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Surgical Efficacy Concerning Pylorus Preserving Gastrectomy Versus Distal Gastrectomy in Early Gastric Cancer (EGC): Meta-Analysis

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Abstract

Aim: The purpose of this study is to evaluate and compare the surgical efficacy following pylorus-preserving gastrectomy and distal gastrectomy in patient with early gastric cancer.

Method: Electronic database such as PubMed, google scholar and Medline were search for original studies from the year 1998 to 2019. Postoperative outcomes, complications and nutritional status were the main outcome of the studies. Selected studies were analyzed by the Review manager 5.3 software.

Result: 18 studies were selected for the meta-analyses comprising of 3285 patients diagnosed with gastric cancer, 2585 patients underwent pylorus preserving gastrectomy and 700 patient with distal gastrectomy showed shorter operative time (Heterogeneity: $Tau^2 = 280.80$; $Chi^2 = 230.95$, df = 7 ($P < 0.00001$); $I^2 = 97\%$ and decrease blood loss as compared to the distal gastrectomy (Heterogeneity: $Chi^2 = 23.82$, df = 4 ($P < 0.0001$); $I^2 = 83\%$). For nutritional status, there was no significant difference for serum protein between the two techniques (Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 10.39$, df = 4 ($P = 0.03$); $I^2 = 61\%$). Moreover, the meta-analyses observed no significant difference for postoperative complications.

Conclusion: Pylorus preserving gastrectomy proves to have shorter operative time, decrease blood loss with nutritional benefit. Although there was no significant difference for postoperative complication between the two surgical methods.

Keywords: Pylorus-preserving gastrectomy; Distal gastrectomy; Conventional; Laparoscopic; Early gastric cancer.

Abbreviations: PPG: Pylorus-Preserving Gastrectomy; DG: Distal Gastrectomy; LAPPG: Laparoscopic Pylorus Preserving Gastrectomy; LADG: Laparoscopic Distal Gastrectomy; EGC: Early Gastric Cancer; OR: Odds Ratio; WMD: Weight Mean Difference; SMD: Standardized Mean Difference; CI: Confidence interval.

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Introduction

As of late, minimally invasive methodologies, like endoscopic therapy or laparoscopic gastrectomy, for early gastric cancer have acquired wide application in clinical practice [1]. In any case, standard gastrectomy with radical lymphadenectomy is largely performed for patients with EGC who have no indications for endoscopic submucosal dissection, yet postgastrectomy dysfunction is one of the issues of standard gastrectomy. Because of the low occurrence of lymph node metastasis and the excellent prognosis in EGC, function-preserving gastrectomy, with an sufficient range of gastric resection and minimal lymphadenectomy, could improve the patient's quality of life [2]. Proximal gastrectomy (PG) and pylorus-preserving gastrectomy (PPG) are examples of function-preserving gastrostomies that can be performed in patients with EGC. PG is an alternative to total gastrectomy (TG) for patients with EGC situated in the upper portion of the stomach, while PPG is an alternative to distal gastrectomy (DG) for patients with EGC situated in the center part of the stomach Pylorus-preserving gastrectomy (PPG) was initially proposed by Maki *et al* [3] in 1967 to treat peptic ulcers, and its use was expanded to include middle-third early gastric cancer in 1991 [3,4]. By maintaining the pyloric ring and its functionality, PPG was expected to decrease the risk of postgastrectomy syndrome though enhancing quality of life. Since the first application of PPG in 1967 [3], this approach has been introduced as a minimally invasive surgery and even extended to combine with laparoscopic technique. Moreover, the retainment of pyloric cuff and vagal nerve in PPG provided advantages such as ameliorating post- operative gastritis, bile reflux, early dumping syndromes, and improving nutritional status [5,6]. In PPG, the infra-pyloric lymph nodes are routinely dissected with preserving the infra-pyloric vessels, and the supra- pyloric LNs are usually omitted to preserve the right gastric artery and the hepatic branch of the vagal nerve [7,8]. However, technical difficulty and incomplete lymph resection, which raise concerns about compromising long-term survival, contribute to the restriction on extensive application of PPG. So far, many studies have reported that PPG has benefits against DG with various reconstructive techniques such as Billroth I, II and Roux-en-Y reconstruction by functional conserving.

Therefore, we executed a meta-analysis to measure the surgical efficacy in terms of postoperative result, complications and nutritional assessment of PPG comparing with DG in the outcomes of gastric cancer.

Method and material

Search strategy

This meta-analysis was carried out by searching for various articles from renowned database such as PubMed, google scholar and Medline between the years of 1998 to 2019. The search terms ranged from pylorus preserving gastrectomy, distal gastrectomy, conventional, laparoscopic, gastric or stomach cancer or neoplasm and function preserving. The searching approach varied per database by the different requirement. After, 18 full papers were collected for the meta-analysis. The patient characteristics included, study, country, year of publication, study design, number of patients, gender and type of anastomosis technique as shown in (Table 1).

Table 1: Characteristics of preferred studies.

Study	Publication Year	Nationality	Study design	Patient (PPG/DG)	PPG(M/F)	DG(M/F)	Anastomosis Technique
Imada et al[7]	1998	Japan	Retrospective	20/25	-	-	-
Zhang et al[9]	1998	Japan	Retrospective	16/28	-	-	Billroth I/ Gastro-gastro
Hotta et al[10]	2001	Japan	Retrospective	19/45	-	-	Billroth I/ Gastro-gastro
Nishikawa et al[11]	2002	Japan	Retrospective	12/12	-	-	-
Tomita et al[12]	2003	Japan	Retrospective	10/22	8/2	22/8	Billroth I
Urushihara et al[13]	2004	Japan	Retrospective	22/26	-	-	-/ Gastro-gastro
Tsuijiura et al[14]	2019	Japan	Retrospective	101/101	71/30	72/79	Billroth I/ Roux-en-Y/Gastro-gastro
Shibata et al[15]	2004	Japan	Prospective	36/38	23/13	25/13	Billroth I/ Gastro-gastro
Park et al[5]	2008	Korea	Prospective	22/17	-	-	Billroth I/Gastro-gastro
Ikeguchi et al[16]	2010	Japan	Retrospective	24/30	-	-	Billroth I/ Gastro-gastro
Lee et al[17]	2010	Japan	Prospective	148/305	-	-	-
Tomikawa et al[18]	2012	Japan	Retrospective	9/12	-	-	Gastroduodenal/ Gastro-gastro
Kim et al[19]	2013	China	-	24/196	13/8	68/41	-
Suh et al[20]	2014	Japan	Retrospective	116/176	-	-	Billroth I,11, Roux-en-Y/ Gastro-gastro
Aizawa et al[21]	2017	Japan	-	502/502	301/201	309/193	Billroth I,11, Roux-en-Y/ Gastro-gastro
Zhu et al[6]	2018	Korea	Prospective	145/61	67/78	34/27	Billroth II,Roux-en-Y/ Gastro-gastro
Xia et al[8]	2019	China	Retrospective	70/97	46/24	63/34	Billroth I/ Gastro-gastro
Eom et al[22]	2019	Korea	-	101/195	54/47	114/81	Billroth II/ Gastro-gastro

Data extraction

Extraction was independently performed and 666 papers was collected. 400 studies were gathered after duplicates removed. The 400 collected studies were screened and after careful examination, 267 were excluded which led to133 studies which were measured for eligibility. Following eligibility, 113 were lacking targeted information needed for the analysis. Finally, 18 studies were included for the meta-analysis as seen in (Figure 1).

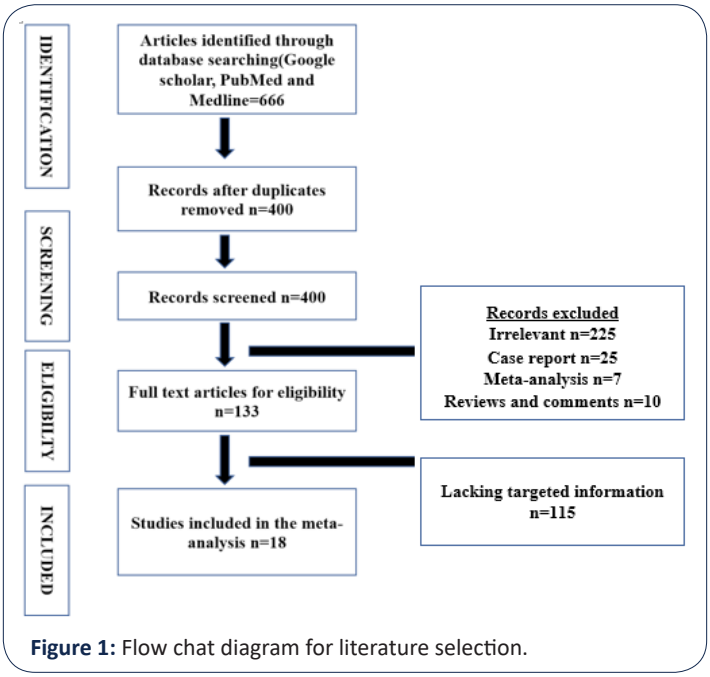

Figure 1: Flow chat diagram for literature selection.

Inclusion criteria

- Only full published article in English.
- Studies comparing pylorus preserving gastrectomy and distal gastrectomy.
- laparoscopically or conventionally with various anastomosis technique.
- All patients should be diagnosed with early gastric cancer or gastric cancer.

Exclusion criteria

- Animal or lab studies excluded.
- Studies with conflicting result and unavailable postoperative outcomes and complications.
- Patients with advance gastric cancer

Statistical analysis

Statistical analysis was accomplished using the Review Manager (RevMan) software, version 5.3 presented by the Cochrane collaboration. Continuous variables were pooled using the mean difference (MD) with a 95% confidence interval (95% CI), and dichotomous variables were pooled using the odds ratio (OR) with a 95% CI. Random effect and fixed effect models were computed under statistical methods of Mantel-Haenszel (for OR or RR). Heterogeneity among studies was evaluated using the inconsistency statistic (*I*). If *I* was < 50%, the eligible studies were considered to be homogenous; hence, the fixed effect model was used. In contrast, if *I* was > 50%, the pooled results were said to be significant, heterogeneous, and the random effect model was used instead.

Surgical efficacy

In this studies, surgical efficacy was outlined as how effective both techniques can minimize postoperative outcomes, complications and increase nutritional status between patients. Although these procedures were performed by multiple surgeons with difference experience and techniques, therefore will be some bias with the outcomes (Figure 2).

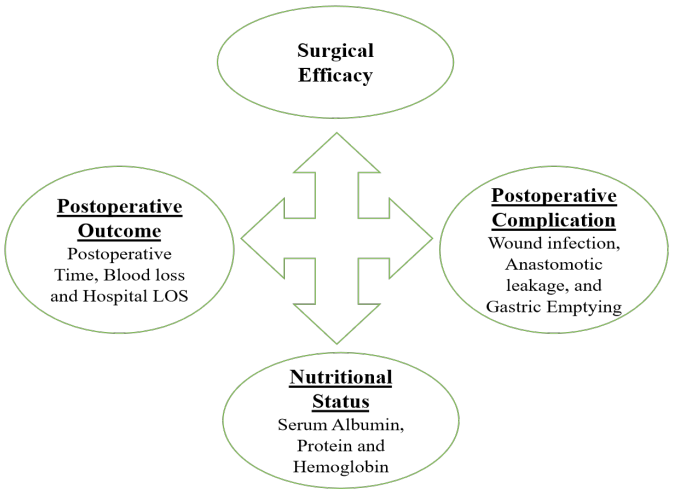

Figure 2: Surgical Efficacy.

Meta-analysis results

Postoperative outcome

Postoperative time: Eight studies [5-8,13,15,18,20] reported postoperative time. A significant different was noted between the two groups. This study was deemed heterogenous, as Heterogeneity: $Tau^2 = 280.80$; $Chi^2 = 230.95$, df = 7 ($P < 0.00001$); $I^2 = 97\%$. Hence the random effect was used (Test for overall effect: Z = 2.99 (P = 0.003). These studies reported decrease operative time for PPG as compared to DG (Figure 3).

Blood loss: After analyzing five studies [6,8,13,15,18], there was a significant difference of blood loss between the PPG and DG. Pylorus preserving gastrectomy observed less blood loss. Heterogeneity was observed their fixed effect model was used (Heterogeneity: $Chi^2 = 23.82$, df = 4 ($P < 0.0001$); $I^2 = 83\%$, Test for overall effect: Z = 3.44 (P = 0.0006) (Figure 4).

Hospital length of stay: Studies conducted between six studies [6,10,15,16,18,20] for hospital length of stay showed no significant difference between the two techniques. Thence there was mild heterogeneity (Heterogeneity: $Tau^2 = 0.71$; $Chi^2 = 8.97$, df = 5 (P = 0.11); $I^2 = 44\%$, Test for overall effect: Z = 0.27 (P = 0.79) (Figure 5).

Nutritional status

Serum protein: There was no significant difference for serum protein between the two methods when five studies [8-10, 15, 20] were analyzed. Heterogeneity: $Tau^2 = 0.03$; $Chi^2 = 10.39$, df

= 4 (P = 0.03); I^2 = 61%, Test for overall effect: Z = 1.30 (P = 0.19) (Figure 6).

Serum albumin: Analyses of six studies [5,8-11,20] indicated a significant difference between PPG and DG. The level of serum albumin was higher the PPG than the DG method. This study was deemed heterogenous, Heterogeneity: Tau^2 = 4.23; Chi^2 = 590.42, df = 5 (P < 0.00001); I^2 = 99%. Hence the random effect model was used (Test for overall effect: Z = 4.01 (P < 0.0001) (Figure 7).

Serum Hemoglobin

The level of serum hemoglobin was high in the DG as compared to the PPG. There was a significant difference between the four studies [8,14,15,18] with Heterogeneity: Tau^2 = 0.03; Chi^2 = 6.65, df = 3 (P = 0.08); I^2 = 55%, Test for overall effect: Z = 2.65 (P = 0.008) (Figure 8).

Postoperative complications

Gastric emptying: Three studies [5,8,13] analyzed for gastric emptying. The result of the meta-analysis showed that the was no significant difference between the two procedures. Heterogeneity: Chi^2 = 13.39, df = 2 (P = 0.001); I^2 = 85%, Test for overall effect: Z = 0.31 (P = 0.76) (Figure 9).

Anastomotic leakage: Eight studies [6,8,14,16,17,20-22] reported anastomotic leakage. The meta-analyses resulted in no significant difference; therefore, no incidence was noted between the two surgical methods. No heterogeneity was observed, Heterogeneity: Chi^2 = 1.91, df = 7 (P = 0.96); I^2 = 0%, Test for overall effect: Z = 1.11 (P = 0.27) (Figure 10).

Wound Infection

Four studies [6,17,21,22] were collected for wound infection and there was no significant difference found between the two groups. No significant heterogeneity was noted; thus, the fixed-effect model was used. Heterogeneity: Chi^2 = 0.40, df = 3 (P = 0.94); I^2 = 0%. Test for overall effect: Z = 0.98 (P = 0.33) (Figure 11).

Publication bias

The funnel plot on the wound infection and anastomotic leakage is shown in figure below.

Because all studies laid inside the 95% CI limits, no evidence of publications bias was noted. Egger test was performed to provide statistical evidence regarding funnel plot symmetry. Result still did not reveal any evidence of publication bias in anastomotic leakage and wound infection Heterogeneity: Chi^2 = 1.91, df = 7 (P = 0.96); I^2 = 0% (Figure 12) and Heterogeneity: Chi^2 = 0.40, df = 3 (P = 0.94); I^2 = 0% (Figure 13).

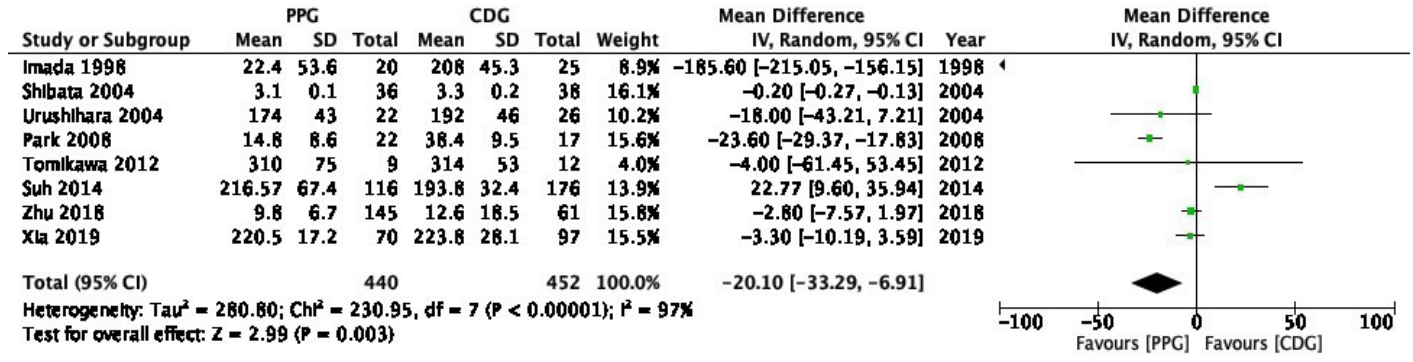

Figure 3: Forest plot of Operative Time.

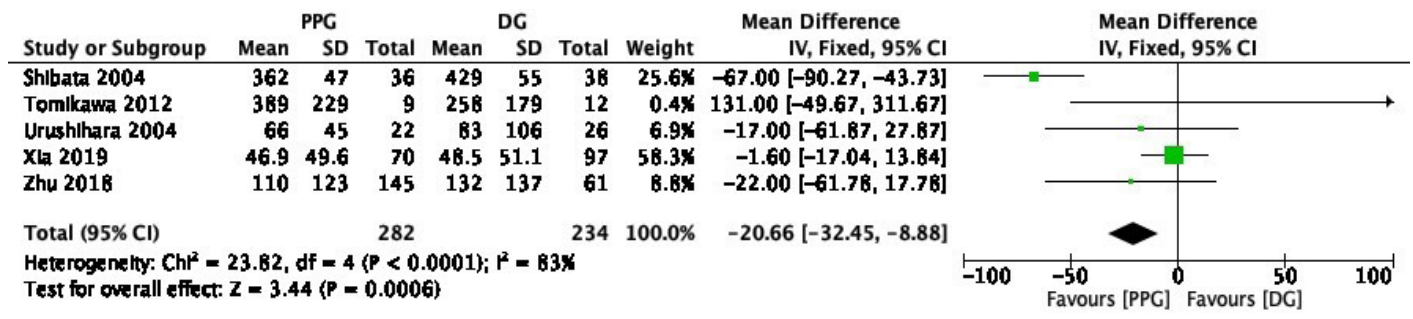

Figure 4: Forest plot of Blood loss.

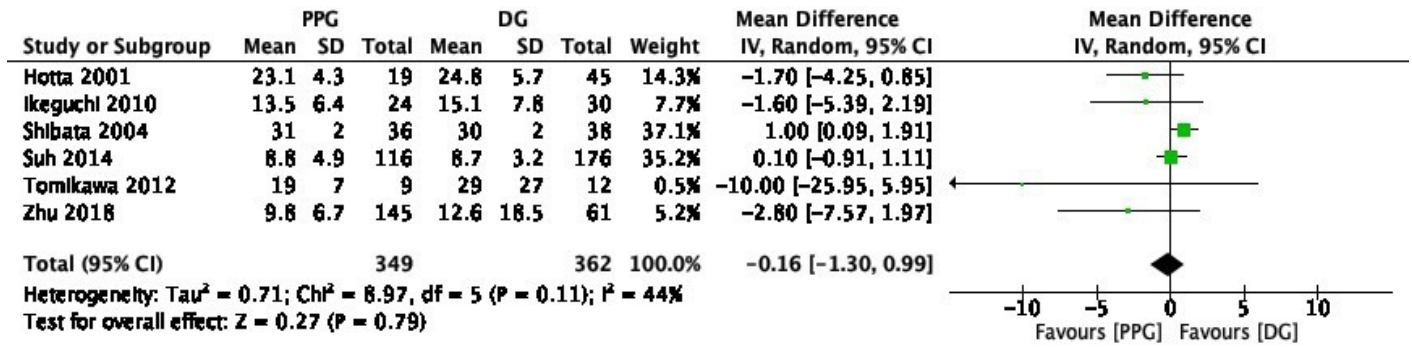

Figure 5: Forest plot of Hospital Length of stay.

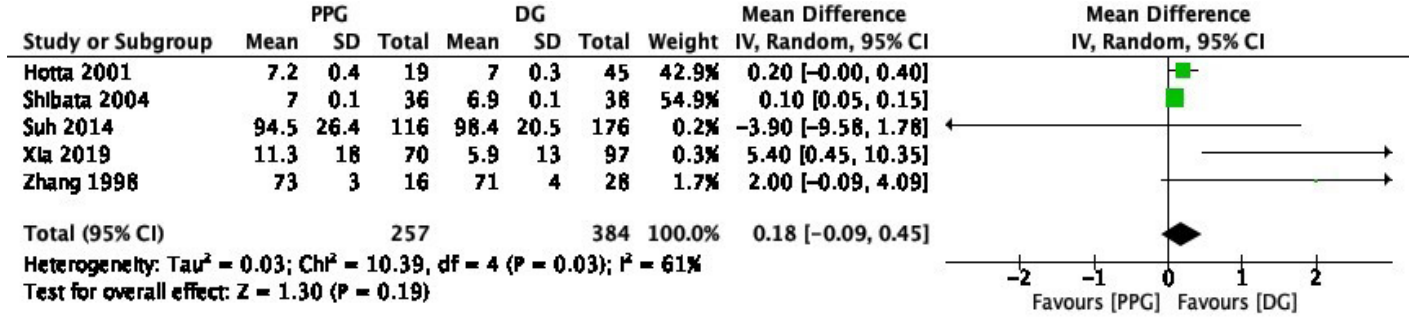

Figure 6: Forest plot of Serum Protein.

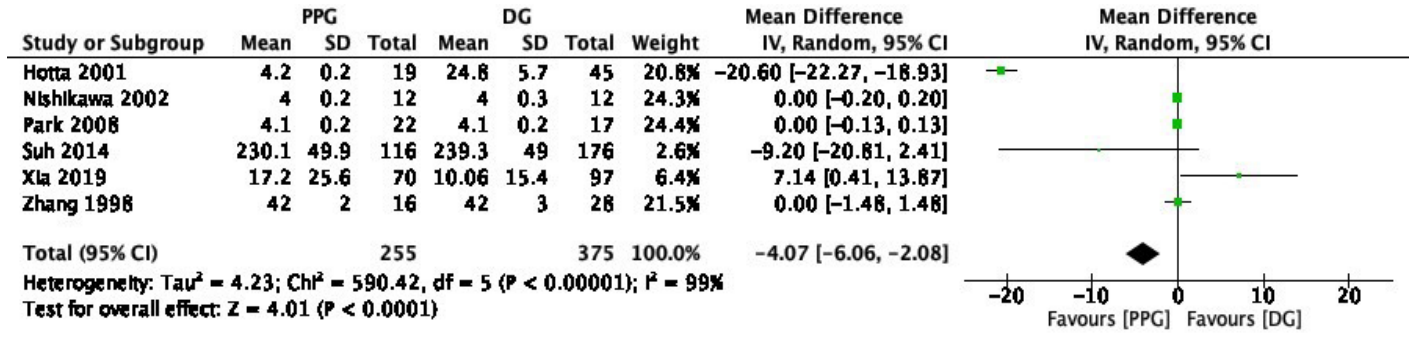

Figure 7: Forest plot of serum Albumin.

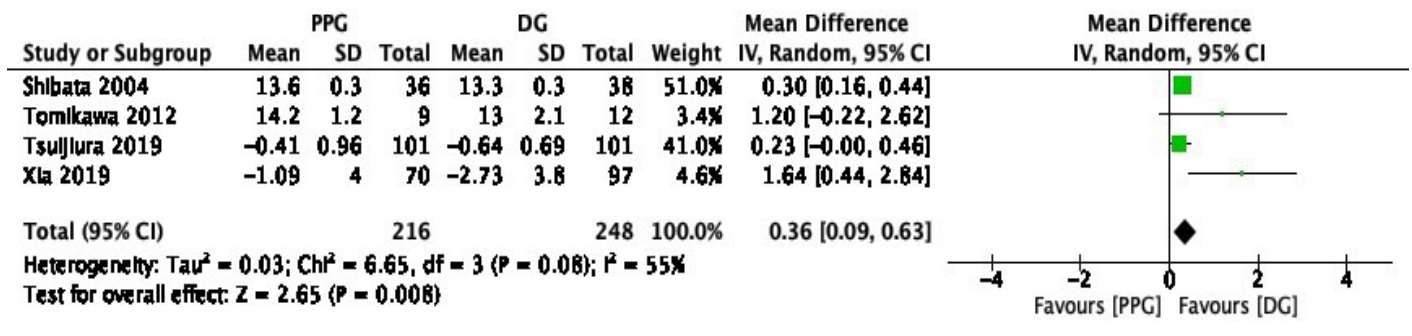

Figure 8: Forest plot of serum Hemoglobin.

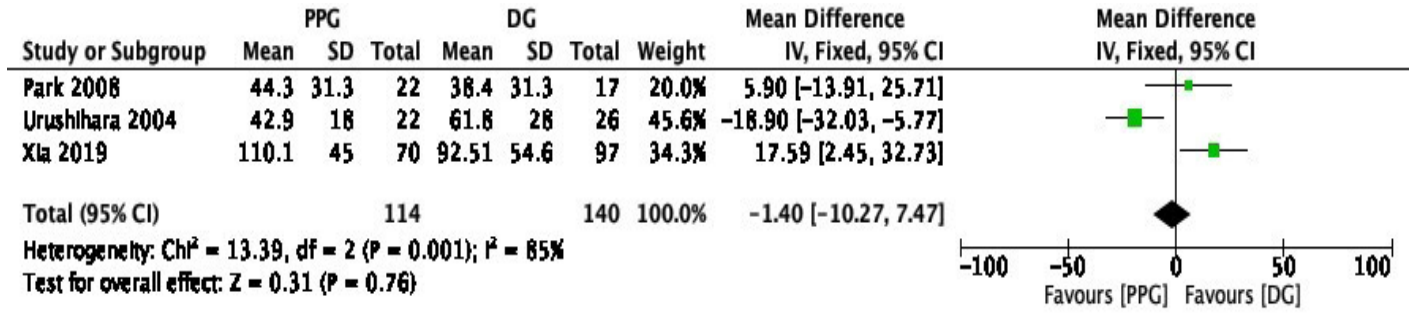

Figure 9: Forest plot of Gastric Emptying.

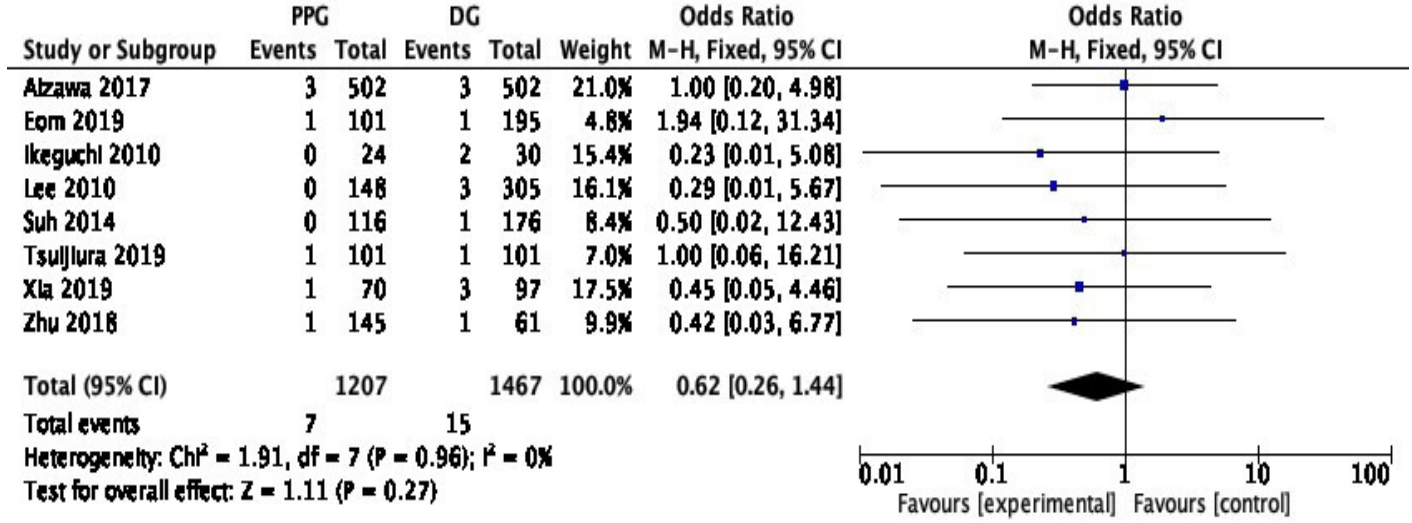

Figure 10: Orest plot of Anastomotic Leakage.

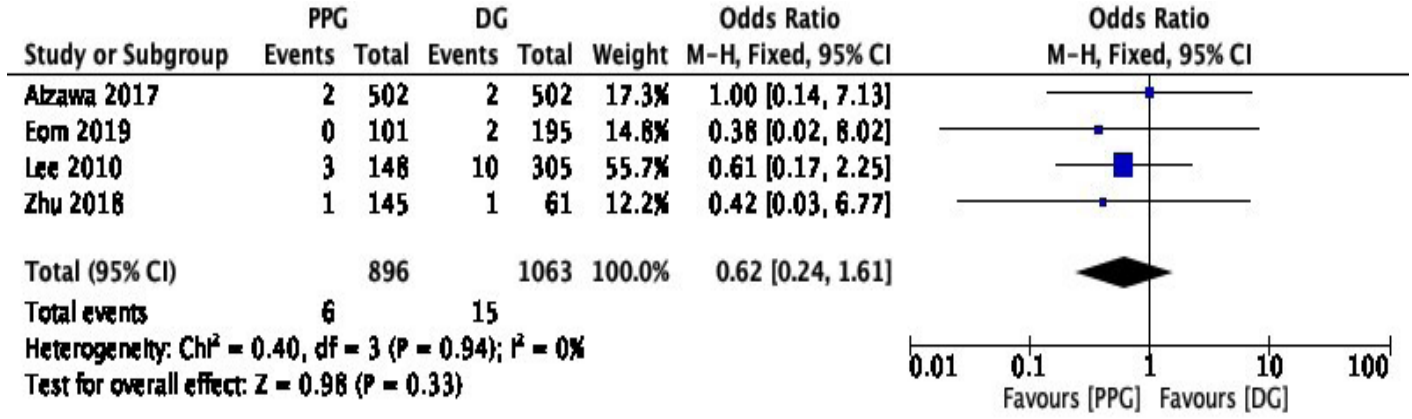

Figure 11: Forest plot of Wound Infection.

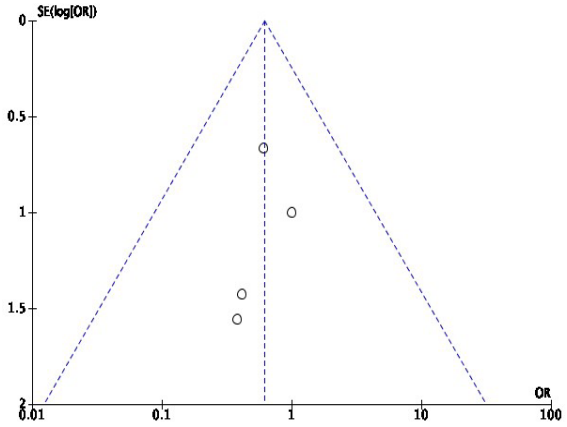

Figure 12: Funnel plot of wound infection.

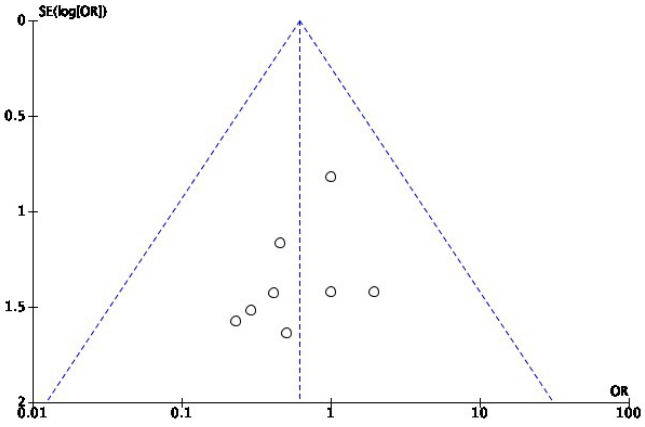

Figure 13: Funnel plot of Anastomotic Leakage.

Discussion

Pylorus preserving gastrectomy has been shown to be a safe technique for early gastric cancer patients with outstanding short and long-term prognosis [23,24]. LAPPG, a less invasive operation compared to PPG, not only had several benefits in early postoperative outcomes, such as decreasing intraoperative blood loss, postoperative pain, hospital stay and accelerate bowel function recovery and fluid oral intake [25], but also could ameliorate early dumping syndromes, body weight loss and duodenogastric reflux although those patients might more frequently experience delayed gastric emptying, abdominal fullness and gastro-esophageal reflux disorder than LADG in short term [20,26,27].

In our meta-analysis, it was established that PPG has several advantages over DG, such as the prevention of long operation time (Heterogeneity: $Tau^2 = 280.80$; $Chi^2 = 230.95$, df = 7 ($P < 0.00001$); $I^2 = 97\%$) and decrease blood loss (Heterogeneity: $Chi^2 = 23.82$, df = 4 ($P < 0.0001$); $I^2 = 83\%$) compared with DG as seen in shibata et al [15]. Hotta et al. [10] described that nutritional status and serum albumin and hemoglobin levels were better in PPG than in DG patients. Nevertheless, this study displayed no significant difference amid the two groups in terms of serum hemoglobin and protein. While, we found that the serum albumin level was higher in PPG than DG (Heterogeneity: $Tau^2 = 4.23$; $Chi^2 = 590.42$, df = 5 ($P < 0.00001$); $I^2 = 99\%$). Gastrectomy significantly reduced absorption and reservoir function of the stomach such as the secretion of gastric acid, and resection of the vagus nerve also impacts the peristalsis of the stomach and duodenum [28]. The length of hospital stay after surgery, serum hemoglobin, serum protein, anastomotic leakage and wound infection were not different between the two techniques. But Xinyu Mao et al showed a significant difference favoring PPG group for hospital duration [28].

Due to preservation of the infra-pyloric vessels and hepatic branch of the vagus nerve, PPG has the advantage of better pyloric function and quality of life. Although comparable postoperative complications were seen in both methods, less anastomotic leakages were found in the PPG groups despite no significant difference was observed in the two techniques,which may be due poor nutrition and anemia as described in previous studies [28]. The decreased anastomotic fistula may be related with better blood supply and function recovery. As defined in preceding reports [29], several risk factors such as advanced age, anemia, and malnourishment may contribute to anastomotic leakage. In our practice, reducing the anastomosis tension and ensuring the blood supply extremity have a useful effect on the healing of anastomosis, no matter to the patients' physical condition. Furthermore, there was no significant difference between the two surgical techniques in terms of gastric emptying. Elder people, infra-pyloric artery and infra-pyloric vein injury, failure to preserve the hepatic branch and pyloric branch of vagal nerve during surgery, and a shorter preserved pyloric cuff are risk factors for delayed gastric emptying [30].

Furthermore, PPG patients had a greater feeling of gastric fullness after meals and food retention in the residual stomach than Billroth I patients [12,31,32]. Delayed gastric emptying is thought to be the cause of this feeling of epigastric fullness. Yet, Imada et al. [7] reported that long after procedures, caloric intake, which reflects gastric emptying, was comparable for PPG and BI patients, and Nakane et al. [31] reported that the frequency of postprandial symptoms after PPG decreased and food intake increased at 2 years postoperatively. He came to the conclusion that PPG should be used in young patients with early gastric cancer who have a good chance of living a long time, because more time is needed for stomach fullness or improved food intake. Because delayed emptying is common following pylorus-preserving gastrectomy, Yamaguchi et al. [8] noted that this treatment should not be advised for elderly patients with simple causes.

Limitations

It's important to think about some of the limitations in this meta-analysis. To begin with, the procedures were performed either conventionally or laparoscopically, with varying surgical experience, which could contribute to prejudice. Second, due to a lack of data, we were unable to assess several critical results, such as anastomotic stricture and bleeding. Finally, due to a lack of data on long-term results, we only focused at postoperative outcomes, complications, and nutritional status for PPG versus DG. Fourth, because the total sample size was small and all of the participants were Asian, there was a risk of publication bias.

Conclusion

Finally, PPG is a safe and effective surgical procedure for patients with EGC. We cannot, however, consider PPG to be completely superior to DG due to the lack of data. Well-designed mul-

ticenter randomized control trial studies are needed to validate these findings.

Declarations

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Authors' contributions: Zakari Shaibu was the chief contributor in data collection, data analysis and textwriting. Jeffrey Joseph Boateng contributed to data collection and analysis. Zhihong Chen was the main contributor of the study design. Zhu Wei was involved in data check and data analysis. All authors read and agreedto the final manuscripts. They have no conflict of interest or family ties to disclose.

Availability of Data and material: The studies included were retrieved from PubMed, Google scholar, and Medline.

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Competing interests: The authors declare they have no competing interest.

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