Palliative Therapy for Gastric Outlet Obstruction Caused by Unresectable Gastric Cancer: A Meta-analysis Comparison of Gastrojejunostomy with Endoscopic Stenting

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Abstract

Background: Gastrojejunostomy (GJJ) and endoscopic stenting (ES) are palliative treatments for gastric outlet obstruction (GOO) caused by gastric cancer. We compared the outcomes of GJJ with ES by performing a meta-analysis.

Methods: Clinical trials that compared GJJ with ES for the treatment of GOO in gastric cancer were included in the meta-analysis. Procedure time, time to resumption of oral intake, duration of hospital stay, patency duration, and overall survival days were compared using weighted mean differences (WMDs). Technical success, clinical success, procedure-related mortality, complications, the rate of re-obstruction, postoperative chemotherapy, and reintervention were compared using odds ratios (*OR*s).

Results: Nine studies were included in the analysis. Technical success and clinical success were not significantly different between the ES and GJJ groups. The ES group had a shorter procedure time (WMD = −80.89 min, 95% confidence interval [*CI*] = −93.99 to −67.78, $P < 0.001$), faster resumption of oral intake (WMD = −3.45 days, 95% *CI* = –5.25 to −1.65, $P < 0.001$), and shorter duration of hospital stay (WMD = −7.67 days, 95% *CI* = −11.02 to −4.33, $P < 0.001$). The rate of minor complications was significantly higher in the GJJ group (*OR* = 0.13, 95% *CI* = 0.04–0.40, $P < 0.001$). However, the rates of major complications (*OR* = 6.91, 95% *CI* = 3.90–12.25, $P < 0.001$), re-obstruction (*OR* = 7.75, 95% *CI* = 4.06–14.78, $P < 0.001$), and reintervention (*OR* = 6.27, 95% *CI* = 3.36–11.68, $P < 0.001$) were significantly lower in the GJJ group than that in the ES group. Moreover, GJJ was significantly associated with a longer patency duration (WMD = −167.16 days, 95% *CI* = −254.01 to −89.31, $P < 0.001$) and overall survival (WMD = −103.20 days, 95% *CI* = −161.49 to −44.91, $P = 0.001$).

Conclusions: Both GJJ and ES are effective procedures for the treatment of GOO caused by gastric cancer. ES is associated with better short-term outcomes. GJJ is preferable to ES in terms of its lower rate of stent-related complications, re-obstruction, and reintervention. GJJ should be considered a treatment option for patients with a long life expectancy and good performance status.

Key words: Endoscopic Stenting; Gastric Cancer; Gastric Outlet Obstruction; Gastrojejunostomy

Introduction

Gastric cancer is the third leading cause of cancer-related mortality and the fifth most common malignancy worldwide.[1] In patients with advanced or metastatic gastric cancer, gastric outlet obstruction (GOO) is commonly reported and leads to nausea, vomiting, dehydration, and malnutrition, thus severely affecting patients' quality of life.[2-4] Given that radical surgery is not indicated in patients with late-stage disease, palliative treatment is required to relieve symptoms of GOO and allow the oral intake to be resumed.[5,6]

Gastrojejunostomy (GJJ) is the standard palliative treatment for GOO and adequately relieves obstructive symptoms in most cases.[7-9] However, the incidence of delayed gastric emptying after conventional GJJ is significant (20%–59%),[10-13] and the postoperative mortality rate reportedly varies from 18% to 24%.[2,13,14] Endoscopic stenting (ES) is increasingly being performed for malignant

Access this article online

Quick Response Code:

Website: www.cmj.org

DOI: 10.4103/0366-6999.180530

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Received: 09-01-2016 **Edited by:** Peng Lyu

How to cite this article: Bian SB, Shen WS, Xi HQ, Wei B, Chen L. Palliative Therapy for Gastric Outlet Obstruction Caused by Unresectable Gastric Cancer: A Meta-analysis Comparison of Gastrojejunostomy with Endoscopic Stenting. Chin Med J 2016;129:1113-21.

GOO.[15] With a shorter procedure time, faster resumption of oral intake, and a shorter hospital stay than GJJ, ES presents an effective and less invasive therapeutic option for the treatment of GOO.[16-18] However, higher rates of complications, reintervention, and recurrent obstructive symptoms have also been reported.[5,15,17]

A previous review suggested that treatment options should depend on the life expectancy of patients,[19] while recent literature has shown that ES is associated with several clinical advantages over GJJ and might be considered a more appropriate treatment for malignant GOO;[7,20,21] however, most studies have compared ES with GJJ in patients with GOO secondary to all forms of periampullary cancer, not gastric cancer alone. Pancreatic cancer is the most common cause of malignant GOO and is associated with a shorter median survival time than gastric cancer.[22,23] Moreover, gastric cancer can develop in the intrinsic pyloric channel with subsequent tumor ingrowth or overgrowth of the ES, leading to re-obstruction.[24] These related factors might have a significant influence on therapeutic strategy, and conclusions from previous reviews did not reach a consensus on the most suitable treatment for GOO secondary to gastric cancer.

Although several studies have previously compared the outcomes of GJJ with ES for the treatment of GOO in gastric cancer,[2,15,16,25-30] most were limited by relatively small sample sizes and inconsistent outcomes. Meta-analysis is a powerful tool that can overcome the small sample sizes of individual studies to identify specific outcomes.[31] Some studies of GJJ compared with ES reported statistically significant results (in terms of clinical success rates, postoperative hospital stay, major complications, re-obstruction, postoperative chemotherapy, reintervention, and overall survival) while others did not show significant differences. Regardless of the limitations in the existing literature, the optimal treatment strategy for malignant GOO secondary to gastric cancer remains unclear. The aim of this study is to systematically compare clinical outcomes of GJJ and ES to determine the most appropriate surgical intervention.

Methods

Search strategy and selection criteria

We conducted a meta-analysis according to the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[32] A literature search was performed of the PubMed, Embase, Cochrane Library, and Web of Science databases for clinical research published before October 2015 that compared ES with GJJ for the treatment of GOO in unresectable gastric cancer. The following terms were used in the search: gastric cancer, GOO, and stent. The references of relevant articles were evaluated to identify other related studies. All studies were carefully examined to avoid inclusion of duplicate data. Two reviewers independently assessed the eligibility of the studies. Agreement regarding discrepancies was reached by discussion.

Inclusion and exclusion criteria

The inclusion criteria were as follows: (1) analyses of the outcomes of ES compared with GJJ for GOO in unresectable gastric cancer; (2) GJJ was a jejunal loop anastomosed with the stomach; and (3) at least one of the following clinical outcomes: technical success, clinical success, procedure time, procedure-related mortality, time to resumption of oral intake, duration of hospital stay, complications, rate of re-obstruction, postoperative chemotherapy, reintervention, patency duration, or overall survival. Where several studies reported on the same patient cohort, only the most recent or detailed study was included.

The exclusion criteria were as follows: (1) GOO caused by other cancers such as pancreatic cancer, ampullary carcinoma, or biliary tract cancer; (2) studies in patients with resectable gastric cancer; (3) inclusion of emergency surgical interventions; and (4) inability to extract effective data from the study's defined clinical outcomes.

Quality assessment of included studies

The quality of each included study was independently assessed by two reviewers. The methodological quality of eligible randomized controlled trials (RCTs) was assessed using the revised Jadad scale,[33] while non-RCT (NRCTs) were assessed using the methodological index for nonrandomized studies.[34] We assessed the quality of RCTs by evaluating four items. Studies with ≥4 points were considered to be of high quality and were included in the meta-analysis. The quality of NRCTs was assessed by evaluating 12 items. Studies with ≥18 points were considered to be of high quality and were included in the meta-analysis.

Data extraction

Two reviewers independently extracted the following relevant data from each study: first author, year of publication, type of study, study period, number of participants, technical success rate, clinical success rate, procedure time, procedure-related mortality, time to resumption of oral intake, duration of hospital stay (number of hospitalization days from procedure to initial discharge), complications, rate of re-obstruction, postoperative chemotherapy, reintervention, patency duration, and overall survival. Where original studies included the median, range, and sample size, we estimated mean and variance using the methods described by Hozo *et al*.[35]

Statistical analysis

Stata 12.0 software (StatCorp., College Station, TX, USA) was used for the statistical analysis. Procedure time, time to resumption of oral intake, duration of hospital stay, patency duration, and overall survival days were compared using weighted mean differences (WMDs). Technical and clinical success rates, procedure-related mortality, complications, rate of re-obstruction, postoperative chemotherapy, and reintervention were compared using odds ratios (*OR*s). A value of $P < 0.05$ was regarded as statistically significant. Heterogeneity was assessed using

Cochran's Q and the I^2 statistic, and considered significant at $P < 0.1$. If heterogeneity existed, the random-effects model was used. Publication bias was evaluated using Begg's funnel plot.

Results

Study selection and characteristics

In total, 174 articles were retrieved using the described search strategies. After screening the title and abstract, 103 reports were excluded. After reading the abstract, 38 reports were excluded as they described reviews, editorials, or case reports. Following full-text review, 16 reports were excluded because they lacked a control group. Eight reports were excluded because they did not evaluate the required outcomes. Therefore, nine studies were eligible for the meta-analysis. The selection process is shown in Figure 1, and the characteristics of the nine eligible studies are summarized in Table 1.[2,15,16,25-30] Eight studies were NRCTs (five from Japan, two from Korea, and one from Finland), and one study was an RCT (from Italy).

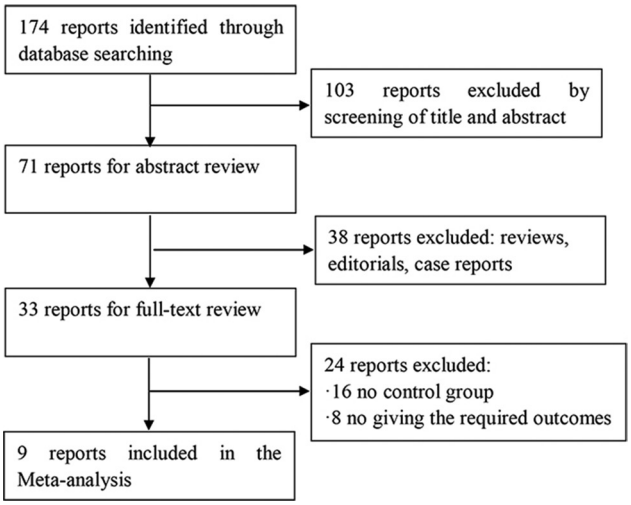

Figure 1: Identification of eligible studies for the meta-analysis comparing the outcomes of gastrojejunostomy and endoscopic stenting for gastric outlet obstruction caused by gastric cancer.

Procedure outcomes

Technical success, defined as successful deployment of a stent across the stricture or the technical possibility of creating an anastomosis, was reported by four studies. The rate of technical success was not significantly different between the ES and GJJ groups ($OR = 0.58$, 95% confidence interval [CI] = 0.06–5.71, $P = 0.637$) [Figure 2a].

Data on procedure time were reported in only two studies. The procedure time was found to be shorter for ES than for GJJ (WMD = −80.89 min, 95% CI = −93.99 to −67.78, $P < 0.001$) [Figure 2b].

Procedure-related mortality, defined as death within the first 30 days after ES or GJJ intervention, was reported by five studies. The rate of mortality was not significantly different between the ES and GJJ groups ($OR = 0.88$, 95% $CI = 0.31$–2.50, $P = 0.814$) [Figure 2c].

Clinical success was defined as improvements in obstructive symptoms and resumption of oral intake and was recorded in five studies; no significant difference was found, however, between the ES and GJJ groups ($OR = 0.54$, 95% $CI = 0.28$–1.01, $P = 0.055$) [Figure 2d].

Postoperative outcomes

The time to resumption of oral intake was reported in six studies and was found to be shorter in the ES group than that in the GJJ group (WMD = −3.45 days, 95% CI = –5.25 to −1.65, $P < 0.001$) [Figure 3a].

The duration of postoperative hospital stay was reported in six studies with ES resulting in a shorter hospitalization than GJJ (WMD = −7.67 days, 95% CI = −11.02 to −4.33, $P < 0.001$) [Figure 3b].

All nine studies reported postoperative complications, information on which was collected separately for comparison under the subgroups of minor complications, major complications, and re-obstruction. Minor complications were defined as those that did not significantly extend the hospital stay and were not life-threatening, such as pneumonia, wound infection, or

Table 1: Major features and quality assessment of the studies comparing the outcomes of GJJ and ES in the meta-analysis

Author	Year	Nation	Study type	Study interval	Sample size, *n*		Quality score*
					ES	GJJ	
Maetani *et al*.[25]	2005	Japan	NRCT	1994.09–2004.09	22	22	22/24
Keränen *et al*.[2]	2013	Finland	NRCT	1999–2010	50	21	21/24
No *et al*.[15]	2013	Korea	NRCT	2001.01–2010.12	72	41	21/24
Fiori *et al*.[16]	2013	Italy	RCT	–	9	9	5/7
Tsuchida *et al*.[28]	2013	Japan	NRCT	2006.09–2012.07	21	17	21/24
Shimazaki *et al*.[27]	2013	Japan	NRCT	2010.05–2012.08	9	9	18/24
Kimura *et al*.[29]	2013	Japan	NRCT	2007.01–2012.06	8	12	18/24
Taniguchi *et al*.[30]	2014	Japan	NRCT	2010.08–2014.02	15	32	21/24
Park *et al*.[26]	2015	Korea	NRCT	2005.11–2012.11	217	39	22/24

*Jadad score for RCT, MINORS score for NRCT; –: Missing data and do not be analyzed in meta-analysis; NRCT: Nonrandomized comparative studies; RCT: Randomized comparative studies; ES: Endoscopic stenting; GJJ: Gastrojejunostomy; MINORS: Methodological index for nonrandomized studies.

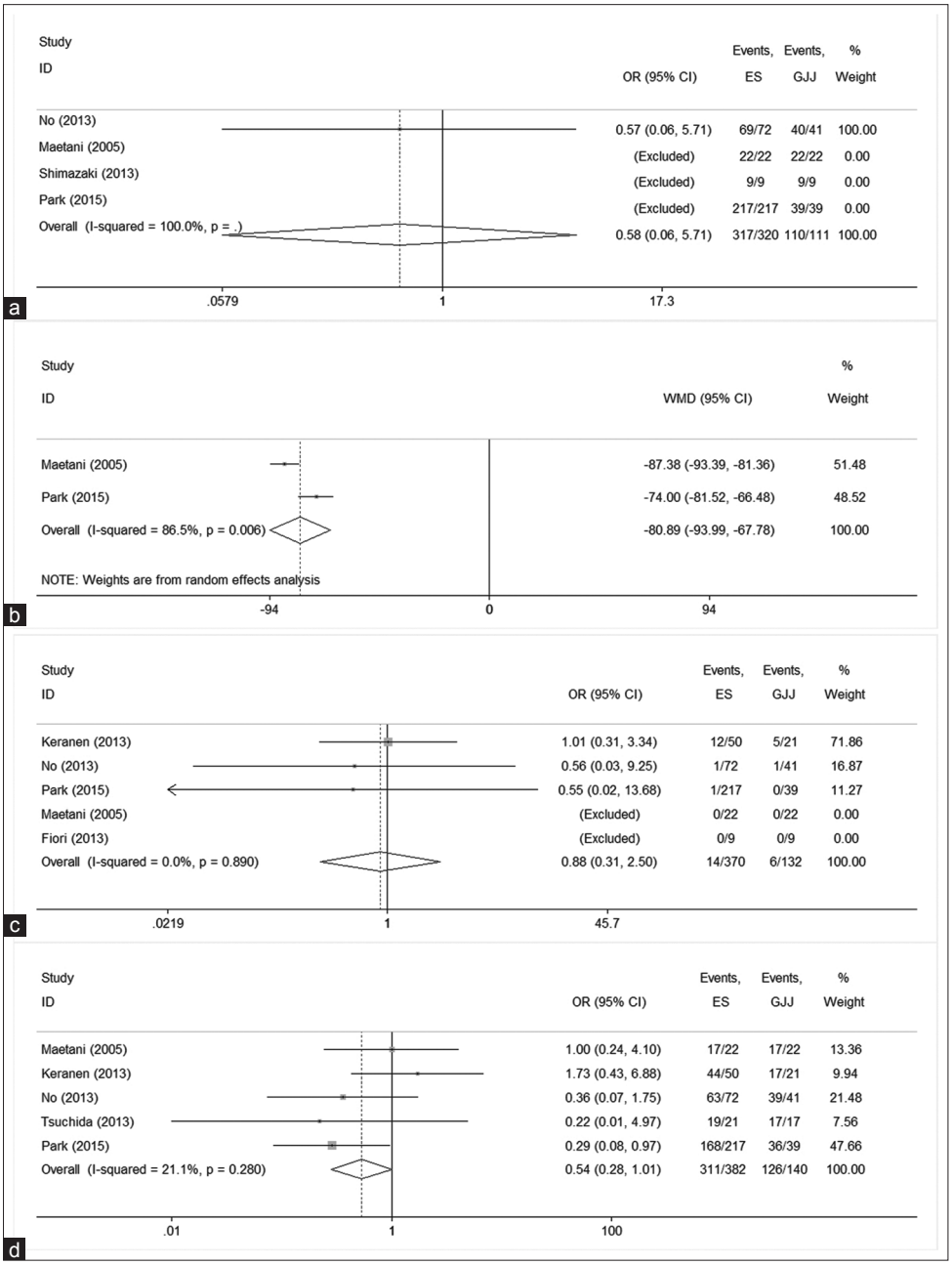

Figure 2: Forest plot results of meta-analysis of procedure outcomes. (a) Meta-analysis on technical success. (b) Meta-analysis on procedure time. (c) Meta-analysis on procedure-related mortality. (d) Meta-analysis on clinical success.

vomiting not related to obstruction. Major complications were defined as life-threatening or severe events such as anastomotic leakage, perforation, stent migration, stent fracture, or stent obstruction and typically required additional treatment and hospitalization. The rate of minor complications was significantly higher in the GJJ group (*OR* = 0.13, 95% *CI* = 0.04–0.40, *P* < 0.001), although the rate of major complications was significantly lower (*OR* = 6.91, 95% *CI* = 3.90–12.25, *P* < 0.001). In particular, the number of stent-related complications was higher in the ES group as was the rate of re-obstruction (*OR* = 7.75, 95% *CI* = 4.06–14.78, *P* < 0.001) [Figure 3c-3e].

Postoperative treatment

Eight studies reported postoperative chemotherapy. After the operative treatment, many patients showed improvements in obstructive symptoms and performance status and could withstand postoperative chemotherapy. The rate of patients who underwent postoperative chemotherapy was not significantly different between the ES and GJJ groups (*OR* = 0.71, 95% *CI* = 0.48–1.05, *P* = 0.087) [Figure 4a].

Several major complications can necessitate reintervention, particularly re-obstruction caused by tumor in-growth followed by stent migration and perforation. The rate of

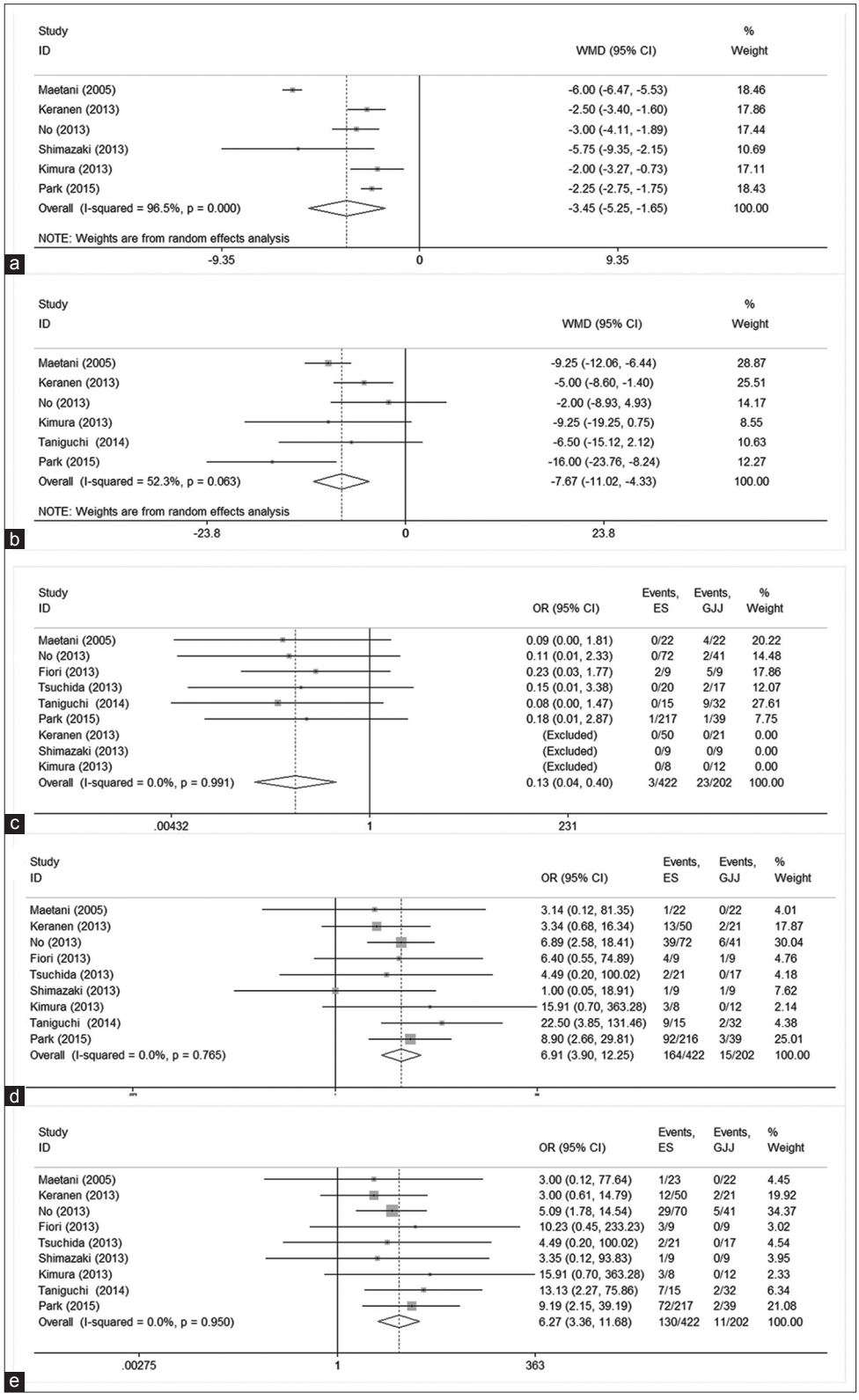

Figure 3: Forest plot results of meta-analysis of postoperative outcomes. (a) Meta-analysis on time to first oral intake. (b) Meta-analysis on postoperative hospital stay. (c) Meta-analysis on minor complications. (d) Meta-analysis on major complications. (e) Meta-analysis on re-obstruction.

reintervention, reported by all nine studies, was significantly higher in the ES group (*OR* = 7.75, 95% *CI* = 4.06–14.78, $P < 0.001$) [Figure 4b].

Patency duration and survival

Six studies reported the patency duration following clinical success. Figure 5a showed a forest plot of the

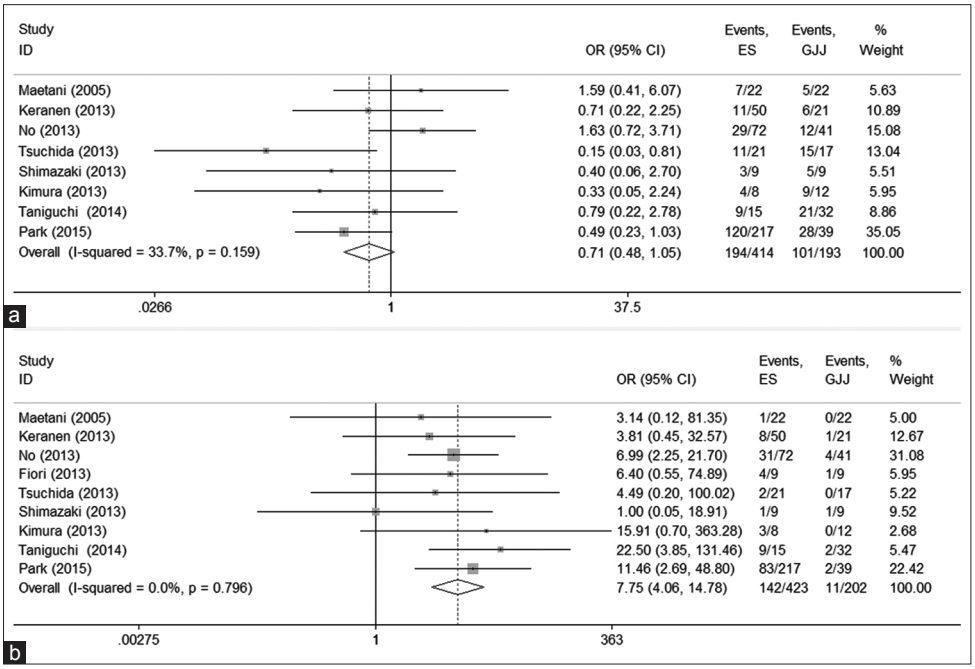

Figure 4: Forest plot results of meta-analysis of postoperative treatment. (a) Meta-analysis on postoperative chemotherapy. (b) Meta-analysis on reintervention.

patency duration in days. GJJ was significantly associated with an enhanced patency duration among patients with GOO secondary to gastric cancer (WMD = −167.16 days, 95% *CI* = −254.01 to −89.31, $P < 0.001$).

Six studies reported overall survival, as illustrated in Figure 5b. GJJ was significantly associated with an enhanced overall survival (WMD = −103.20 days, 95% *CI* = −161.49 to −44.91, $P = 0.001$).

Publication bias

Publication bias, based on postoperative complications, was evaluated using Begg's test and found to be nonexistent among the nine studies ($P = 0.602$). Furthermore, funnel plots for publication bias demonstrated a certain degree of symmetry [Figure 6] supporting the absence of publication bias.

Discussion

Development of GOO in patients with gastric cancer is typically associated with advanced forms of the disease (Stage IV) and short survival times.[36] The main objectives of palliative treatment are therefore to improve patients' general condition, relieve GOO symptoms, and minimize intervention-associated morbidity. GJJ is considered the standard treatment for malignant GOO but is associated with high complication and mortality rates.[37] With the development of endoscopic devices and technology in recent years, ES has become increasingly more popular as a primary treatment modality for patients with malignant GOO because of its minimal invasiveness, early resumption of oral intake, rapid recovery, and equivalent long-term prognosis compared with GJJ.[14,20,21,38,39] However, most previous studies included all types of periampullary cancer and a significant proportion of pancreatic cancer. Gastric cancer has a better prognosis than pancreatic cancer, and patients typically have good performance status.[15,23] The conclusions from existing studies are therefore not entirely appropriate for extrapolation to patients with gastric cancer. To the best of our knowledge, no reviews to date have explored treatment modalities for patients with GOO secondary to gastric cancer. Here, we compared ES with GJJ, specifically in patients with gastric cancer to identify the optimal treatment option for malignant GOO secondary to gastric cancer.

In our meta-analysis, technical success and clinical success were not significantly different between the ES and GJJ groups. Our results suggest that both of these procedures can be thus considered effective in terms of relieving symptoms of GOO caused by gastric cancer.

Both groups had similar procedure-related mortality rates in our analysis. Wong *et al*.[13] found that GJJ had a higher mortality rate than ES (17.64% vs. 0, respectively), a difference which could be mainly attributed to tumor type. Patients with pancreatic cancer typically have a poorer performance status than those with gastric cancer and cannot tolerate the major tissue damage associated with open surgery. In addition, most of the studies included in our meta-analysis were conducted in Japan and Korea, where surgeons typically have extensive experience in surgical intervention for gastric cancer.

In our study, ES was found to be associated with a shorter procedure time, faster resumption of oral intake, and shorter duration of hospital stay. The rate of minor complications was also significantly lower in the ES group. These results

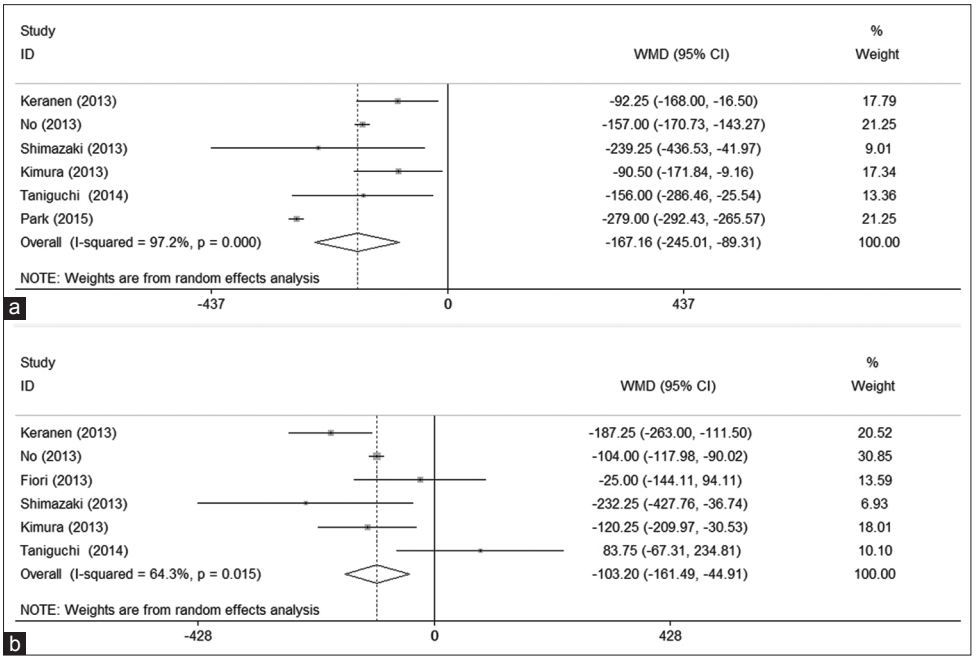

Figure 5: Forest plot results of meta-analysis of patency duration and survival. (a) Meta-analysis on patency duration. (b) Meta-analysis on overall survival.

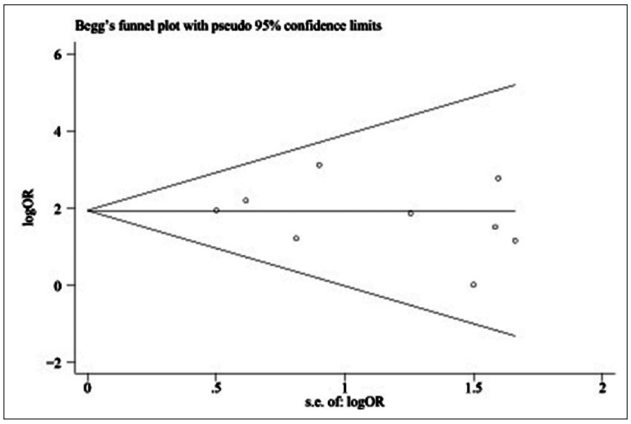

Figure 6: Funnel plot depicting the distribution of odds ratios comparing postoperative complications.

are similar to those of other meta-analyses.[7,19] Patients who undergo ES might recover more quickly than patients who undergo GJJ because ES is less invasive. ES might therefore be indicated for patients with a poor performance condition who require rapid nutritional support and resolution of GOO. However, in our study, ES was associated with a higher rate of major complications than GJJ with perforation, bleeding, and stent-related complications more commonly reported in the ES group. Re-obstruction occurred more frequently in the ES group than in the GJJ group because of tumor ingrowth or outgrowth and obstruction resulting from intake of food. The higher rate of re-obstruction led to a significantly higher rate of reintervention in the ES group.

The ultimate aim of palliative treatment for GOO secondary to gastric cancer is a prolongation of both the patency duration and survival time. ES had a shorter patency duration than GJJ because of the high rate of re-obstruction. Although a second successful ES procedure was achieved in the ES group, the patency duration remained shorter in the ES group than in the GJJ group. In addition, GJJ was significantly associated with enhanced survival. With such superiorities in terms of long-term prognosis, GJJ might be the optimal choice for patients with gastric cancer who have a longer life expectancy. Furthermore, chemotherapy is a significant independent prognostic factor for survival time in patients with unresectable or metastatic gastric cancer.[2,6,36] In our study, the number of patients who received posttreatment chemotherapy did not differ between the ES and GJJ groups. Therefore, the prolonged survival time of patients in the GJJ group might be associated with the surgical procedure. However, in retrospective studies, the selection of treatment was shown to be dependent on clinician's decision, patient's choice, or the specific department that patients were referred to. Therefore, further verification of the data is required to eliminate bias associated with these characteristics.

Our review compared ES with GJJ, specifically in patients with GOO secondary to gastric cancer; however, it had several limitations. First, few prospective randomized studies were eligible for inclusion in this review. Therefore, some key factors, including disease stage, performance status, GOO scoring system scores, and chemotherapy prior to treatment, were either not recorded or not comparable between the two groups. Second, some studies did not describe the detailed condition of patients and the time to resumption of a solid diet. Finally, comparisons between laparoscopic GJJ with ES and open GJJ could not be performed due to a lack of sufficient data.

Based on our results, GJJ appears to be a superior intervention to ES in patients with a longer life expectancy. However, patient selection for surgery and prediction of survival time

are challenging. Although GJJ is a less invasive surgery than gastrectomy, it might nonetheless cause substantial trauma in patients with malignant GOO. One retrospective study reported that poor performance was associated with a high mortality rate after GJJ for gastric cancer.[40] Jeurnink *et al*.[5] found that patients' life expectancy was an important factor that could influence the final treatment options and suggested that GJJ was more suitable for patients with a longer life expectancy (>2 months) while ES was indicated for those with a shorter expected survival time of <2 months. In addition, a recent study showed that GJJ was more effective than ES for the treatment of GOO in incurable or metastatic gastric cancer in patients with a good performance status.[15] These results might facilitate surgeons in determining the suitability of patients for surgery and identifying the appropriate indications for GJJ.

At present, few available studies comparing ES with GJJ in the management of GOO secondary to gastric cancer have been reported, and all previous reviews have included studies in patients with various cancers. Although most of the studies included in our review are retrospective, we consider our findings to be of value as significant differences between ES and GJJ were identified in a large patient sample size, and our results might enable better decision making on the treatment for GOO in gastric cancer alone.

In conclusion, our study has shown that both ES and GJJ are safe and effective procedures for GOO caused by unresectable or metastatic gastric cancer. ES has superior short-term outcomes, such as a shorter operating time, faster resumption of oral intake, and shorter hospitalization. GJJ is preferable to ES in terms of its lower rate of stent-related complications, re-obstruction, and reintervention. We suggest that GJJ should be considered a treatment option for patients with a long life expectancy and good performance status. However, further well-designed randomized studies are needed to establish a standard treatment modality for patients with GOO secondary to gastric cancer.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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