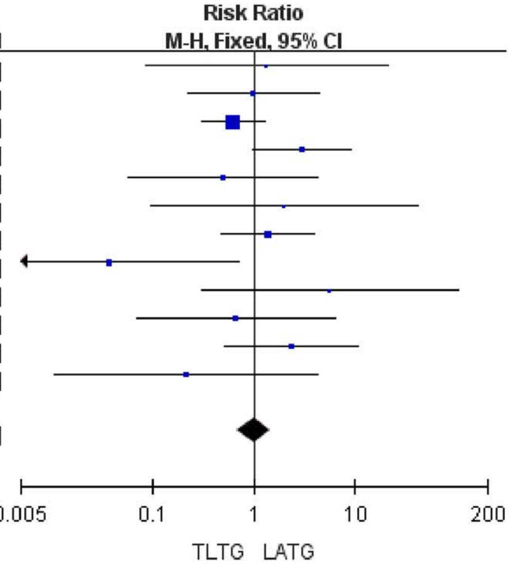

Figure 9. Meta-analysis results of the anastomotic fistula. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

Study or Subgroup	TLTG Events	TLTG Total	LATG Events	LATG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chen 2016	3	108	2	145	7.1%	2.01 [0.34, 11.84]
Gong 2017	2	421	3	266	15.2%	0.42 [0.07, 2.50]
Han WH 2020	2	92	3	110	11.3%	0.80 [0.14, 4.67]
Huang 2017	0	51	2	102	6.9%	0.40 [0.02, 8.10]
Ito 2014	2	117	2	46	11.9%	0.39 [0.06, 2.71]
Jeong 2019	0	118	13	292	32.2%	0.09 [0.01, 1.52]
Kim 2013	4	90	0	23	3.3%	2.37 [0.13, 42.58]
Kim HB 2016	3	30	0	24	2.3%	5.65 [0.31, 104.25]
Qiu 2022	0	46	2	51	9.8%	0.22 [0.01, 4.49]
Total (95% CI)		**1073**		**1059**	**100.0%**	**0.63 [0.33, 1.21]**
Total events	16		27			

Heterogeneity: Chi² = 7.50, df = 8 (P = 0.48); I² = 0%
Test for overall effect: Z = 1.38 (P = 0.17)

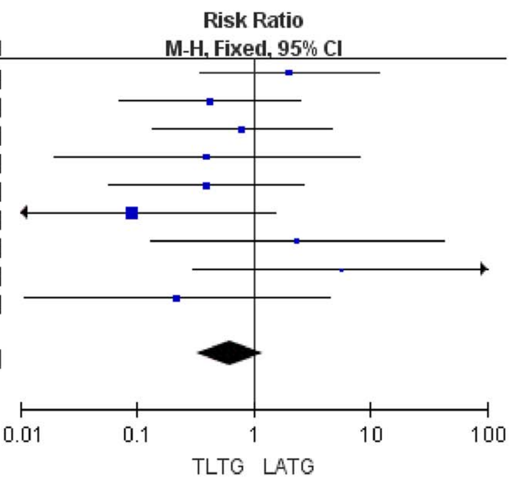

Figure 10. Meta-analysis results of the anastomotic stenosis. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

Study or Subgroup	TLTG Events	TLTG Total	LATG Events	LATG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chen 2019	0	26	2	26	16.9%	0.20 [0.01, 3.97]
Han WH 2020	2	92	0	110	3.1%	5.97 [0.29, 122.76]
Jeong 2019	0	118	16	292	64.3%	0.07 [0.00, 1.23]
Qiu 2022	0	46	1	51	9.6%	0.37 [0.02, 8.83]
Yamamoto 2017	4	100	0	9	6.1%	0.89 [0.05, 15.38]
Total (95% CI)		**382**		**488**	**100.0%**	**0.36 [0.12, 1.04]**
Total events	6		19			

Heterogeneity: Chi² = 5.07, df = 4 (P = 0.28); I² = 21%
Test for overall effect: Z = 1.89 (P = 0.06)

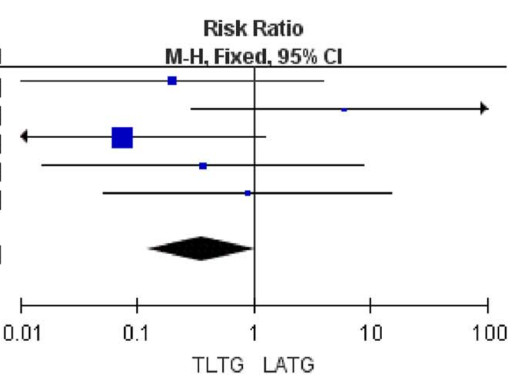

Figure 11. Meta-analysis results of the anastomotic bleeding. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

Study or Subgroup	TLTG Events	TLTG Total	LATG Events	LATG Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Chen 2016	1	108	4	145	7.7%	0.34 [0.04, 2.96]
Chen 2019	6	26	5	26	11.3%	1.20 [0.42, 3.45]
Han WH 2020	1	92	2	110	4.1%	0.60 [0.06, 6.49]
Kim 2013	2	90	0	23	1.8%	1.32 [0.07, 26.56]
Lin 2022	5	104	12	208	18.0%	0.83 [0.30, 2.30]
Lu 2016	3	25	2	25	4.5%	1.50 [0.27, 8.22]
Park 2021	17	213	12	111	35.6%	0.74 [0.37, 1.49]
Qiu 2022	5	46	7	51	15.0%	0.79 [0.27, 2.32]
Yamamoto 2017	5	100	0	9	2.1%	1.09 [0.06, 18.29]
Total (95% CI)		**804**		**708**	**100.0%**	**0.83 [0.55, 1.26]**
Total events	45		44			

Heterogeneity: Chi² = 1.91, df = 8 (P = 0.98); I² = 0%
Test for overall effect: Z = 0.88 (P = 0.38)

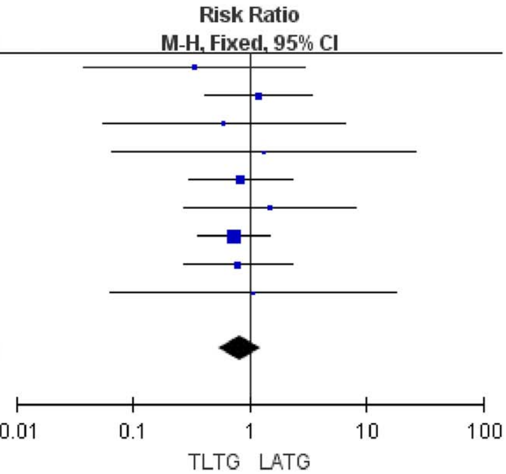

Figure 12. Meta-analysis results of the postoperative pulmonary infection. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

Study or Subgroup	TLTG Mean	TLTG SD	TLTG Total	LATG Mean	LATG SD	LATG Total	Weight	Mean Difference IV, Fixed, 95% CI
Chen 2016	9.2	3	108	9.4	2.5	145	35.0%	-0.20 [-0.90, 0.50]
Chen 2019	14.4	18.4	26	16.2	20.3	26	0.2%	-1.80 [-12.33, 8.73]
Gong 2017	6.75	13	421	7.02	185.33	266	0.0%	-0.27 [-22.58, 22.04]
Huang 2017	12.6	4.3	51	15.4	8.9	102	3.9%	-2.80 [-4.89, -0.71]
Jeong 2019	9.9	7.7	118	9.9	9.2	292	5.6%	0.00 [-1.74, 1.74]
Kim 2013	7.9	4.3	90	9.5	7.5	23	1.7%	-1.60 [-4.79, 1.59]
Kim HB 2016	8	6.75	30	7	1.25	24	2.8%	1.00 [-1.47, 3.47]
Lin 2022	12.4	8.2	104	11.9	8.9	208	4.3%	0.50 [-1.49, 2.49]
Lu 2016	8.8	5	25	9.6	3.9	25	2.8%	-0.80 [-3.29, 1.69]
Park 2021	11.8	6.7	213	10.8	6.7	111	7.2%	1.00 [-0.54, 2.54]
Qiu 2022	8	1.4	46	9.5	2	51	36.6%	-1.50 [-2.18, -0.82]
Total (95% CI)			**1232**			**1273**	**100.0%**	**-0.66 [-1.07, -0.25]**

Heterogeneity: Chi² = 19.99, df = 10 (P = 0.03); I² = 50%
Test for overall effect: Z = 3.13 (P = 0.002)

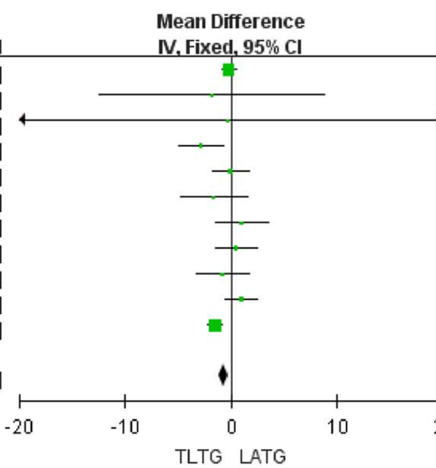

Figure 13. Meta-analysis results of the postoperative hospital duration. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

Study or Subgroup	TLTG Mean	TLTG SD	TLTG Total	LATG Mean	LATG SD	LATG Total	Weight	Mean Difference IV, Random, 95% CI
Chen 2016	3.4	1.1	108	3.4	1	145	12.8%	0.00 [-0.26, 0.26]
Gong 2017	3.3	1	421	3.6	1	266	15.7%	-0.30 [-0.45, -0.15]
Han WH 2020	3.8	0.6	92	3.5	0.8	110	14.7%	0.30 [0.11, 0.49]
Huang 2017	3.8	1.2	51	3.6	1.2	102	9.4%	0.20 [-0.20, 0.60]
Jeong 2019	2.9	0.9	118	2.9	0.9	292	14.7%	0.00 [-0.19, 0.19]
Kim 2013	3.4	1	90	3.2	0.7	23	10.6%	0.20 [-0.15, 0.55]
Lin 2022	5.7	3.2	104	5.2	3	208	4.5%	0.50 [-0.24, 1.24]
Lu 2016	3.1	0.8	25	3.1	0.8	25	8.6%	0.00 [-0.44, 0.44]
Qiu 2022	3.1	0.9	46	3.3	1.2	51	9.1%	-0.20 [-0.62, 0.22]
Total (95% CI)			**1055**			**1222**	**100.0%**	**0.04 [-0.14, 0.22]**

Heterogeneity: Tau² = 0.05; Chi² = 28.61, df = 8 (P = 0.0004); I² = 72%
Test for overall effect: Z = 0.45 (P = 0.65)

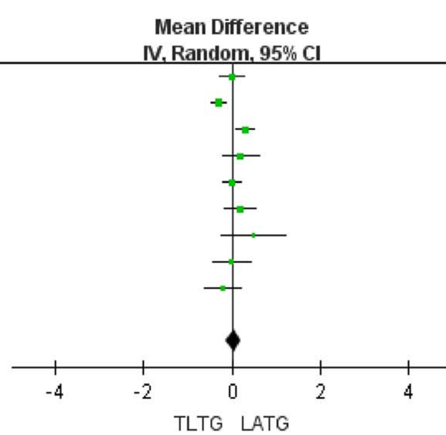

Figure 14. Meta-analysis results of the time to first flatus. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

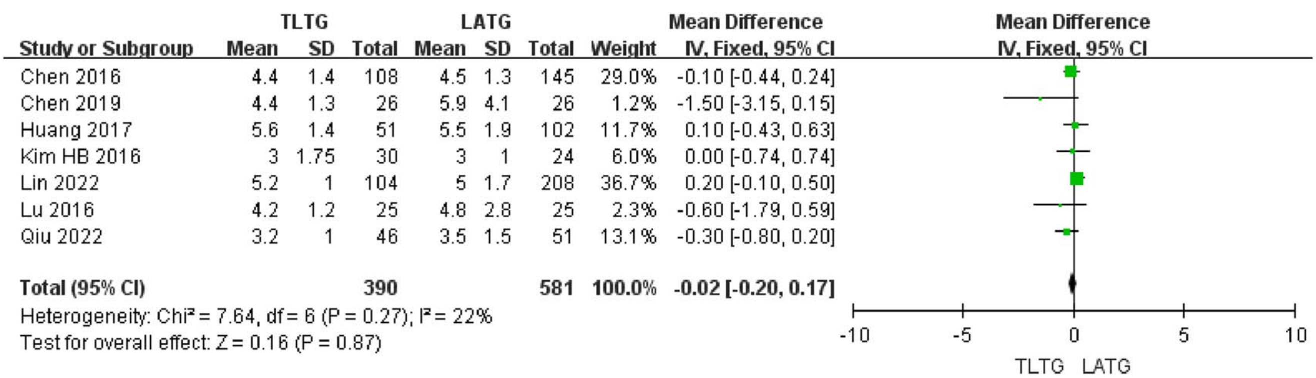

Figure 15. Meta-analysis results of the time to first liquid diet. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

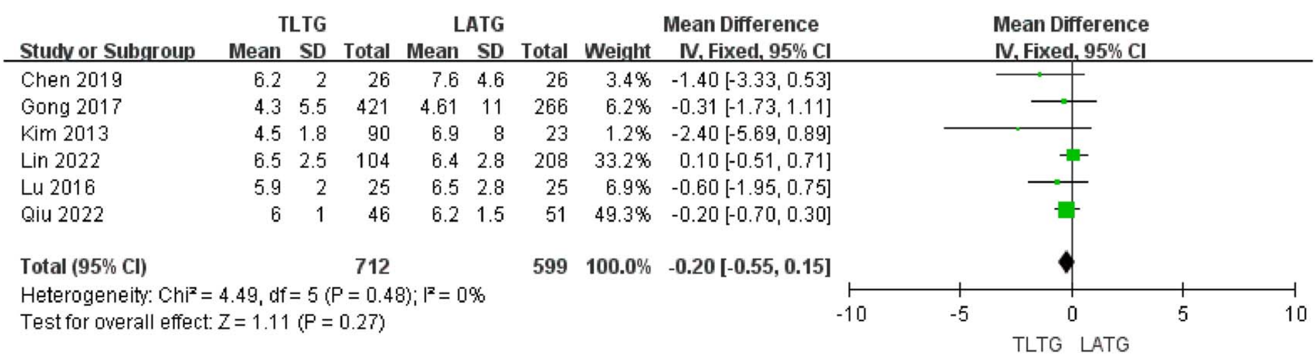

Figure 16. Meta-analysis results of the time to soft diet. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

Table 3

Summary of the meta-analysis of short-term outcomes between TLTG and LATG.

Short outcomes	Studies (n)	Participants (TLTG/LATG)	Risk Ratio/Mean Difference (95% CI)	Heterogeneity	Test for overall effect
Overall postoperative complications	15	1562/1461	0.97 [0.84–1.11]	$I^2=23\%$; $P=0.20$	$P=0.65$
Anastomotic fistula	12	1391/1376	1.01 [0.69–1.48]	$I^2=26\%$; $P=0.19$	$P=0.97$
Anastomotic stenosis	9	1073/1059	0.63 [0.33–1.21]	$I^2=0\%$; $P=0.48$	$P=0.17$
Anastomotic bleeding	5	382/488	0.36 [0.12–1.04]	$I^2=21\%$; $P=0.28$	$P=0.06$
Postoperative pulmonary infection	9	804/708	0.83 [0.55–1.26]	$I^2=0\%$; $P=0.98$	$P=0.38$
Postoperative hospital duration	11	1232/1273	− 0.66 [− 1.07– − 0.25]	$I^2=50\%$; $P=0.03$	$P=0.002$
Time to first flatus	9	1055/1222	0.04 [− 0.14–0.22]	$I^2=72\%$; $P=0.0004$	$P=0.65$
Time to first liquid diet	7	390/581	− 0.02 [− 0.20–0.17]	$I^2=22\%$; $P=0.27$	$P=0.87$
Time to soft diet	6	712/599	− 0.20 [− 0.55–0.15]	$I^2=0\%$; $P=0.48$	$P=0.27$
Operative time	15	1562/1461	− 8.29 [− 17.33–0.74]	$I^2=80\%$; $P<0.001$	$P=0.07$
Blood loss	10	725/928	− 26.31 [− 39.48– − 13.14]	$I^2=57\%$; $P=0.01$	$P<0.0001$
Number of lymph nodes removed	10	1110/979	2.52 [1.37–3.68]	$I^2=50\%$; $P=0.03$	$P<0.0001$
Proximal resection margin	8	1005/730	− 0.20 [− 0.65–0.25]	$I^2=78\%$; $P<0.0001$	$P=0.38$
Distal resection margin	4	633/423	0.32 [− 0.28–0.91]	$I^2=0\%$; $P=0.72$	$P=0.30$
Anastomosis time	2	133/170	4.43 [− 15.56–24.42]	$I^2=97\%$; $P<0.0001$	$P=0.66$

subgroups. The first subgroup, stapler of the different types, used linear staplers in the TLTG group and circular staplers in the LATG group. The second subgroup, stapler of the same type, used circular staplers or linear staplers in both the TLTG and LATG groups (Table 4).

Stapler of the same type

Subgroup analysis showed that there were no statistically significant differences between the TLTG and LATG groups in terms of overall postoperative complications (RR = 0.84, 95% CI: 0.65–1.09, $P=0.19$; Fig. 17), anastomotic fistula (RR = 1.28,

Table 4

Stapler types of included studies.

	Group Stapler type	
References	**TLTG**	**LATG**
Chen *et al.* 2016[32]	Circular stapler	Circular stapler
Chen *et al.* 2019[22]	Circular stapler	Circular stapler
Ito *et al.* 2014[34]	Circular stapler	Circular stapler
Park *et al.* 2021[23]	Circular stapler	Circular stapler
Lu *et al.* 2016[33]	Circular stapler	Circular stapler
Qiu *et al.* 2022[25]	Linear stapler	Circular stapler
Han *et al.* 2020[26]	Linear stapler	Circular stapler
Gong *et al.* 2017[27]	Linear stapler	Circular stapler
Huang *et al.* 2017[28]	Linear stapler	Circular stapler
Kim *et al.* 2016[31]	Linear stapler	Circular stapler
Kim *et al.* 2013[35]	Linear stapler	Circular stapler
Yamamoto *et al.* 2017[29]	Linear stapler	Circular stapler
Jeong *et al.* 2019[30]	Linear stapler	Circular stapler
Lin *et al.* 2022[24]	Linear stapler	Circular stapler
Xing *et al.* 2021[36]	Linear stapler	Linear stapler

95% CI: 0.55–3.00, $P=0.57$; Fig. 18), anastomotic stenosis (RR = 1.00, 95% CI: 0.30–3.34, $P=1.00$; Fig. 19), pulmonary infection (RR = 0.83, 95% CI: 0.49–1.41, $P=0.50$; Fig. 20). Lymphatic node dissection (MD = 1.83, 95% CI: – 0.08 to 3.75, $P=0.06$; Fig. 21), and no statistically significant difference in blood loss (MD = – 22.47, 95% CI: – 61.48 to 16.55, $P=0.26$; Fig. 22).

Stapler of the different type

Subgroup analysis showed no statistically significant differences between the TLTG and LATG groups in terms of overall postoperative complications (RR = 1.03, 95% CI: 0.87–1.21, $P=0.77$; Fig. 17), anastomotic fistula (RR = 0.94, 95% CI: 0.61–1.44, $P=0.77$; Fig. 18), anastomotic stenosis (RR = 0.54, 95% CI: 0.25–1.19, $P=0.13$; Fig. 19), and no statistically significant differences in pulmonary infection (RR = 0.83, 95% CI: 0.43–1.61, $P=0.58$; Fig. 20). However, there were statistically significant difference in lymphatic node dissection (MD = 2.93, 95% CI: 1.47–4.38, $P<0.0001$; Fig. 21) and blood loss (MD = – 30.39, 95% CI: – 46.21 to – 14.58, $P=0.0002$; Fig. 22).

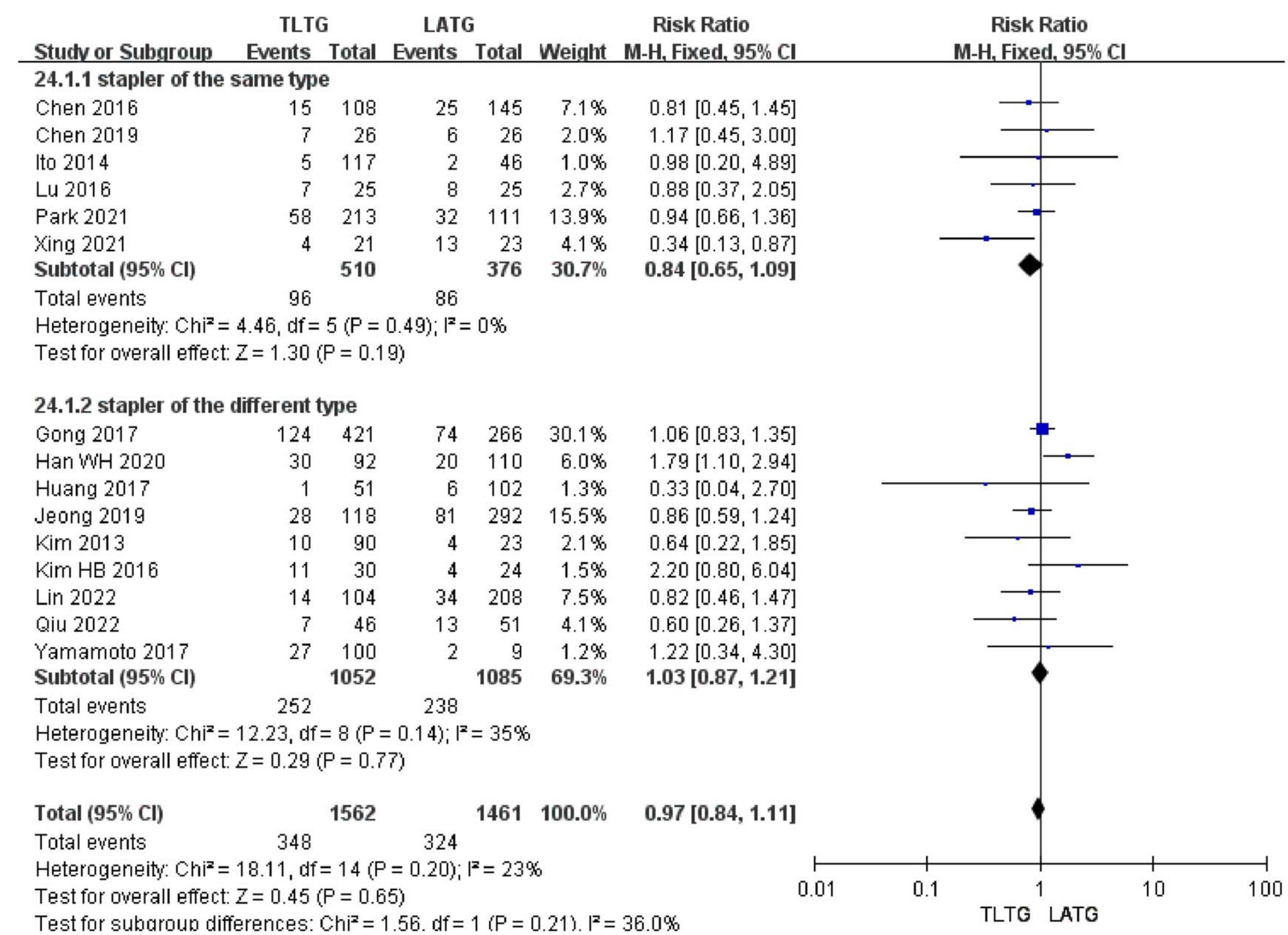

Figure 17. Subgroup analysis results of the overall postoperative complications stratified by stapler type. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

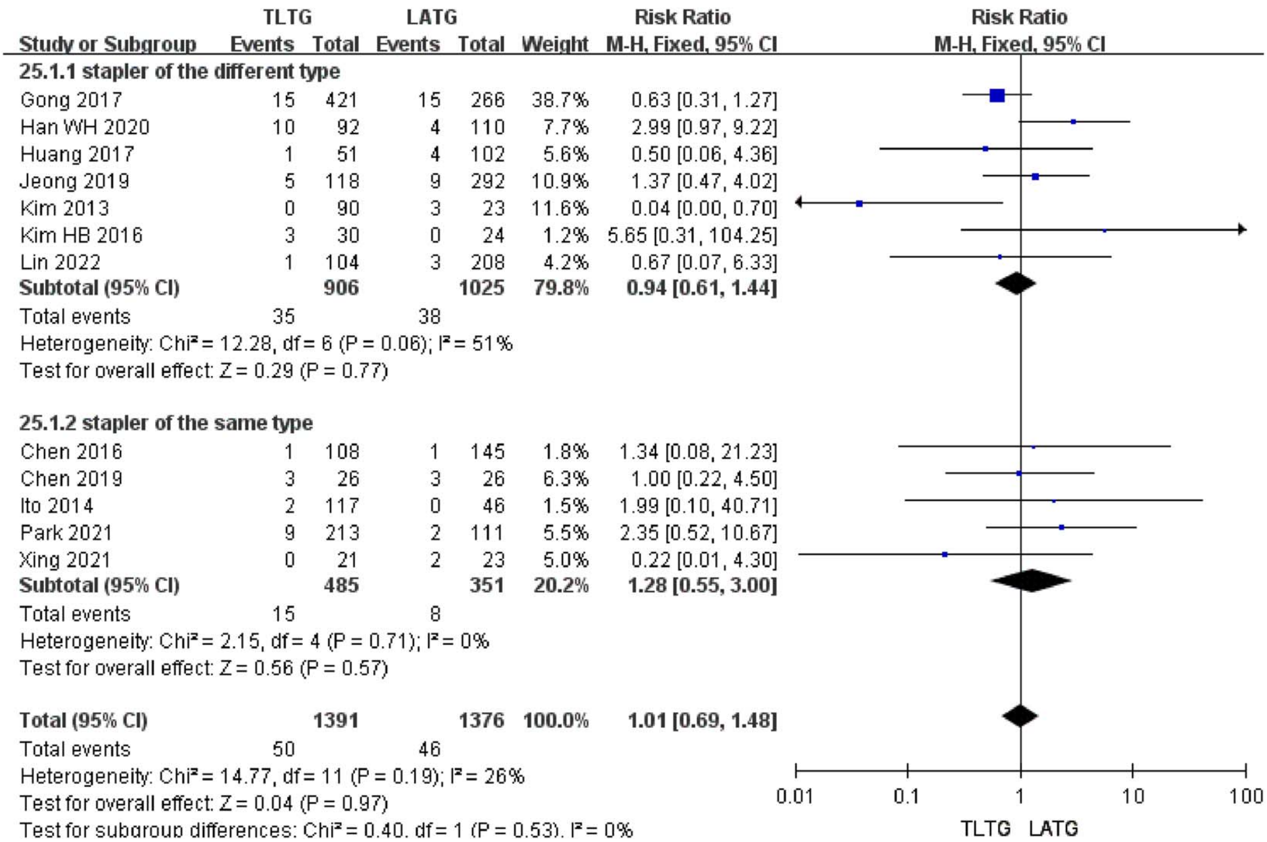

Figure 18. Subgroup analysis results of the anastomotic fistula stratified by stapler type. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

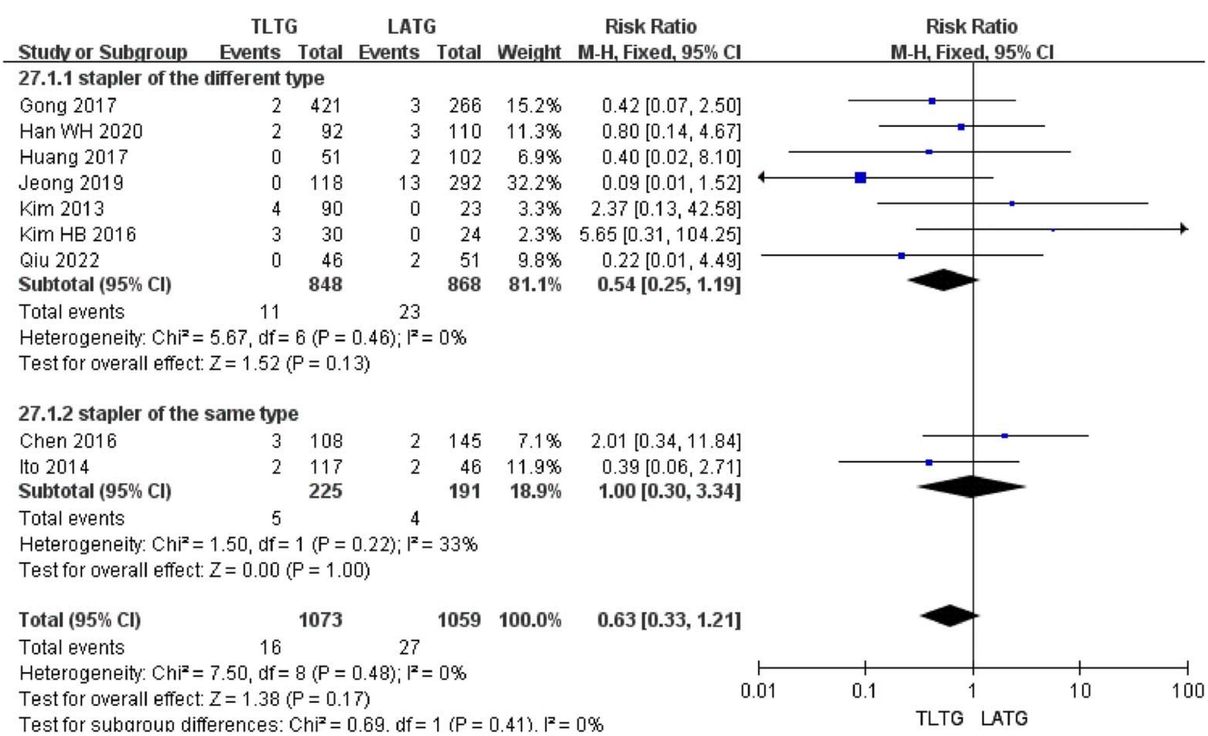

Figure 19. Subgroup analysis results of the anastomotic stenosis stratified by stapler type. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

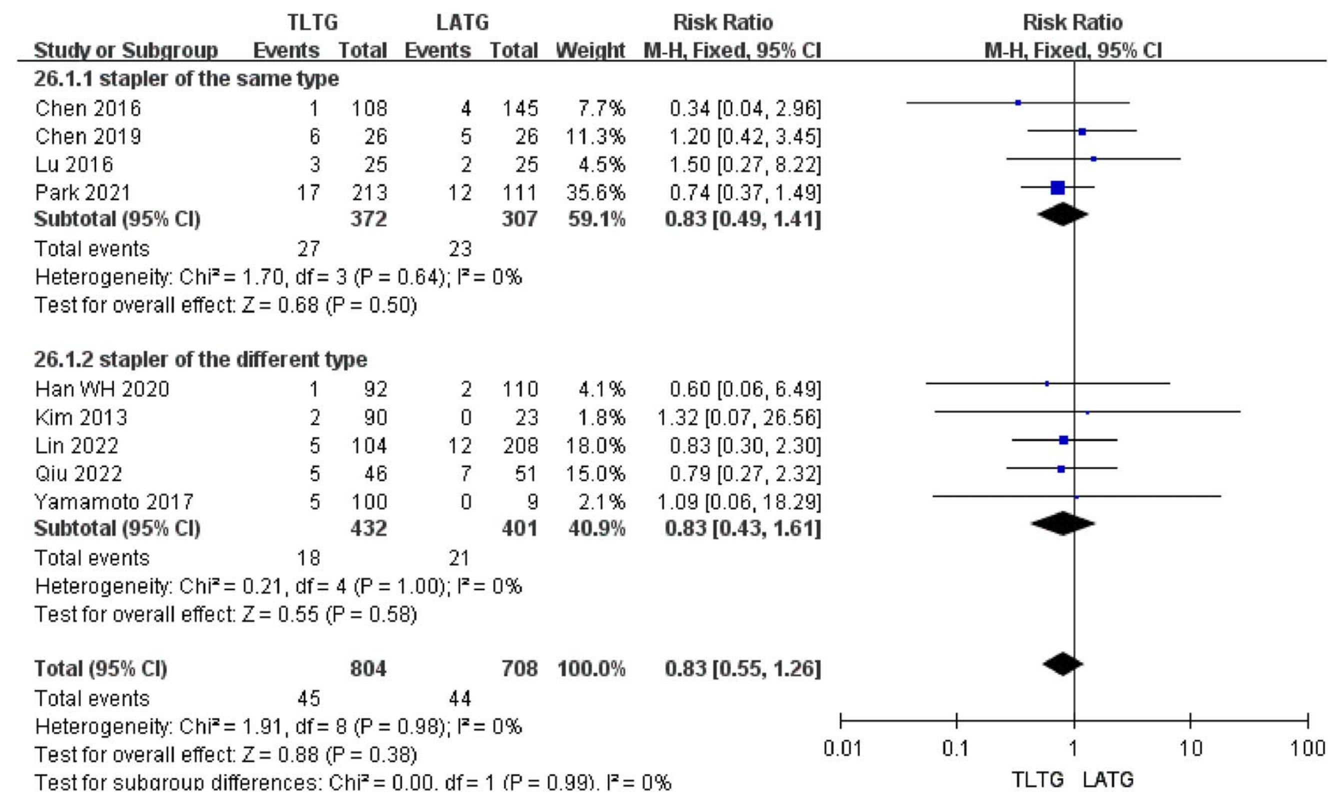

Figure 20. Subgroup analysis results of the postoperative pulmonary infection stratified by stapler type. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

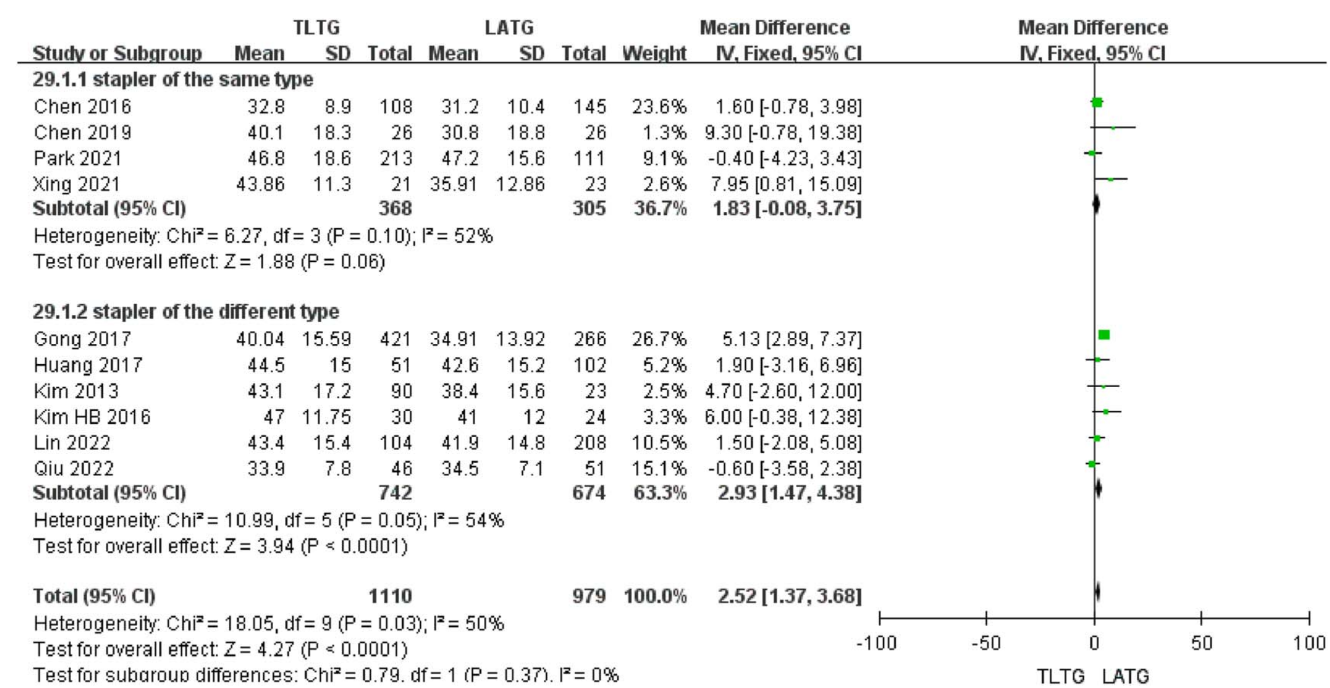

Figure 21. Subgroup analysis results of the number of lymph nodes removed stratified by stapler type. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

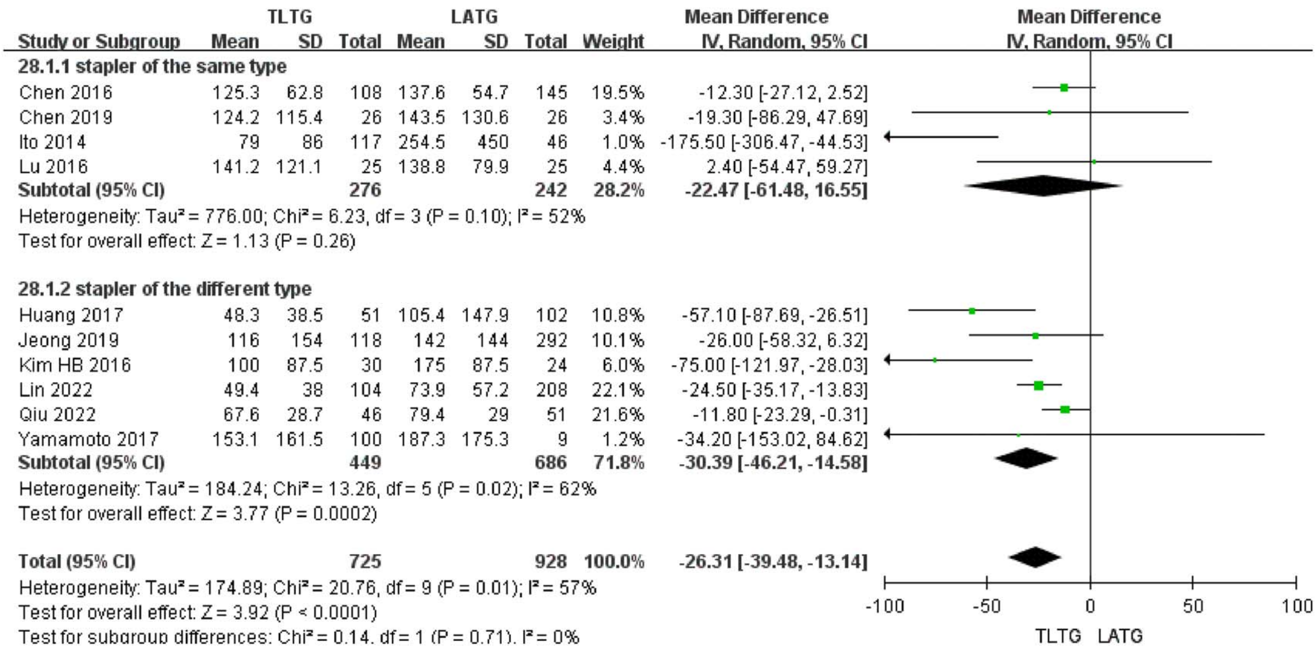

Figure 22. Subgroup analysis results of the blood loss stratified by stapler type. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

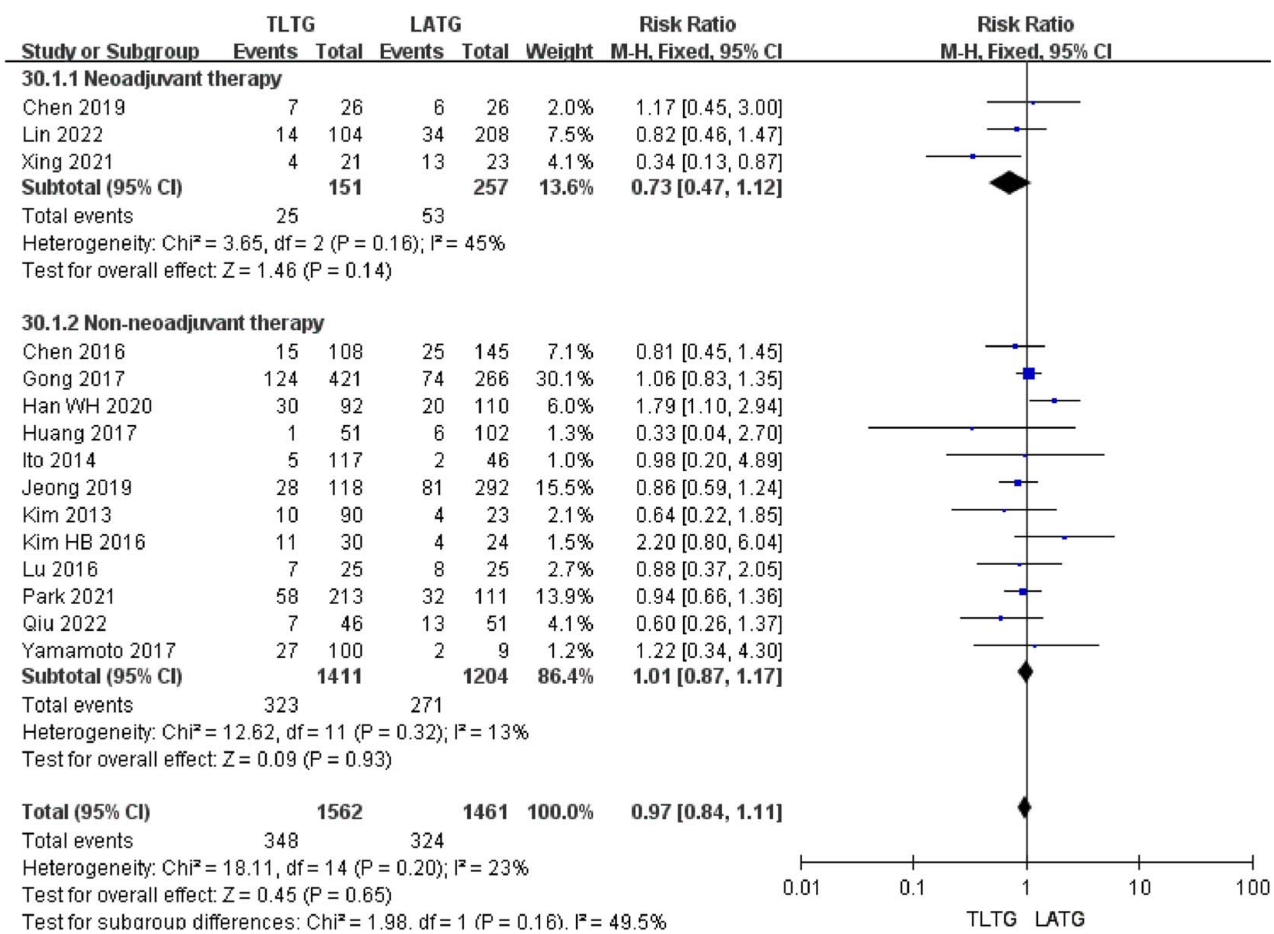

Figure 23. Subgroup analysis results of the overall postoperative complications stratified by neoadjuvant therapy. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

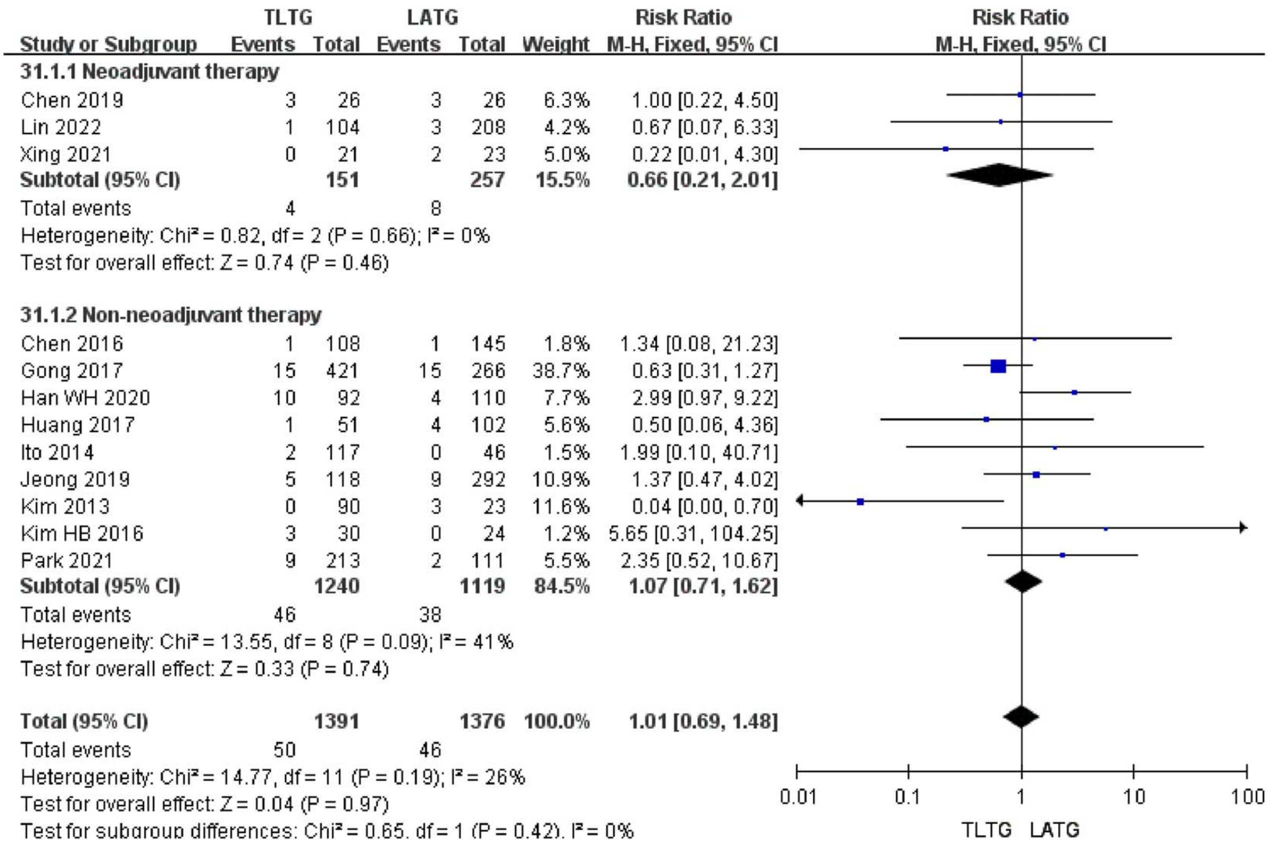

Figure 24. Subgroup analysis results of the anastomotic fistula stratified by neoadjuvant therapy. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

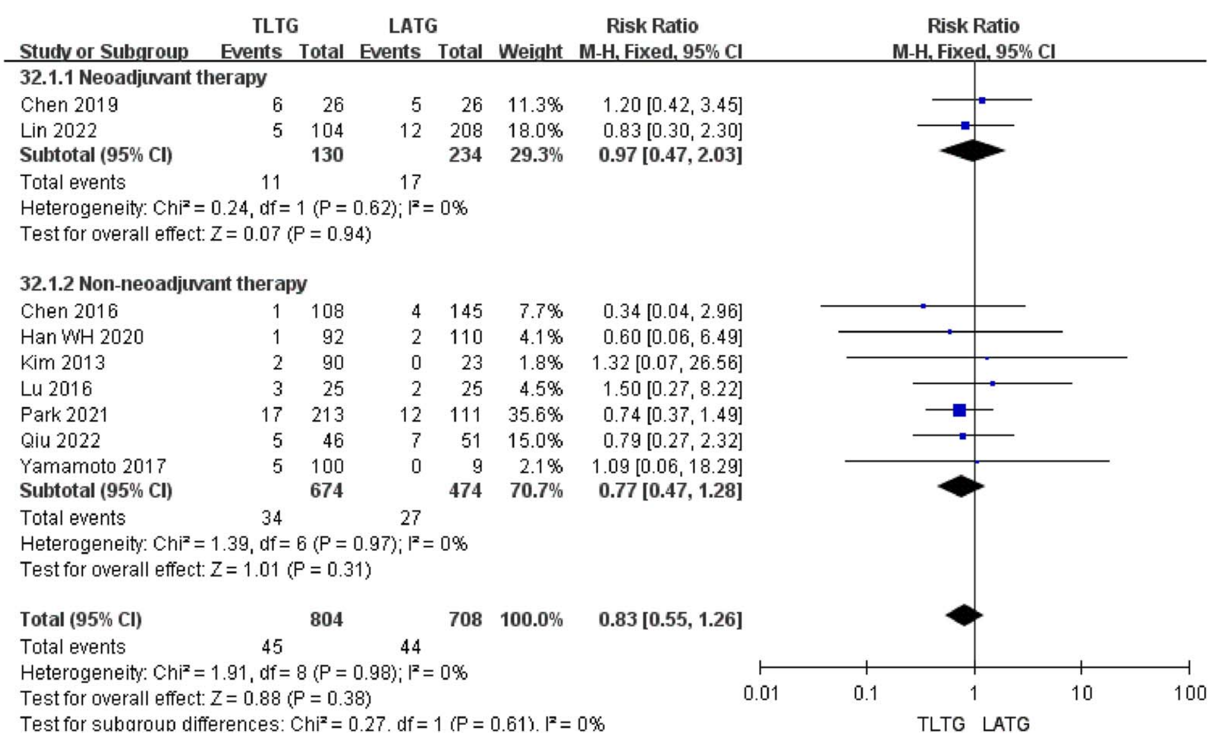

Figure 25. Subgroup analysis results of the postoperative pulmonary infection stratified by neoadjuvant therapy. LATG, laparoscopic-assisted total gastrectomy; TLTG, totally laparoscopic total gastrectomy.

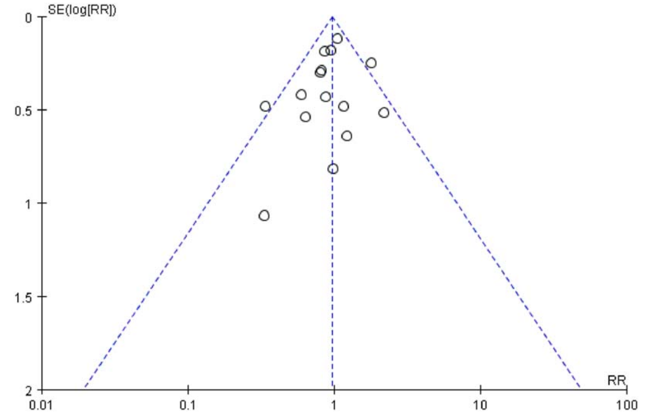

Figure 26. Funnel plot of overall postoperative complications. RR, risk ratio; SE, standard error.

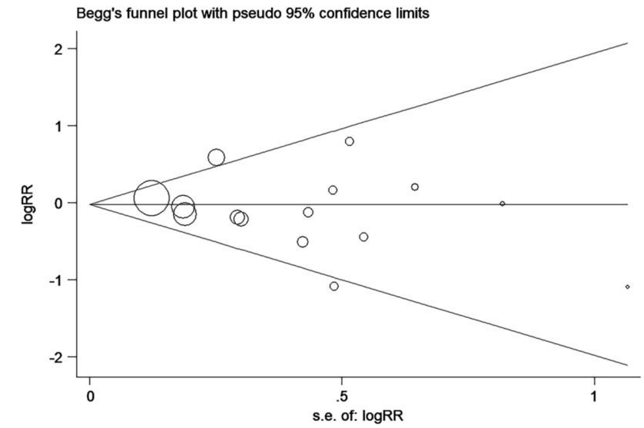

Figure 28. Begg's funnel plot of the overall postoperative complications.

Subgroup analyses stratified by neoadjuvant therapy

The included studies were categorized two groups based on the utilization of neoadjuvant therapy in the respective studies. One group is neoadjuvant therapy, the other group is non-neoadjuvant therapy.

Neoadjuvant therapy

Subgroup analysis showed no statistically significant differences between the TLTG and LATG groups in terms of overall postoperative complications (RR = 0.73, 95% CI: 0.47–1.12, *P* = 0.14; Fig. 23), anastomotic fistula (RR = 0.66, 95% CI: 0.21–2.01, *P* = 0.46; Fig. 24), pulmonary infection (RR = 0.97, 95% CI: 0.47–2.03, *P* = 0.94; Fig. 25).

Non-neoadjuvant therapy

Subgroup analysis showed no statistically significant differences between the TLTG and LATG groups in terms of overall postoperative complications (RR = 1.01, 95% CI: 0.87–1.17, *P* = 0.93; Fig. 23), anastomotic fistula (RR = 1.07, 95% CI: 0.71–1.62, *P* = 0.74; Fig. 24), pulmonary infection (RR = 0.77, 95% CI: 0.47–1.28, *P* = 0.31; Fig. 25).

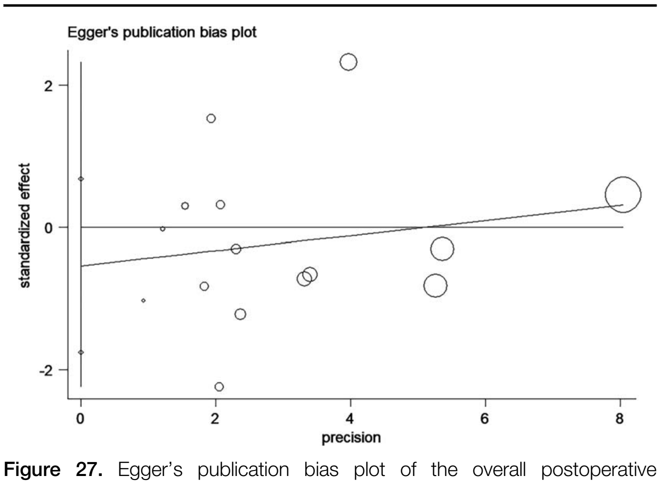

Figure 27. Egger's publication bias plot of the overall postoperative complications.

Publication bias and sensitivity analysis

For overall postoperative complications, funnel plots were used to assess publication bias (Fig. 26), which was accurately evaluated using Egger's and Begg's tests (Figs 27 and 28). The results showed that the funnel plot was not asymmetric, and the *P* values of Egger's and Begg's tests were 0.359 and 0.428, respectively, indicating no publication bias in the study. Sensitivity analysis of overall postoperative complications, blood loss, operative time, anastomosis time, time to first flatus, and proximal resection margin showed that removing any of the studies did not significantly affect the total effect size, indicating that the results were statistically stable (Figs 29–34).

Heterogeneity analysis

For outcomes with high heterogeneity, meta-regression was performed to explore the sources of heterogeneity. The results of the meta-regression showed that the p values of region, publication year, stapler type, and neoadjuvant therapy in operative time were 0.434, 0.721, 0.776, 0.404, in proximal resection margin were 0.283, 0.865, 0.254, 0.985. in time to first flatus were 0.917, 0.866, 0.823, 0.297, in blood loss were 0.239, 0309, 0.492, 0.768. It indicated that these factors were not the sources of heterogeneity (Supplementary Tables 1–4, Supplemental Digital Content 4, http://links.lww.com/JS9/B434, Supplemental Digital Content 5, http://links.lww.com/JS9/B435, Supplemental Digital Content 6, http://links.lww.com/JS9/B436, Supplemental Digital Content 7, http://links.lww.com/JS9/B437).

Discussion

Surgery remains the primary treatment for gastric cancer, including lymph node dissection and gastrectomy. In addition, D1 resection is indicated for differentiated cT1bN0 tumors ≤1.5 cm in diameter and D2 resection is indicated for cT2-T4 stage tumors and cT1N + tumors[37]. LATG and TLTG are extensively used to treat gastric cancer. However, the effect of surgery remains controversial owing to the lack of large sample studies.

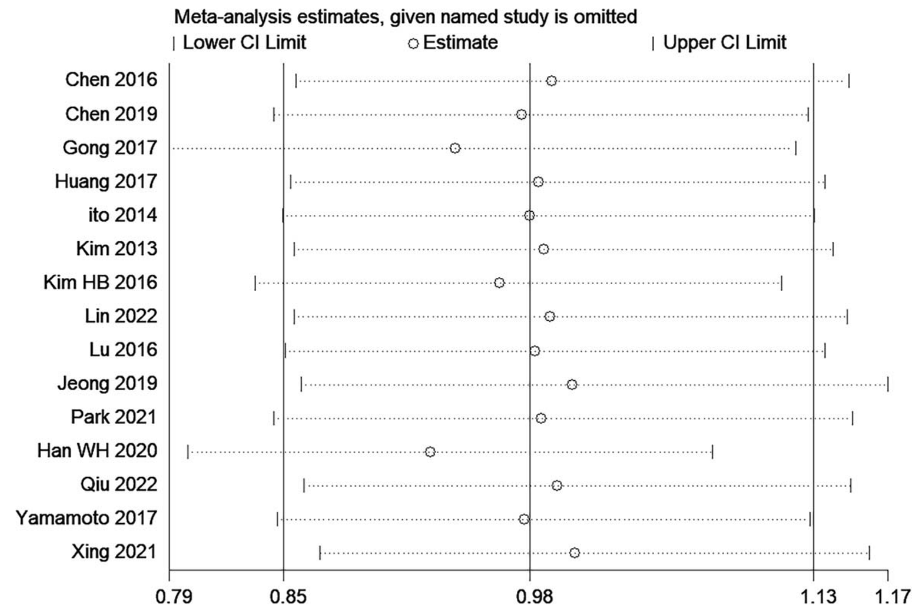

Figure 29. Sensitivity analysis of overall postoperative complications.

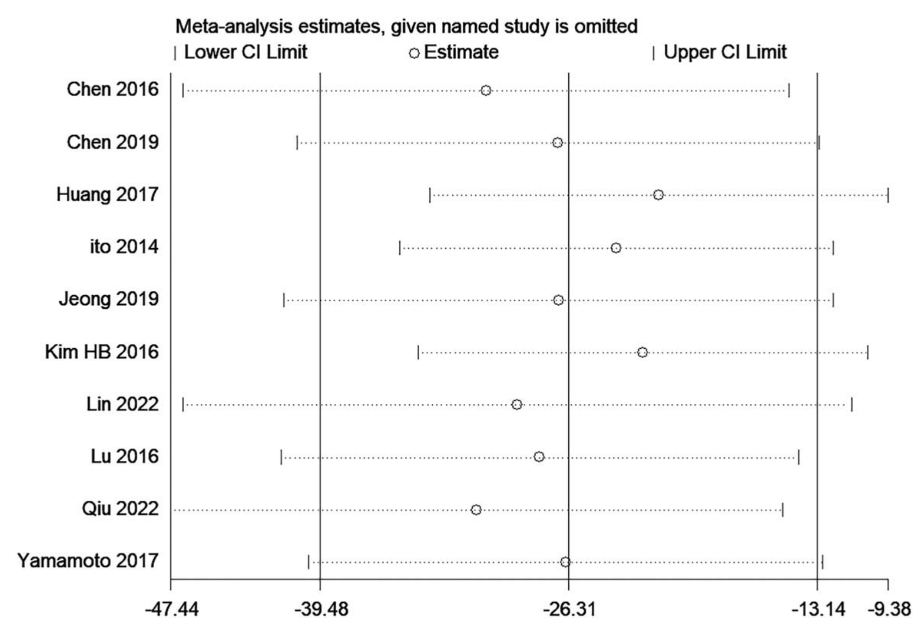

Figure 30. Sensitivity analysis of the blood loss.

Usually, extracorporeal anastomosis with the LATG is performed through a 5–7 cm small incision in the middle upper abdomen. In addition, for obese patients with a higher BMI, extension of the incision is a prerequisite for obtaining a better safety field of view. What is more, extracorporeal esophagojejunostomy is performed in a limited space, and intraoperative anastomosis suturing appears to be challenging. When the exposed length of the esophagus is short, contraction of the esophagus and peristalsis of the jejunum increases the tension of the anastomosis, thereby increasing the risk of an anastomotic fistula[38]. For TLTG, esophagojejunal anastomosis was performed under full laparoscopic vision, which provided a more comprehensive surgical view and reduced anastomotic tension. Compared to LATG, TLTG is less invasive and traumatic. Kim *et al.*[35] concluded that TLTG can improve early surgical outcomes; however, esophagojejunostomy is challenging to popularize widely.

This meta-analysis included high-quality cohort studies from databases that compared the two surgical approaches. As is well known, the overall postoperative complications are more representative and significantly correlated with recurrence and poor survival in patients with gastric cancer. To obtain better surgical outcomes and long-term prognosis, postoperative complications should be minimized as much as possible[39]. In this meta-analysis, there were no statistically significant differences between the LATG and TLTG groups in terms of overall postoperative

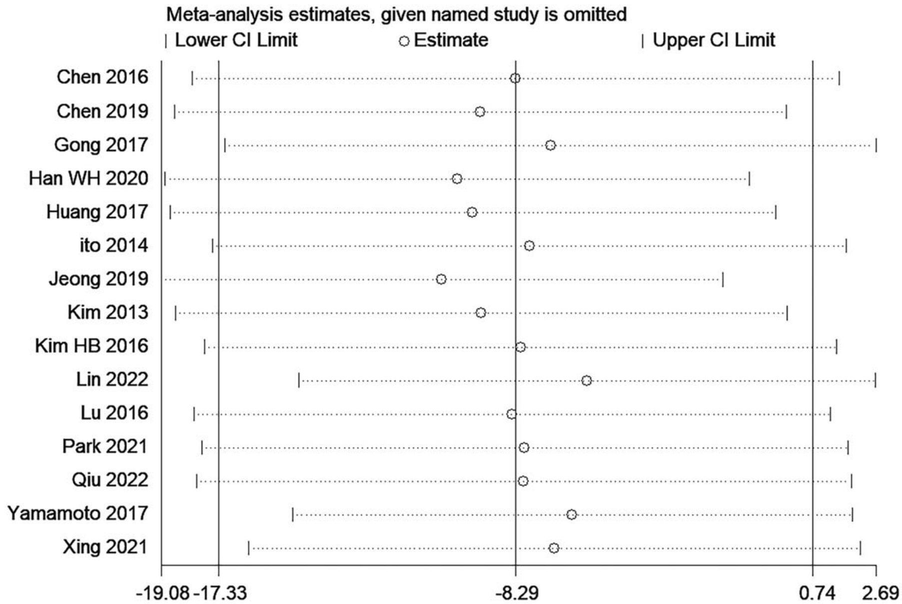

Figure 31. Sensitivity analysis of the operative time.

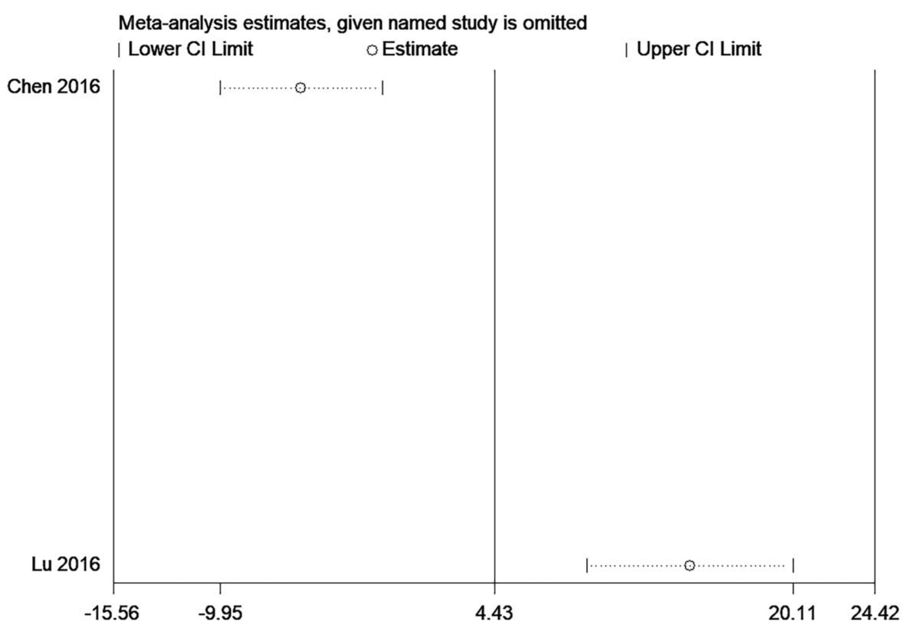

Figure 32. Sensitivity analysis of the anastomosis time.

complications, including anastomotic fistula, anastomotic stenosis, anastomotic bleeding, and pulmonary infection. In general, the intracorporeal anastomosis using a linear stapler may be considered more feasible than the extracorporeal anastomosis using a circular stapler[27]. Therefore, the subgroup analysis was performed to explore the effect of types of staplers on overall postoperative complications. The results show no statistically significant differences in the two subgroups between TLTG and LATG, indicating no association between the postoperative complications and the types of staplers. Furthermore the effectiveness of neoadjuvant therapy remains controversial[40,41], and this subgroup analysis showed no difference in overall postoperative complications between TLTG and LATG regardless of whether neoadjuvant therapy was used or not, which showed that neoadjuvant therapy may not have a significant effect on overall postoperative complications. In conclusion, the reasons are as follows: First, the two surgical approaches in terms of anastomotic tension and anastomotic blood flow may not show much difference. Second, this may be related to the development of anastomotic techniques and the operative proficiency of surgeons. It also shows that although TLTG is challenging to perform, it does not increase postoperative-related complications, proving a safe technique. In addition, the operative and anastomosis times of the two groups were similar in this meta-

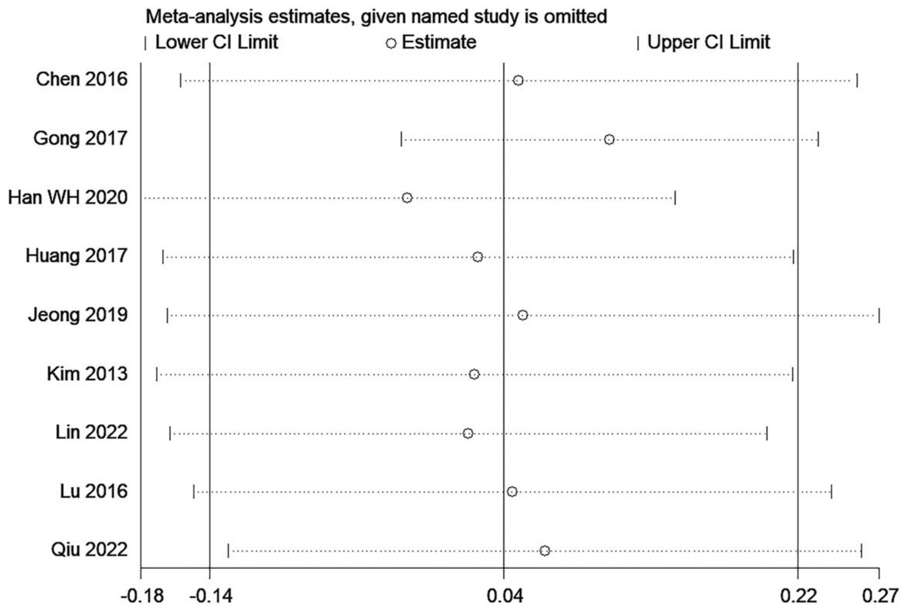

Figure 33. Sensitivity analysis of the time to first flatus.

analysis. This may be the surgeons have become proficient in this technique after a certain amount of practice. Furthermore, the fact that TLTG does not require additional incisions is also a significant reason. The intraoperative blood loss in the TLTG group was lower than that in the LATG group. Based on clinical practice, it has been observed that using linear staplers may reduce the risk of bleeding[42]. Therefore, subgroup analyses were performed in this article, which showed no difference in blood loss between TLTG and LATG when both used the same type of stapler, but there was a statistically significant difference between TLTG and LATG when used different types of staplers. It showed that the lower blood loss in TLTG group may be attributed to the use of linear staplers. Of course, it could be related to the fact that using linear staplers may eliminated the process of purse suture and placemen of anvil head when closing the anastomosis with circular staplers. In addition, intracorporeal anastomosis causes less strain on the anastomosis, less damage to the surrounding tissue and requires a relatively small incision. The duration of hospitalization in the TLTG group was shorter than that in the LATG group, which may be associated with a smaller wound, less bleeding, and less pain in the TLTG group. Compared with patients who underwent LATG, there were no significant

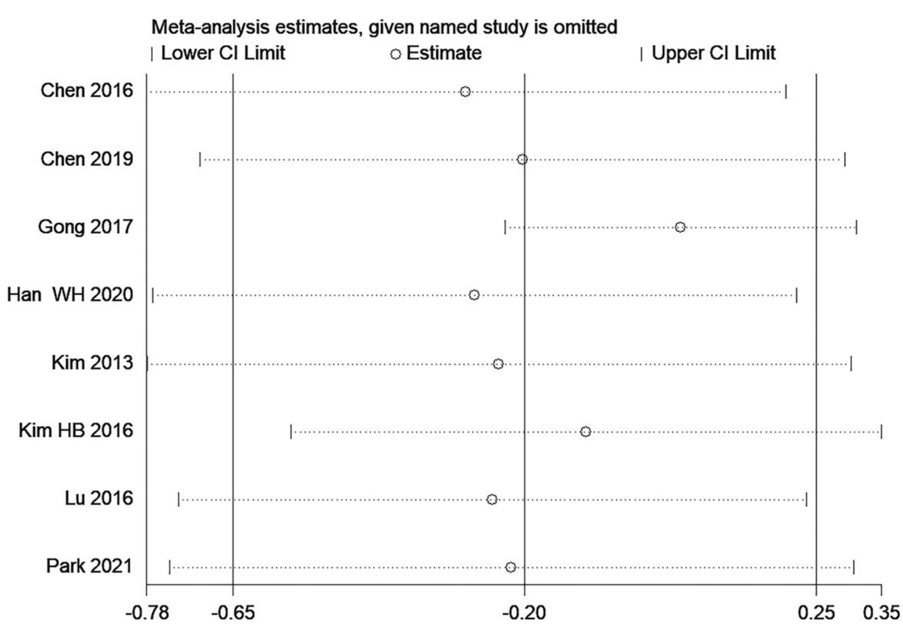

Figure 34. Sensitivity analysis of the proximal resection margin.

Table 5

Tumor location of included studies.

References	Tumor location
Chen *et al.* 2016[32]	Upper, Middle
Chen *et al.* 2019[22]	EGJ
Ito *et al.* 2014[34]	Upper, Middle, Lower
Park *et al.* 2021[23]	NA
Lu *et al.* 2016[33]	EGJ, Non-EGJ
Qiu *et al.* 2022[25]	Cardia, Body
Han *et al.* 2020[26]	Upper, Middle, Combined
Gong *et al.* 2017[27]	NA
Huang *et al.* 2017[28]	Upper, Middle, Whole
Kim *et al.* 2016[31]	Upper, Middle
Kim *et al.* 2013[35]	NA
Yamamoto *et al.* 2017[29]	NA
Jeong *et al.* 2019[30]	NA
Lin *et al.* 2022[24]	Upper, Middle, Lower, Combined
Xing *et al.* 2021[36]	Upper, Middle, Lower

differences in the time to first liquid diet, time to first flatus, or time to first soft diet in patients who underwent TLTG, and these postoperative outcomes may not be related to the surgical approach.

Regarding tumor resection, oncological outcomes is a reflection of surgical outcome[43]. The two groups had no significant differences in proximal and distal margins. This may be because surgeons paid more attention to the resection margin, as resection margin involvement is associated with a negative prognosis after gastrectomy[44]. Patients in the TLTG group had more lymph nodes were removed during surgery than those in the LATG group, possibly because the TLTG group in most of the studies in this meta-analysis used linear staplers for esophagojejunostomy and anastomosis with linear staplers requires a longer esophagus to be dissociated than circular staplers; therefore, more paraoesophageal lymph nodes were removed in the TLTG group than in the LATG group. And, the subgroup analyses confirmed this view to some extent, which indicated that the TLTG showed a significant advantage over the LATG in lymph node dissection when TLTG and LATG used different types of staplers and there was no statistically significant difference between TLTG and LATG when both used the same type of stapler. Sensitivity analysis and Egger's and Begg's tests for overall postoperative complications were also performed, and no high heterogeneity or publication bias was found. The following outcomes, including blood loss, operative time, anastomosis time, time to first flatus, and proximal resection margin, showed high heterogeneity in the meta-analysis. Thus, random-effects models were used to analyze these outcomes. Furthermore, meta-regression was also performed to explore the sources of heterogeneity, with the results showing that region, publication year, stapler type, and neoadjuvant therapy were not sources of higher heterogeneity for operative time, proximal resection margin, time to first flatus, and blood loss. Due to only two studies reporting the anastomosis time, identifying the source of heterogeneity is challenging. Nevertheless, sensitivity analyses for each of these outcomes indicated that the results of the respective meta-analyses were relatively reliable. There are several certain limitations in this meta-analysis. Firstly, these articles were only from East Asian countries, with no studies from Western countries. Secondly, all the studies were nonrandomized controlled trials, and although the quality of the included studies was high, there may still be related risks of bias. Thirdly, since the surgical approaches in the studies were performed in different hospitals, the procedures' criteria may be inconsistent, which may affect the results. Fourthly, it should be noted that not all of the included studies underwent D2 resection, but these studies adhered to surgical guidelines[37]. According to a previous study, there is an association between different extent of lymph node dissection and complications[45]. However, distinguishing between D1 and D2 lymph node dissections in all the included studies is challenging because D1 and D2 dissections often co-occur within the same study. Therefore, future studies with large samples are needed to investigate the relationship between lymph node dissection and postoperative complications. Fifthly, incomplete characteristics of some studies prevented sources of heterogeneity from being further identified despite meta-regression being performed and hindered the inclusion of all studies in subgroup analyses which also could lead to confounding factors affecting the results. To begin with, it may not be possible to analyze the relationship between forms of gastric replacement and postoperative outcomes as only one study performed isoperistaltic jejunum-later-cut overlap method (IJOM) for digestive tract reconstruction and subgroup analyses stratified by esophagojejunostomy techniques are challenging to conduct due to some studies being grouped separately (e.g. Xing2021, Yamamoto 2017, and Qiu2022). What is more, comorbidities were mentioned in only two studies and follow-up time was not mentioned in any studies. Thus, in future studies, it is essential to conduct a rigorous assessment of the impact of these confounders on postoperative complications in patients. Additionally, based on our clinical experience, studies that did not reported neoadjuvant therapy was allocated to a subgroup that did not undergo neoadjuvant therapy. So more rigorous validation of the effect of neoadjuvant on postoperative complications is needed. Sixthly, Whether or not the margins are negative is one of the challenges in the surgical treatment of cardia cancer[46]. Among all the included studies, there was no detailed description of cardia cancer margins. Only one study specifically reported on cardia cancer and the rest studies both cardia and other gastric malignancies were combined, which hindered the ability of this meta-analysis to extract and analyze data specifically for patients with cardia cancer (Table 5). Seventhly, the qualifications, experience, and proficiency of the surgeons performing the procedures differed, which might impact the results.

Conclusion

TLTG did not lead to an increase in overall postoperative complications, which is a reliable surgical approach for treatment of gastric cancer. Moreover, it may reduce harm to patients and enable them to obtain better surgical outcomes.

Ethical approval

This study has no ethical implications.

Consent

None.

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Author contribution

The study proposal and design, data collection and analysis were done by Q.W., F.T., C.J., Y.W.L.L., Q.P., M.B., Z.S.; and the writing of the article was completed by Q.W. and F.T.

Conflicts of interest disclosure

The authors promise that this research has no conflict of interest with any party.

Research registration unique identifying number (UIN)

I have already registered on the prospero, and my registration number is CRD42023441065.

Guarantor

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Data availability statement

The data of this study were searched from databases and all findings were analyzed using data from the included studies, which are authentic and reliable.

Provenance and peer review

Not commissioned, externally peer-reviewed.

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