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Postoperative Outcome Of Laparoscopic Pylorus Preserving Gastrectomy And Distal Gastrectomy For Early Gastric Cancer: Meta-Analysis

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Abstract
Purpose*: The aim of this meta-analysis is to assess the effectiveness and outcomes of laparoscopic pylorus preserving gastrectomy (LPPG) and laparoscopic distal gastrectomy (LDG) in patient with early gastric cancer (EGC).*
Methods*: Renowned databases such PubMed, Google scholar and Medline were searched from the year 2004 to 2023.Postoperative outcomes recorded were operation time, blood loss, hospital length of stay, lymph node dissection, anastomotic leakage, gastric emptying, gastric stasis, wound infection and ileus. All included studies were analyzed by Review manager software 5.4 (RevMan).*
Results*: A total of 10 studies involving 1,481 patients met the eligibity criteria for this meta-analysis, 578 patients underwent LPPG gastrectomy and 903 LDG. Pooled data for LDG showed shorter operative time as compared to LPPG (Heterogeneity: Chi² = 486.04, df = 6 (P < 0.00001); I² = 99%). There was significant difference for blood loss and hospital length of stay between the two surgical methods with Heterogeneity: Chi² = 21.12, df = 4 (P = 0.0003); I² = 81% and Heterogeneity: Chi² = 2.11, df = 4 (P = 0.72); I² = 0% respectively. Furthermore, both techniques reported no significant difference for postoperative complications such as anastomosis leakage, gastric emptying, gastric stasis, wound infection and ileus.*
Conclusions*: For EGC, LDG can be considered as a better option than LPPG in terms of operative time. However, there was no significant difference for postoperative complication between the two techniques.*

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I. Introduction

Gastric cancer is the fourth most prevalent type of cancer and ranks third for cancer-related deaths among men and fifth among women globally[1]. There are two categories of gastric cancer, namely EGC and advanced gastric cancer. The Japanese Gastric Cancer Association defines EGC as a stomach lesion that is limited to the mucosa or submucosa, regardless of its size or whether it has spread to the lymph nodes[2]. Thanks to the progress in medical techniques, the quantity of people detected with EGC is progressively increasing. Surgery is the fundamental basis for administering conclusive therapy for this cancerous ailment[3, 4].

Despite numerous research studies that have compared PPG and DG in relation to surgical and functional outcomes, there is still a debate surrounding whether PPG is a better option than DG for EGC without compromising oncological safety. This is due to the lack of long-term oncologic outcomes and high-level evidence from randomized clinical trials (RCTs) [5-7]. In 2014, the first meta-analysis was published [10], which showed that PPG provided superior benefits, such as a lower incidence of early dumping syndrome, gastritis, and bile reflux, as well as weight recovery[8].

During the 2000s, there was a substantial assessment of the practicability and feasibility of minimally invasive methods, and the LPPG was also introduced and assessed during this period[9-12]. In comparison to the conventional PPG, LPPG offered numerous advantages of minimal invasion, such as reduced bleeding, decreased postoperative discomfort, and quicker restoration of intestinal function[13-15]. Additionally, LPPG led to a decreased possibility of postgastrectomy syndrome and better nourishing outcomes as compared to LDG [16-18]. There have been limited investigations examining the effectiveness of LPPG and LDG. Therefore, our meta-analysis aims to compare these methods regarding the postoperative outcomes and complications of EGC.

II. Material and Method

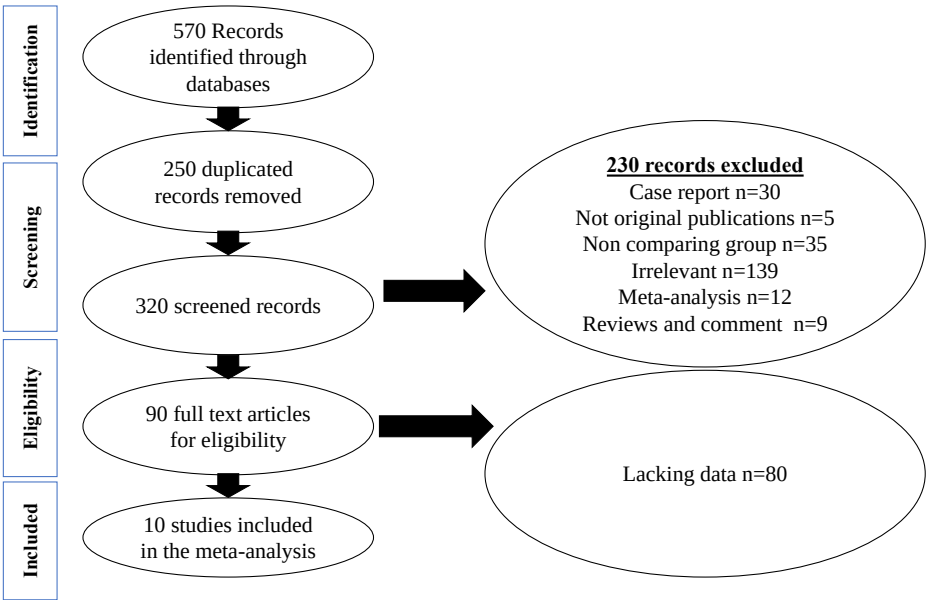
Search strategy

This meta-analysis was conducted through a thorough search of credible databases, including PubMed, Google Scholar, and Medline, spanning from 2004 to 2023. The search terms encompassed various types of laparoscopic gastrectomies, such as pylorus preserving and distal gastrostomies for the treatment of gastric or stomach cancer or neoplasms while preserving function. The search methodology varied depending on the database requirements. Ultimately, 10 comprehensive papers were gathered for the meta-analysis. Patient characteristics, including study location, publication year, study design, number of patients, age and type of anastomosis technique, were documented as seen in Table 1. Our study was conducted according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines[19].

Data Extraction

The retrieval process was conducted independently, resulting in the collection of 570 papers. After eliminating duplicates, 320 studies were obtained. These 320 studies were scrutinized, and 230 were excluded after careful examination, leaving 90 studies that were evaluated for eligibility. Among these, 80 studies lacked the required targeted information for analysis. Ultimately, 10 studies were selected for the meta-analysis, as depicted in Figure 1.

Figure 1.Prisma flow diagram of selected studies



Inclusion and Exclusion criteria

The inclusion are as follows:(1) Only full published article in English, (2) Studies comparing laparoscopic pylorus preserving gastrectomy and distal gastrectomy with various anastomosis technique, (3) Any kind of comparative studies, (4) Revealed adequate data, (5) All patients should be diagnosed with clinical stage 1 early gastric cancer or gastric cancer.

Exclusion criteria are as follows:(1) Animal or lab studies excluded, (2) Studies with conflicting result and unavailable postoperative outcomes and complications, (3) Patients with advance gastric cancer

Statistical Analysis

The statistical analysis was carried out utilizing the Review Manager (RevMan) software, version 5.4, presented by the Cochrane collaboration. The MD with a 95% CI was employed to pool continuous variables, while the OR with a 95% CI was used to pool dichotomous variables. The Mantel-Haenszel statistical method was utilized to compute random effect and fixed effect models for OR or RR. The inconsistency statistic (I^2) was employed to assess heterogeneity among studies. If I^2 was less than 50%, the eligible studies were deemed to be homogenous, and the fixed effect model was utilized. Conversely, if I^2 was greater than 50%, the pooled results were deemed significant, heterogeneous, and the random effect model was used instead.

Assessment of Quality

In this investigation, we employed the Cochrane Handbook for Systematic Reviews of Interventions, Version 5.1 risk of partiality instrument to individually evaluate the quality of the experiments [20]. We assessed sequence generation, allocation concealment, blinding, incomplete data, selective reporting, and other potential sources of partiality. The term "high risk" was utilized to denote a study that had a significant risk of partiality for one or more crucial domains. A study was considered to be "low risk" if it had a low partiality risk across all crucial domains. If not, it was categorized as "unclear," as depicted in Figure 11 A and B. Any disparities between the researchers were resolved through discussion with the corresponding author.

III. Results

Patients' Characteristics

A total of 570 potential records with LPPG and LDG were identified, of which 90 of them were fully examined. Finally, 10 articles were included in the meta-analysis including 1,481 patients diagnosed of EGC as shown in Figure 1. Among these patients, 578 underwent LPPG and 903 were LDG. The characteristics of the included studies are summarized in Table 1. Postoperative outcomes recorded were operation time, blood loss, hospital length of stay, lymph node dissection, anastomosis leakage, gastric emptying, gastric stasis, wound infection, and ileus as seen in Table 2.

Table 1.Descriptions of Included studies

Study and Publication year	Country	Type of Study design	Age(years)	Number of Patients LPPG/LDG	Anastomosis Method
Tsuijiura et al[21],2019	Japan	Retrospective	59.5± 9.3/59.4± 11.1	101/101	Billroth I/ Roux-en-Y/Gastro-gastro
Ikeguchi et al[22],2010	Japan	Retrospective	NR	24/30	Billroth I/ Gastro-gastro
Tomikawa et al[17],2012	Japan	Retrospective	69.2± 6.9/68.7± 4.8	9/12	Gastroduodenal/ Gastro-gastro
Suh et al[16],2014	Japan	Retrospective	54.1± 12.3/59.1± 12.0	116/176	Billroth I,11, Roux-en-Y/ Gastro-gastro
Xia et al[5],2019	China	Retrospective	56.8± 10.9/57.5± 12.1	70/97	Billroth I/ Gastro-gastro
Eom et al[23],2019	Korea	NR	58.3± 12.0/56.5± 11.8	101/195	Billroth II/ Gastro-gastro
Hosoda et al[24],2016	Japan	Retrospective	64.0± 9.5/63.2± 8.8	32/32	NR
Lee et al[25],2023	Korea	Retrospective	59.8± 11.1/60.4± 11.2	63/183	Billroth I, /Billroth II
Huang and Yu et al[26],2020	China	NR	NR	40/51	NR/Billroth I
Urushihara et al[11],2004	Japan	Retrospective	NR	22/26	NR/Gastro-gastro

Table 2.Postoperative Outcomes

Study and Publication year	Operative time	Blood loss	Hospital stays	Lymph node dissection	Anastomosis leakage	Gastric emptying	Gastric stasis	Wound Infection	Ileus
Tsuijiura et al[21],2019	254± 72.5 / 268± 88.75	35 ± 100 / 45± 110	11± 7 / 10± 11.5	39 ± 17.75/38± 25.5	1/1	NR	NR	NR	NR
Ikeguchi et al[22],2010	NR	NR	NR	NR	0/1	NR	0/1	NR	NR
Tomikawa et al[17],2012	310 ± 75 /314 ± 53	389 ± 279 /258 ± 179	19 ± 7 /29 ± 27	NR	NR	NR	NR	NR	NR
Suh et al[16],2014	193.8 ± 32.4/216. 57 ± 67.4	NR	8.8 ± 4.9 /8.7 ± 3.2	NR	0/1	NR	NR	2/7	2/1

Xia et al[5],2019	220.5 ± 17.2/223.8 ± 28.1	46.9 ± 49.6/48.5 ± 51.1	8± 5.75 /8± 5	NR	1/3	34.04 ± 15.3/27.32 ± 15.9	4/2	NR	NR
Huang et al[26],2020	NR	NR	NR	NR	NR	NR	NR	NR	NR
Eom et al[23],2019	210.0± 12.5/150.0 ± 13.75	100.0 ± 37.5/ 100.0± 46.88	7.0 ± 0.38/ 7.0 ± 0.25	30.5 ± 11.6/33.5 ± 12.2	1/1	NR	NR	0/1	1/3
Hosoda et al[24],2016	NR	NR	NR	NR	NR	NR	NR	NR	NR
Lee et al[25],2022	224 ± 46/214 ± 46	NR	NR	NR	4/4	NR	NR	2/1	NR
Urushihara et al[11],2004	174 ± 43 /192 ± 46	66 ± 45 /83 ± 106	NR	NR	NR	42.9 ± 18 /61.8 ± 28	NR	NR	NR

Operation Time, Blood loss, Hospital length of stay and lymph node dissection

Seven studies[5, 11, 16, 17, 21, 23, 25] pooled for operation time included 482 patients in LPPG and 790 in the LDG group. The analyses showed a significant difference between the two methods. The LDG saw a shorter operative time than the LPPG. Heterogeneity: $Chi^2 = 486.04$, df = 6 ($P < 0.00001$); $I^2 = 99\%$. Test for overall effect: Z = 31.08 ($P < 0.00001$). Figure 2. Five studies[5, 11, 17, 21, 23] were collected for blood loss reported no significant difference between the two groups. Heterogeneity: $Chi^2 = 21.12$, df = 4 ($P = 0.0003$); $I^2 = 81\%$. Test for overall effect: Z = 0.22 ($P = 0.83$). Figure 3. Both LPPG and LDG recorded no difference when it comes to hospital length of stay when five studies[5, 16, 17, 21, 23] were analyzed. Heterogeneity: $Chi^2 = 2.11$, df = 4 ($P = 0.72$); $I^2 = 0\%$. Test for overall effect: Z = 0.03 ($P = 0.97$). Figure 4. Two studies[21, 23] recorded lymph node dissection. However, the two methods did not show any statistical difference. Heterogeneity: $Chi^2 = 1.38$, df = 1 ($P = 0.24$); $I^2 = 28\%$. Test for overall effect: Z = 1.74 ($P = 0.08$). Figure 5

Anastomosis leakage, Gastric emptying, Gastric stasis, Wound infection and Ileus

Postoperative complications such anastomosis leakage collected from six studies [5, 16, 21-23, 25] reported no significant difference after the analysis between the LPPG (475 patients) and LDG (782 patients). Heterogeneity: $Chi^2 = 3.18$, df = 5 ($P = 0.67$); $I^2 = 0\%$. Test for overall effect: Z = 0.42 ($P = 0.67$). Figure 6. Two studies[5, 11] collected for gastric emptying showed no significant difference between LPPG (92 patients) and LDG (123 patients). Heterogeneity: $Chi^2 = 12.91$, df = 1 ($P = 0.0003$); $I^2 = 92\%$. Test for overall effect: Z = 1.62 ($P = 0.10$). Figure 7. Two studies[5, 22] retrieved for gastric stasis showed no significant difference between the two techniques (LPPG with 94 patients and LDG includes 127 patients). Heterogeneity: $Chi^2 = 1.11$, df = 1 ($P = 0.29$); $I^2 = 10\%$. Test for overall effect: Z = 0.78 ($P = 0.44$). Figure 8. There was no difference for wound infection collected from three studies[16, 23, 25] between LPPG (280 patients) and LDG (554 patients). Heterogeneity: $Chi^2 = 3.26$, df = 2 ($P = 0.20$); $I^2 = 39\%$. Test for overall effect: Z = 0.29 ($P = 0.77$). Figure 9. Two studies [16, 23] recorded for ileus saw no significant difference between the two methods (LPPG with 217 patients and LDG with 371 patients). Heterogeneity: $Chi^2 = 0.86$, df = 1 ($P = 0.35$); $I^2 = 0\%$. Test for overall effect: Z = 0.35 ($P = 0.72$). Figure 10

Figure 2.Forest plot of Operative Time

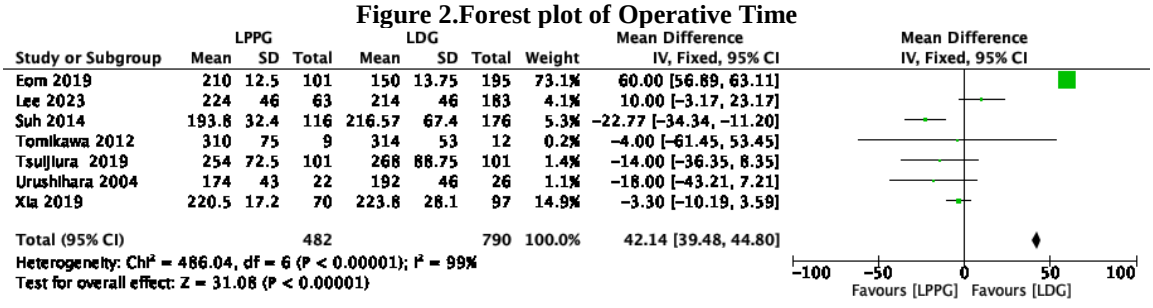


Figure 3.Forest plot of Blood Loss

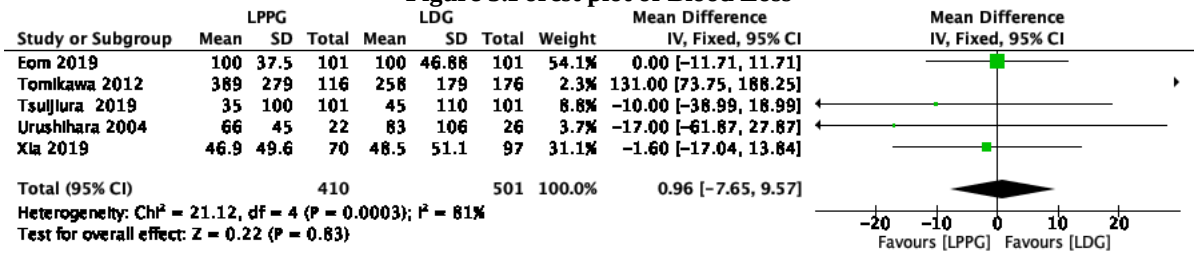


Figure 4.Forest plot of Hospital length of stay

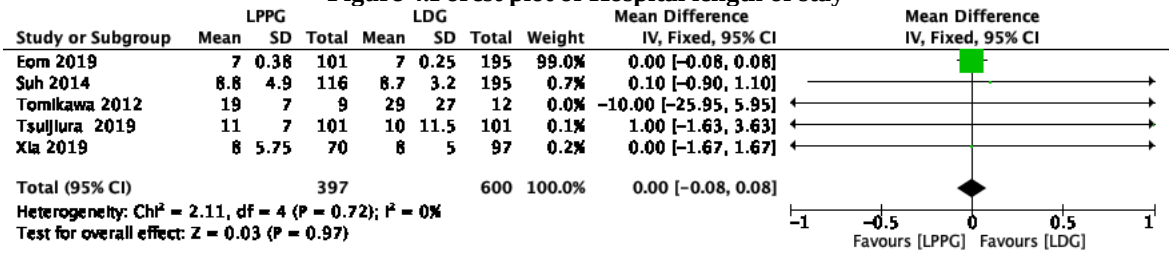


Figure 5.Forest plot of Lymph node dissection

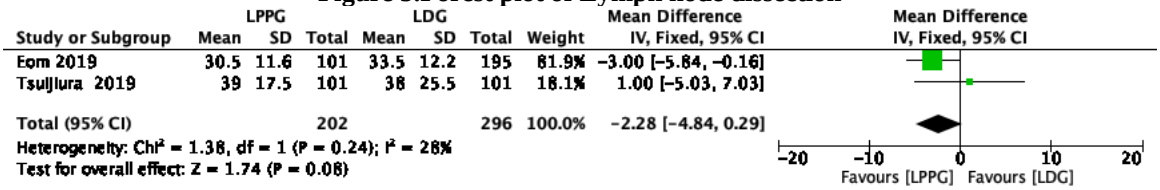


Figure 6.Forest plot of Anastomosis Leakage

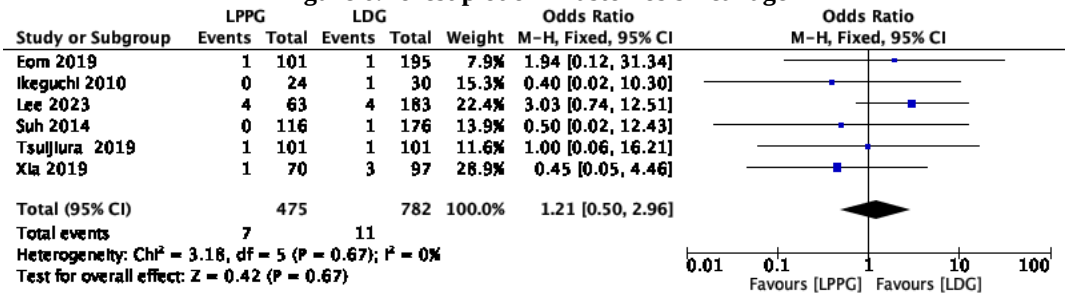


Figure 7.Forest plot of gastric Emptying

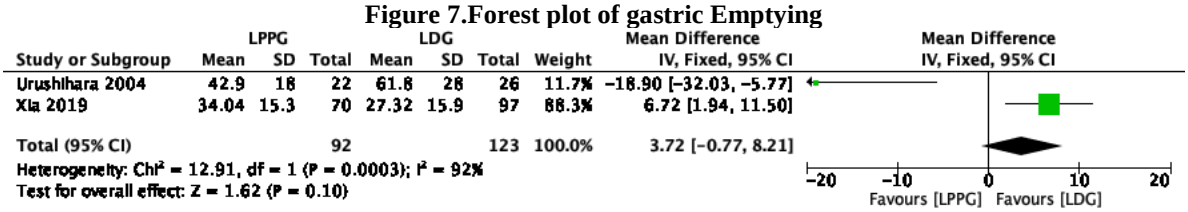


Figure 8.Forest plot of gastric stasis

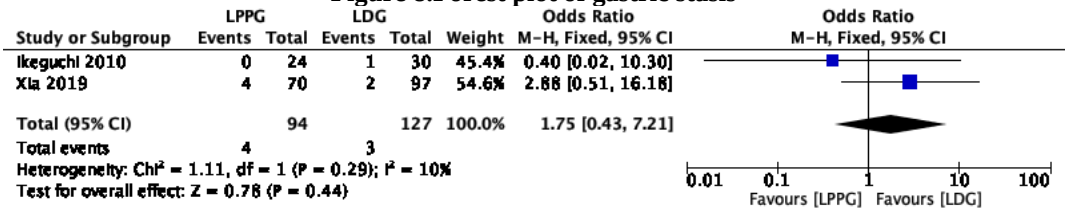


Figure 9.Forest plot of wound Infection

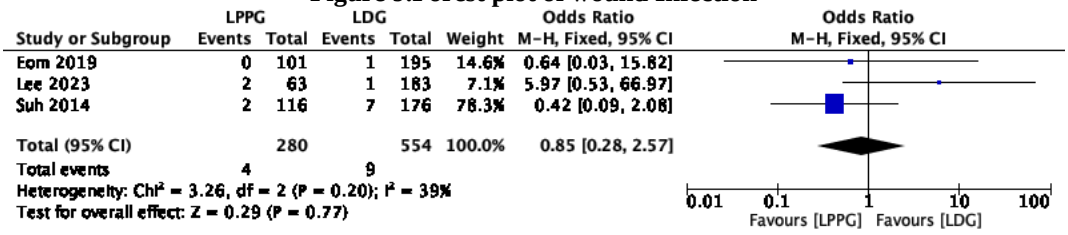
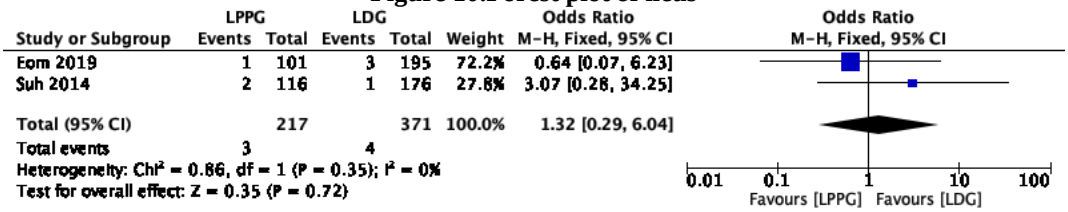
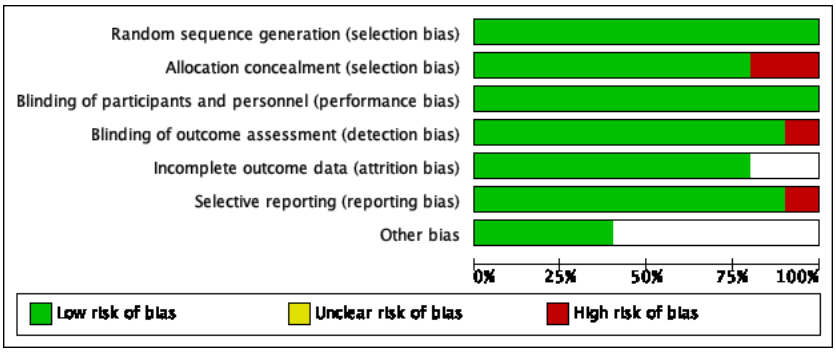


Figure 10.Forest plot of ileus



A



B

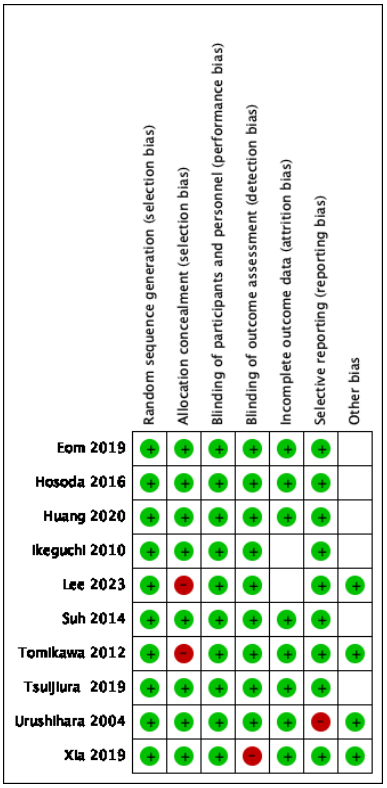


Figure 11.A: Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies. B: Risk of bias summary: review authors' judgements about each risk of bias item for each included study.

IV. Discussion

Function-preserving surgeries, like Billroth-I, Billroth-II, and Roux-en-Y, have been frequently conducted on patients who underwent distal gastrectomy due to their uncomplicated nature. Nevertheless, they frequently resulted in dumping syndrome, gastritis, and bile reflux, which impacted the patients' quality of life. The PPG technique, which involves minimal stomach removal and preserving the antral cuff, is a surgery that conserves function. The efficacy of PPG in enhancing postoperative quality of life continues to be a topic of debate[8].

Preserving the pylorus during gastrectomy has been demonstrated to be a secure technique for patients with early gastric cancer, resulting in exceptional short and long-term prognosis [27, 28]. LPPG is a less invasive procedure when compared to PPG, providing multiple benefits in the early postoperative phase. These benefits include decreased intraoperative blood loss, postoperative pain, hospital stay, and accelerated recovery of bowel function and oral fluid intake [29]. Furthermore, LPPG can improve early dumping syndromes, body weight loss, and duodenogastric reflux, although patients who undergo this procedure may experience delayed gastric emptying, abdominal fullness, and gastro-esophageal reflux disorder more frequently than those treated with LDG in the short-term[16, 24, 30]. Despite several published research studies verifying the comparable surgical outcomes and superior functional status of LPPG, there are still disputes due to the absence of high-quality randomized controlled trials.

The initial meta-analysis that was released in 2014 revealed that PPG offered advantages in terms of averting the early onset of dumping syndrome, bile reflux, and gastritis[8].We accordingly performed an updated meta-analysis to compare the postoperative outcome of LPPG and LD. This meta-analysis demonstrated that, LDG has shorter operative time as compared with the LPPG (Heterogeneity: $Chi^2 = 486.04$, df = 6 ($P < 0.00001$); $I^2 = 99\%$). The above occurrence can be clarified by an increase in LPPG incompetence. Nevertheless, additional research involving large sample sizes or randomized controlled trials is necessary. Although, other meta-analysis showed that operation time was significantly shorter in the LAPPG group[8]. The analysis showed that, the blood loss in both procedures reported no significant difference (Heterogeneity: $Chi^2 = 21.12$, df = 4 ($P = 0.0003$); $I^2 = 81\%$). Furthermore, the duration of hospital stay after surgery is a crucial factor for recuperation and hospital costs. Both surgical methods demonstrated comparable results for hospital length of stay (Heterogeneity: $Chi^2 = 2.11$, df = 4 ($P = 0.72$); $I^2 = 0\%$).

There was no significant difference in the occurrence of postoperative complications, such as anastomosis leakage, gastric emptying, gastric stasis, wound infection, and ileus, between LPPG and LDG. A study conducted by Song et al. also revealed that there was no difference in postoperative complications, including gastric stasis and anastomotic leak, between the two groups[8]. PPG has an advantage over LDG due to the preservation of the infra-pyloric vessels and hepatic branch of the vagus nerve, resulting in better pyloric function and improved quality of life. Although both techniques had comparable postoperative complications, fewer anastomotic leakages were observed in the PPG group, which may be attributed to poor nutrition and anemia, as previously reported [31]. The reduced incidence of anastomotic fistula may be due to better blood supply and function recovery. Previous studies have identified several risk factors, such as advanced age, anemia, and malnourishment, that may contribute to anastomotic leakage. In our experience, reducing anastomosis tension and ensuring the blood supply extremity have a beneficial effect on anastomosis healing, regardless of the patient's physical condition[32]. Additionally, there was no significant difference in gastric emptying between the two surgical techniques. Risk factors for delayed gastric emptying include elderly patients, infra-pyloric artery and infra-pyloric vein injury, failure to preserve the hepatic branch and pyloric branch of the vagal nerve during surgery, and a shorter preserved pyloric cuff[33].

The primary constraint of our investigation is that the operations were executed by surgeons with varying levels of experience, which may have led to bias. Additionally, each operation was performed using a distinct reconstructive procedure. Thirdly, due to insufficient data, we were unable to examine some crucial outcomes. Fourthly, we only assessed short-term results for LPPG versus LDG because there is a paucity of literature on long-term outcomes. Lastly, the overall sample size was limited, and all participants were from Asia, implying a potential publication bias. Thus, further research is required to assess the advantages of PPG in other ethnic groups.

To sum up, LDG proves to be a proficient surgical technique for EGC patients concerning the duration of operation. Nevertheless, we cannot assert that LDG is entirely better than LPPG as there is insufficient evidence. To verify these results, meticulously planned randomized control trial studies conducted across multiple centers are necessary.

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