



Is the routine placement of a feeding jejunostomy during esophagectomy worthwhile? – a systematic review and meta-analysis

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Background: Malnutrition dramatically increases the risk of postoperative complications and delays patient recovery. Therefore, a feeding jejunostomy tube (FJT) is routinely placed during esophagectomy to maintain the postoperative nutrition supply. However, recently published studies have questioned the need of a FJT in every esophageal cancer patient. Because most patients can resume oral intake shortly after surgery, the nutrition-providing function of a FJT becomes much less critical. In contrast, FJT-related complications could be severe.

Methods: Relevant publications were found out by systemic searching of four medical databases (PubMed, EMBASE, Medline, and Cochrane Center Register of Controlled Trials). By reading the titles and the abstracts, potentially relevant studies were screened from the search results. The incidence of postoperative complications and FJT-related complications were calculated and compared to evaluate the efficacy of a FJT.

Results: Eighteen studies were included in the meta-analysis. The no-FJT group had a similar or even lower incidence of postoperative complications [anastomotic leakage (AL), pulmonary complications, and wound infections] compared with the FJT group. Ileus and FJT site infections were the most common FJT-related complications. The incidence of ileus was approximately 6% (95% CI: 3–12%), and over 63% of the patients with an ileus required re-operation to relieve the obstruction. The pooled mean rate of FJT site infections was 7% (95% CI: 6–9%). Approximately 7% of patients had dysfunction (obstruction or dislocation) of the jejunostomy tube (95% CI: 3–14%).

Conclusions: The non-selective placement of a FJT during esophagectomy provides few benefits to the patients and may even increase the risk of postoperative complications. Therefore, an intraoperative FJT should be selectively prescribed, but not routinely in the surgical treatment of esophageal cancer.

Keywords: Esophagectomy; enteral nutrition; jejunostomy; meta-analysis

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Introduction

Surgery with or without neoadjuvant therapy is now the standard treatment for locally advanced esophageal cancer (1). However, the surgical procedure is highly invasive, involving the abdomen, thorax, and even the neck. Moreover, malnutrition is common in patients with esophageal cancer (2). Malnutrition dramatically increases the risk of postoperative complications and delays patient recovery (3). Therefore, a feeding jejunostomy tube (FJT) is routinely placed during surgery to ensure adequate postoperative nutrition.

Recent studies have questioned the need for a FJT in all esophageal cancer patients (4-6). Because most patients resume oral intake shortly after surgery, providing nutrition via a FJT is not critical. In contrast, FJT-related complications, such as ileus and jejunum perforation, can be severe (7,8). Therefore, these studies recommend selective placement of a FJT during esophagectomy.

We compared the postoperative outcomes between patients with and without a FJT to evaluate the need for a FJT in every patient, and calculated the incidence of FJT-related complications to assess the safety of FJT. In addition, the characteristics of patients who benefited from a FJT were summarized.

We present the following article in accordance with the PRISMA reporting checklist (available at <http://dx.doi.org/10.21037/apm-20-2519>).

Methods

The study was designed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-analyses) statement. The online searching of four medical databases (PubMed, EMBASE, Medline, and Cochrane Center Register of Controlled Trials) were performed on 18 November 2019. The searching was conducted basing on the following terms: (enteral nutrition OR jejunostomy OR nasogastric feeding OR nasoduodenal OR nasojejunoscopy OR nasojejunal) AND (esophagectomy OR oesophagectomy OR esophagus OR esophageal OR oesophagus OR oesophageal) AND (tumor OR tumour OR cancer OR carcinoma OR neoplasm).

Inclusion and exclusion criteria

The inclusion criteria were as follows: (I) studies that enrolled patients who underwent esophagectomies for

esophageal cancer; and (II) studies that compared the postoperative outcomes between patients who did and did not have an FJT placed intraoperatively.

The exclusion criteria were as follows: (I) non-English publications; (II) reviews, meta-analyses, study protocols, case reports, abstracts presented at a conference, comments, and replies; and (III) in the case of duplicate data, the study with the smaller sample size.

Study screening and quality assessment

By reading the titles and abstracts, irrelevant studies were removed. Then, the full texts of the selected studies were carefully read and the data of targeted outcomes were extracted to confirm the eligibility of the included studies. According to the MINORS (Methodological Index for Non-Randomized Studies) score, the quality of included studies was assessed. Study selection and data extraction were independently performed by two authors (Shen and Zhuo); disagreements were resolved by discussion with a third author (Lin).

Statistical analysis

The odds ratio (OR) was used to compare dichotomous data. I^2 was used as an indicator of heterogeneity. Specifically, $I^2 < 25\%$, $25\% \leq I^2 < 50\%$, and $I^2 \geq 50\%$ indicated low, moderate, and high heterogeneity, respectively. A random-effects model would be adopted when high heterogeneity was detected, otherwise, a fixed-effects model was adopted. Publication bias was evaluated by Begg's and Egger's tests. The difference was considered statistically significant when the p-value was less than 0.05. All the data analyses were performed by RevMan 5.3 software and STATA (version 12.0; Stata Corporation, College Station, TX, USA).

Results

The online database search identified 3,029 potentially relevant studies. After removing 1,276 duplicate studies, 1,753 studies entered the first round of screening, during which the titles and abstracts were read. Of the 1,753 studies, 26 were *in vitro* or animal studies, 755 were ineligible publication types, and the targeted intervention of 928 did not satisfy the aim of our study. Thus, 44 highly-relevant studies remained for further evaluation. By reading the full texts of the 44 studies, three conference abstracts, 10 non-English publications, and

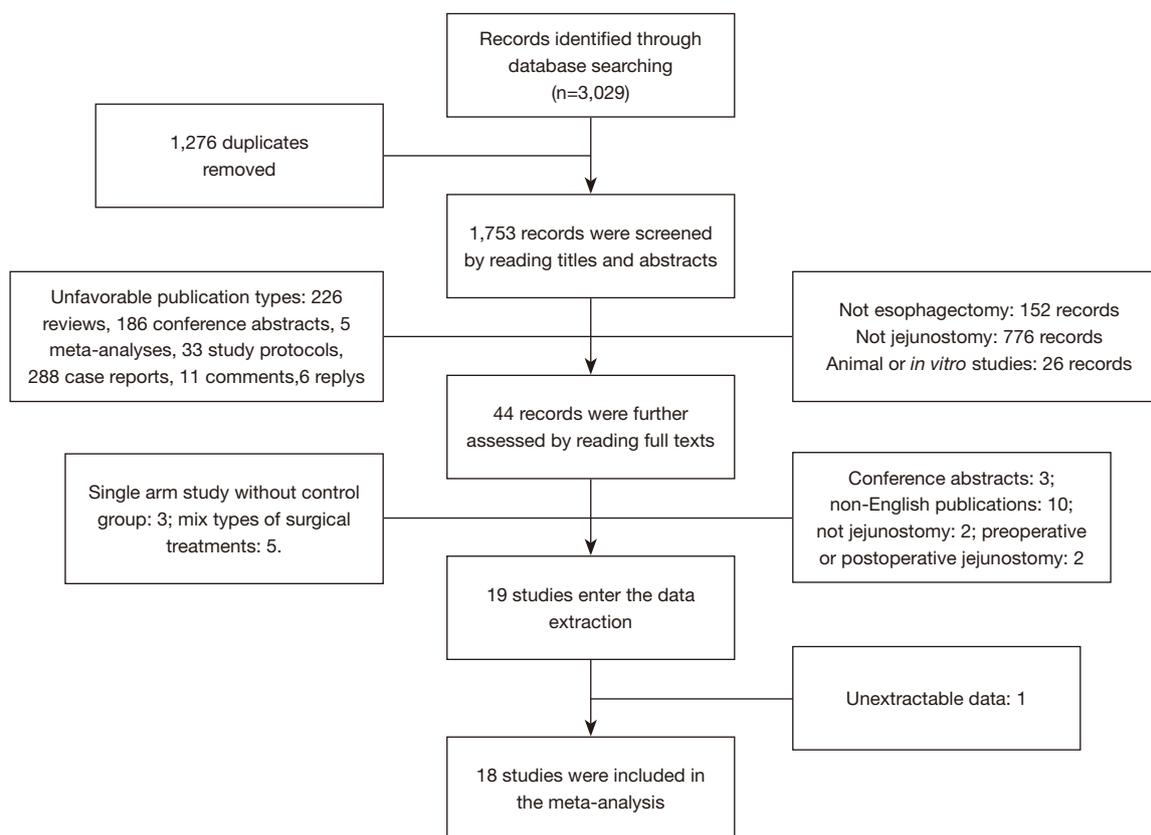


Figure 1 The screening procedures of the studies included in the meta-analysis.

eight studies with disqualifying interventions were excluded. Three single-arm studies (9-11) without controls were also excluded. Nineteen studies met the inclusion criteria for this meta-analysis, thus, data extraction was performed. The target outcomes of one study (12) could not be extracted, therefore, 18 studies (4-8,13-25) were included in the final analysis. The details of the study selection procedures are shown in *Figure 1*, and *Table 1* shows the base line characteristics of the studies included in the meta-analysis.

Postoperative complications

Sixteen studies reported the incidence of anastomotic leakage (AL). The overall prevalence of AL in the feeding jejunostomy tube group (FJT-G) was 10.04% and 8.48% in the no feeding jejunostomy tube group (no FJT-G). The rate of AL was quite close between the two groups, but the pooled analysis indicated a statistically significant difference (OR =1.27, 95% CI: 1.02–1.59, $P=0.03$; *Figure 2A*). The no FJT-G also had a significantly lower incidence of pulmonary complications

(OR =1.24, 95% CI: 1.01–1.51, $P=0.04$; *Figure 2B*). Ten studies were included in the comparison of postoperative ileus. The FJT-G had a higher incidence of ileus. The overall rates of ileus in the FJT-G and no FJT-G were 5.87% and 0.74%, respectively. The meta-analysis showed a statistically significant difference in the occurrence of ileus (OR =7.49, 95% CI: 3.78–14.85, $P<0.001$; *Figure 2C*). The FJT-G also had a higher incidence of wound infections (7.00% vs. 3.74%) and the difference was statistically significant (OR =2.01, 95% CI: 1.46–2.75, $P<0.001$; *Figure 2D*). The FJT-G and no FJT-G had a similar prevalence of chyle (3.16% vs. 3.82%; OR =0.89, 95% CI: 0.51–1.55, $P=0.67$).

Jejunostomy-related complications

Ileus and jejunostomy site infections were the most frequent jejunostomy-related complications. The overall mean jejunostomy-related ileus rate was 6% (95% CI: 3–12%; *Figure 3A*). Among the 33 patients who had an ileus, 21 (63.64%) required re-operation to relieve the obstruction.

Table 1 The baseline characteristics of the studies included in the meta-analysis

Study	Design	Sample size (FJT:no FJT)	Surgery type	FJG nutrition intervention	NFJG nutrition intervention	MINORS score
Kroese 2019	R	135:53	MIE	EN through FJT, OI on the 5 th POD	OI on the 5 th POD	11
Koterazawa 2020	R	139:139	MIE or OE	EN through FJT, OI on the 7 th POD	NA	11
Álvarez-Sarrado 2019	R	47:53	NA	EN through FJT	PN	11
Akiyama 2018	R	33:43	MIE or OE	EN through FJT, PN, OI on 6–7 th POD	PN, OI on the 6–7 th POD	12
Gong 2015	NA	38:76	OE	EN through FJT	PN or EN through NJT	12
Scarpa 2014	R	40:69	OE	EN through FJT	NA	11
Huang 2014	R	153:121	NA	EN through FJT, OI on the 5 th POD	EN through gastrostomy, OI on the 5 th POD	11
Konishi 2018	R	82:133	NA	EN through FJT, OI on the 7 th POD	EN through gastrostomy, OI on the 7 th POD	11
Al-Temimi 2019	R	841:841	MIE or OE	EN through FJT	NA	11
Arif 2018	P	162:163	OE	EN through FJT	NA	13
Kawai 2017	R	214:206	OE	EN through FJT, OI on the 8 th POD	EN through gastrostomy, OI on the 8 th POD	12
Elshaer 2016	R	14:41	MIE or OE	EN through FJT	EN through NJT	11
Takesue 2015	P	24:23	MIE	EN through FJT, OI on the 8 th POD	PN, OI on the 8 th POD	15
Rajabi Mashhadi 2015	P	20:20	NA	EN through FJT, OI on the 7 th POD	PN, OI on the 7 th POD	13
Oya 2015	R	267:111	NA	EN through FJT, OI on the 7 th POD	EN through duodenostomy, OI on the 7 th POD	11
Cao 2013	R	55:57	NA	EN through FJT, OI on the 4 th POD	EN through NJT, Oral intake on 7 th POD	11
Fenton 2011	R	143:8	MIE or OE	EN through FJT, OI on 5–7 th POD	NA	11
Lidder 2010	P	16:14	NA	EN through FJT and PN, OI on 4 th POD	PN, OI on 4 th POD	15

R, retrospective; P, prospective; NA, not available; MIE, minimal invasive esophagectomy; OE, open esophagectomy; EN, enteral nutrition; PN, parenteral nutrition; OI, oral intake; POD, postoperative day; FJT, feeding jejunostomy tube; MINORS, Methodological Index for Non-Randomized Studies.

Eight studies were included in the analysis of jejunostomy site infections and the mean pooled rate was 7% (95% CI: 6–9%; *Figure 3B*). Approximately 7% of patients had obstruction or dislocation of the jejunostomy tube (95% CI: 3–14%; *Figure 3C*). The details of the jejunostomy-related complications data are summarized in *Table 2*.

Indications for intraoperative placement of a FJT

Among the included studies, seven selected patients who were recommended to have the intraoperative placement of a FJT. The recommendations are summarized in *Table 3*. Patients at high risk for postoperative complications (AL

and pulmonary complications) were widely recommended to have the intraoperative placement of a FJT. The nutritional status was also considered. The body mass index (BMI), NRS-2002 screening test, and severe preoperative dysphagia were included in evaluating patient nutrition status. Patients undergoing open surgery or a McKeown esophagectomy were also candidates for a FJT due to the greater extent of surgical trauma. The decision for intraoperative placement of a FJT was also made based on the patient's condition during surgery. Specifically, placement of a FJT was considered in the case of an intraoperative bilateral vocal code palsy or a depressed bloodstream of conduit. Older age and neoadjuvant therapy were also indications for an

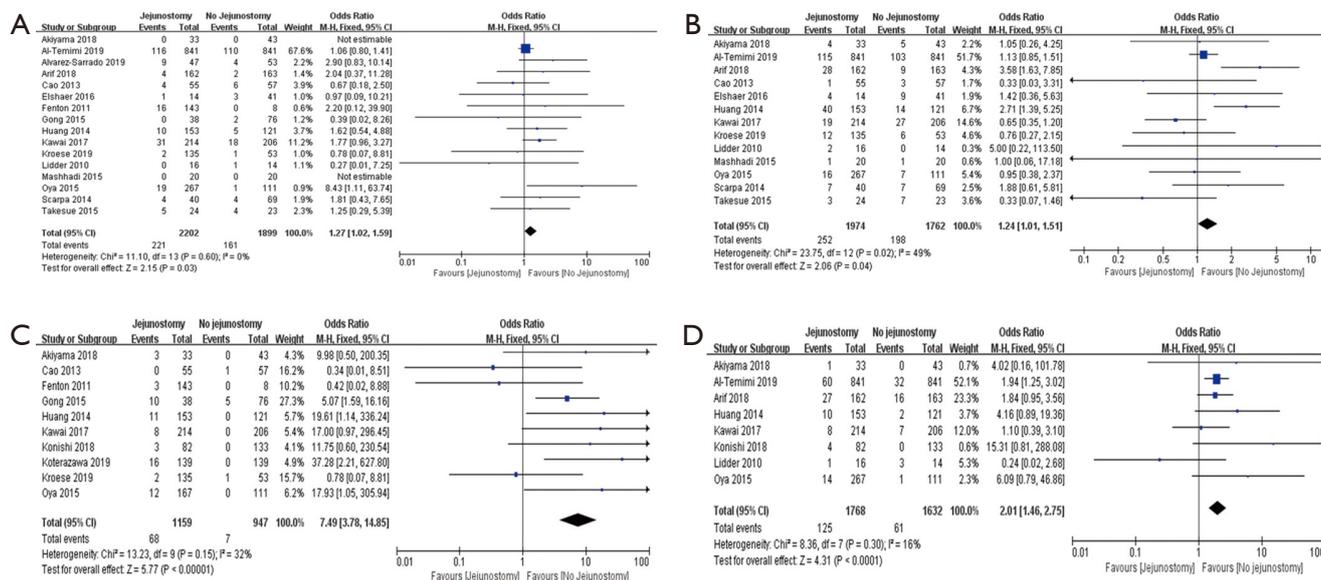


Figure 2 The comparison of postoperative complication between JG and NJG. (A) JG had a significantly higher incidence of anastomotic leakage than NJG [OR =1.27, 95% CI: 1.02 to 1.59; P=0.03]. (B) JG had a significantly higher incidence of pulmonary complications than NJG (OR =1.24, 95% CI: 1.01 to 1.51; P=0.04). (C) JG had a significantly higher incidence of ileus than NJG (OR =7.49, 95% CI: 3.78 to 14.85; P<0.001). (D) JG had a significantly higher incidence of wound infection than NJG (OR =2.01, 95% CI: 1.46 to 2.75; P<0.001).

intraoperative FJT.

Publication bias and heterogeneity

All meta-analyses had low or moderate heterogeneity except the single-arm analysis of jejunostomy-related complications. Therefore, the random effect model was adopted in these analyses. The Begg’s (P=0.381; Figure 4A) and Egger’s tests (P=0.382; Figure 4B) indicated no publication bias.

Discussion

Our study showed that the routine intraoperative placement of a FJT did not decrease the incidence of postoperative complications in esophageal cancer. The analyses indicated that patients who received an intraoperative FJT had a significantly higher risk of postoperative complications than patients who did not receive an intraoperative FJT. Moreover, an intraoperative FJT may lead to severe jejunostomy-related complications that require surgery. Therefore, an intraoperative FJT should be selectively, not routinely prescribed in the surgical treatment of esophageal cancer.

The perioperative nutritional status is associated with the rehabilitation and prognosis of esophageal cancer patients (26,27). Malnutrition may increase the risk of postoperative complications (13,28). The studies conducted by Álvarez-Sarrado *et al.* (4) and Akiyama *et al.* (5) demonstrated that the total protein and albumin levels were similar between the FTJ-G and no FTJ-G on postoperative day 7. The changes in body weight or BMI 1, 3, and 6 months after surgery were also comparable between the FJT-G and no FJT-G (5,6,13). These results indicated that the postoperative nutrition status of patients in the FJT-G and no FJT-G was similar. The Kroese *et al.* (13) reported that only 4 patients (7.5%) in the no FJT-G needed a FJT after surgery and only 1 patient (0.7%) in the no FJT-G received a FJT postoperatively in the study conducted by Koterazawa *et al.* (6). Therefore, these surgeons were of the opinion that the intraoperative placement of a FJT is not necessary for every patient, especially patients without severe complications.

The non-selective placement of a FJT has limited benefits to the patient and may even increase the risk of postoperative complications. Scarpa *et al.* (15) reported comparable postoperative outcomes between the FJT-G and no FJT-G; however, Al-Temimi *et al.* (7) and Arif *et al.* (8)

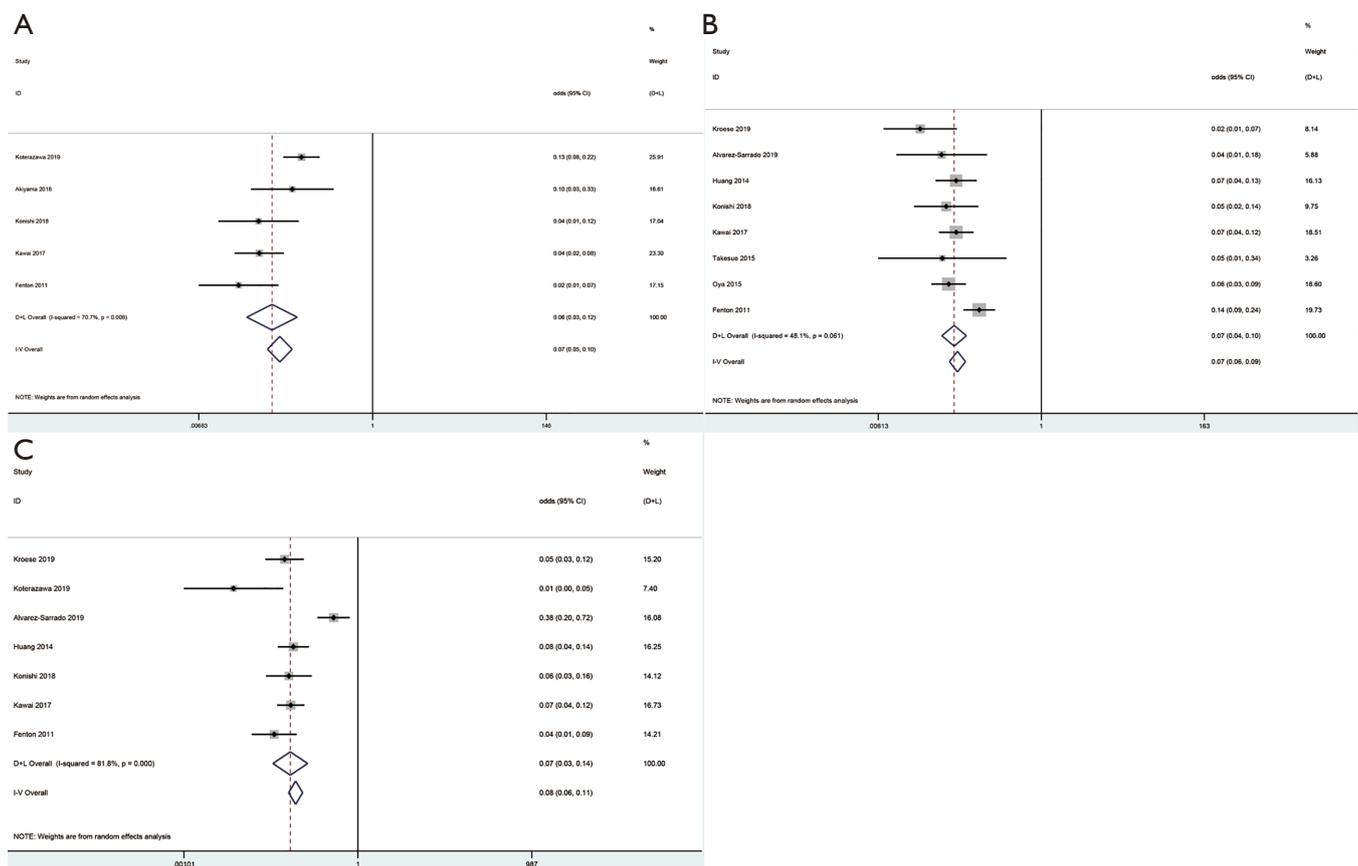


Figure 3 The single-arm analysis of the jejunostomy-related complications. (A) The mean incidence of jejunostomy-related was 6% (95% CI: 3–12%). (B) The mean incidence of jejunostomy site infection was 7% (95% CI: 6–9%). (C) The mean incidence of jejunostomy dysfunction was 7% (95% CI: 3–14%).

revealed a higher incidence of morbidities in patients who received a FJT. Although a statistically significant difference was detected in our meta-analysis, the overall rate of AL and pulmonary complications was very close between the two groups. The overall AL rate was 8.5% in the no FJT-G and 10.0% in the FJT-G. The incidence of pulmonary complications was 11.2% in the no FJT-G and 12.9% in the FJT-G. The incidence of complications in the two groups was close; however, the statistically significant difference is unlikely to be clinically meaningful. Therefore, we believe the incidence of AL and pulmonary complications are comparable between the two groups. The FJT-related complications are the most important reason why we recommend that the FJT should be prescribed selectively, but not routinely. The FJT-related complications included ileus, infection of the jejunostomy site, and obstruction or dislocation of the FJT. Between 10% and 40% of patients

have a FJT-related complication and between 2% and 15% have a severe FJT-related complication (7,13). From the perspective of the patient, the FJT is the complication.

In fact, a FJT is not always unhelpful. A FJT plays a vital role in the recovery of patients who have severe postoperative complications, such as an AL and a pulmonary infection (6,7). Koterazawa *et al.* (6) reported that age (>75 years), neoadjuvant therapy, AL, and pulmonary complications are independent risk factors for long-term FJT placement. Thus, Koterazawa *et al.* (6) recommended that older patients or patients at high risk for postoperative complications are candidates for the intraoperative placement of a FJT. For patients who resume oral intake early, the function of a FJT is not quite as important (29). The FJT may even affect the patient's emotions and decrease the quality of life. Scarpa *et al.* (15) reported that patients who received a FJT had poor emotional function compared

Table 2 The detail data of jejunostomy-related complications in each study

Study	Jejunostomy-related complications	The overall rate of Jejunostomy-related complications	The overall rate of reoperation for Jejunostomy-related complications
Kroese 2019	Wound infection: 3/135; jejunostomy dysfunction: 15/135	18/135 (13.33%)	2/18 (11.11%)
Koterazawa 2020	Ileus: 16/139; jejunostomy dysfunction: 1/139	17/139 (12.23%)	13/17 (76.47%)
Álvarez-Sarrado 2019	Wound infection: 2/47; jejunostomy dysfunction: 13/47; other: 9/47	24/47 (51.06%)	2/24 (8.33%)
Akiyama 2018	Ileus: 3/33	3/33 (9.09%)	3/3 (100%)
Huang 2014	Wound infection: 10/153; jejunostomy dysfunction: 11/153	21/153 (13.73%)	NR
Konishi 2018	Ileus: 3/82; wound infection: 4/82; jejunostomy dysfunction: 5/82	12/82 (14.63%)	3/12 (25%)
Kawai 2017	Ileus: 8/214; wound infection: 14/214; jejunostomy dysfunction: 14/214	36/214 (16.82%)	2/36 (5.56%)
Takesue 2015	Ileus: 0/23; wound infection: 1/23	1/23 (4.35%)	NR
Oya 2015	Wound infection: 14/267	14/267 (5.24%)	NR
Fenton 2011	Ileus: 3/143; wound infection: 18/143; jejunostomy dysfunction: 5/143	26/143 (18.18%)	0/26 (0%)

NR, not reported.

Table 3 Indications for intraoperative placement of feeding jejunostomy tube from included studies

Study	Indications for intraoperative placement of FJT
Kroese 2019	1) Patients undergo open surgery 2) Patients could not start early oral intake after the surgery 3) Patients under high risk of pneumonia
Koterazawa 2020	1) Elderly patients (>75 years old) 2) Patients received neoadjuvant treatment 3) Patients under high risk of pulmonary complication and anastomosis leakage
Álvarez-Sarrado 2019	1) Patients with severe dysphagia or aphagia prior to surgery 2) Malnourished patients prior to surgery (NRS-2002 screening test ≤ 3) 3) Patients undergoing McKeown esophagectomy
Akiyama 2018	1) Elderly patients with reduced function of swallowing preoperatively 2) Patients with intraoperatively confirmed bilateral vocal cord palsy or depressed bloodstream of conduit
Scarpa 2014	Patients under high risk of anastomotic complications
Al-Temimi 2019	Patients at high risk of an anastomotic leak
Fenton 2011	Patients with a BMI less than 18.5 kg/m ²

FJT, feeding jejunostomy tube; BMI, Body mass index; NRS 2002, Nutritional risk screening 2002.

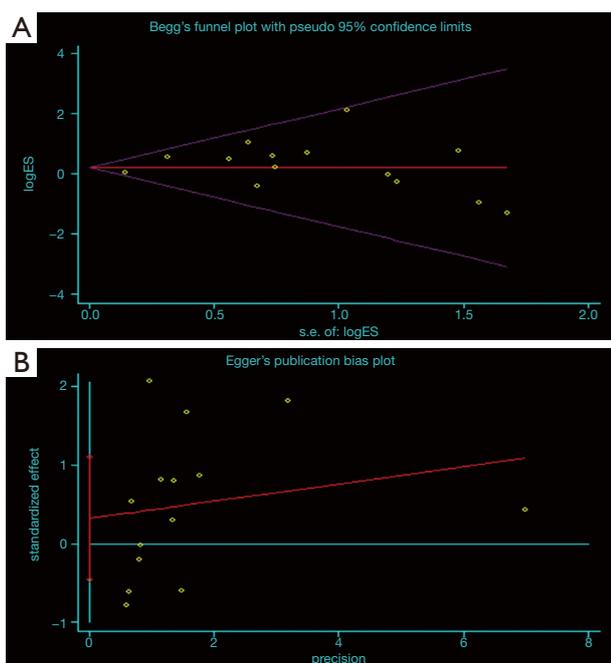


Figure 4 Begg's and Egger's test for the detection of publication bias. Both the Begg's ($P=0.381$) and Egger's test ($P=0.382$) detected no publication bias.

to patients who did not receive a FJT.

We summarized the indications for intraoperative placement of a FJT from included studies. The risk for postoperative complications, age, nutritional status, surgery type, intraoperative conditions, and neoadjuvant therapy should be taken into consideration when deciding if a FJT is placed during surgery.

Our meta-analysis had some limitations. First, the reported FJT-related complication rate varied among the studies, so a single-arm analysis of FJT-related complications had high heterogeneity. The single-arm analysis was thought to provide a rough evaluation of the rate of FJT-related complications. Despite high heterogeneity, the meta-analysis provided the data we sought. Second, postoperative nutritional supplementation in the no FJT-G also varied among the included studies, and decreased the level of evidence in the meta-analysis. Finally, if the FJT affected long-term survival or long-term nutrition status was not analyzed in our study due to limited data.

Nevertheless, our study indicated that the intraoperative placement of a FJT was not suitable and beneficial for every esophageal cancer patient. A FJT should be prescribed selectively, but not routinely. How to accurately identify

the patients who need a FJT will be the focus of corollary studies.

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Footnote

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Ethical Statement: The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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