Diseases of the Esophagus (2023), **36**, 1–9
https://doi.org/10.1093/dote/doac105

DISEASES OF THE ESOPHAGUS

ISDE The International Society for Diseases of the Esophagus

Original Article

Feeding gastrostomy and duodenostomy using the round ligament of the liver versus conventional feeding jejunostomy after esophagectomy: a meta-analysis

Tomohiko Yasuda,[1] Akihisa Matsuda,[2,*] Hiroki Arai,[1] Daisuke Kakinuma,[1] Nobutoshi Hagiwara,[2] Youichi Kawano,[1] Keisuke Minamimura,[1] Takeshi Matsutani,[3] Masanori Watanabe,[1] Hideyuki Suzuki,[1] Hiroshi Yoshida,[2]

[1]*Department of Surgery, Nippon Medical School Chiba Hokusoh Hospital, Chiba, Japan,* [2]*Department of Gastrointestinal and Hepato-Biliary-Pancreatic Surgery, Nippon Medical School, Tokyo, Japan, and* [3]*Department of Digestive Surgery, Nippon Medical School Musashikosugi Hospital, Kawasaki-shi, Kanagawa Japan*

SUMMARY. **Esophageal cancer patients require enteral nutritional support after esophagectomy. Conventional feeding enterostomy to the jejunum (FJ) is occasionally associated with small bowel obstruction because the jejunum is fixed to the abdominal wall. Feeding through an enteral feeding tube inserted through the reconstructed gastric tube (FG) or the duodenum (FD) using the round ligament of the liver have been suggested as alternatives. This meta-analysis aimed to compare short-term outcomes between FG/FD and FJ. Studies published prior to May 2022 that compared FG or FD with FJ in cancer patients who underwent esophagectomy were identified via electronic literature search. Meta-analysis was performed using the Mantel–Haenszel random-effects model to calculate Odds Ratios (ORs) with 95% confidence intervals (CIs). Five studies met inclusion criteria to yield a total of 1687 patients. Compared with the FJ group, the odds of small bowel obstruction (OR 0.09; 95% CI, 0.02–0.33), catheter site infection (OR 0.18; 95% CI, 0.06–0.51) and anastomotic leakage (OR 0.53; 95% CI, 0.32–0.89) were lower for the FG/FD group. Odds of pneumonia, recurrent laryngeal nerve palsy, chylothorax and hospital mortality did not significantly differ between the groups. The length of hospital stay was shorter for the FG/FD group (median difference, −10.83; 95% CI, −18.55 to −3.11). FG and FD using the round ligament of the liver were associated with lower odds of small bowel obstruction, catheter site infection and anastomotic leakage than FJ in esophageal cancer patients who underwent esophagectomy.**

KEY WORDS: **esophagectomy, enterostomy, enteral nutrition, post-operative complications.**

INTRODUCTON

Advanced esophageal cancer is associated with a high frequency of lymph node metastasis and has a very poor prognosis.[1] In patients with resectable disease, a surgical approach is generally most effective in terms of long-term survival.[1] However, subtotal esophagectomy with extensive lymph node dissection is quite invasive and involves the thorax, abdomen and neck.[1,2] Furthermore, the patients may be malnourished and immunocompromised owing to disease- or treatment-related dysphagia and anorexia.[3] Both conditions are associated with increased incidence of surgical complications, higher mortality and worse prognosis.[2,4]

Aggressive nutritional support for esophageal cancer patients early after surgery assists with early recovery of post-operative immune function and reduces the incidence of post-operative complications.[5] However, early oral feeding may not be possible because of impaired swallowing and/or concerns regarding the surgical anastomosis. Feeding enterostomy is therefore performed in conjunction with esophagectomy, most commonly feeding jejunostomy (FJ),[6] which enables placement of a feeding tube into the intestinal tract. However, FJ involves fixing the jejunum to the abdominal wall, which can cause complications such as small bowel obstruction, volvulus and internal hernia.[6–8]

As an alternative, feeding via an enteric feeding tube inserted through the reconstructed gastric tube or the duodenum using the round ligament of the liver has been suggested (FG or FD, respectively). With these techniques, a tube is placed from the abdominal

Address correspondence to: Akihisa Matsuda, Department of Gastrointestinal and Hepato-Biliary-Pancreatic Surgery, Nippon Medical School, 1-1-5 Sendagi, Bunkyo-ku, Tokyo 113-8603, Japan. E-mail: a-matsu@nms.ac.jp
Authors' contributions: TY: project development, data analysis and collection, manuscript writing, AM: data analysis and collection, manuscript writing/editing, HA: manuscript writing/editing, DK: manuscript writing/editing, NH: manuscript writing/editing, YK: manuscript writing/editing, KM: manuscript writing/editing, TM: manuscript writing/editing, MW: manuscript writing/editing, HS: manuscript writing/editing, HY: manuscript writing/editing, study supervision. Conflict of interest statement: None declared.

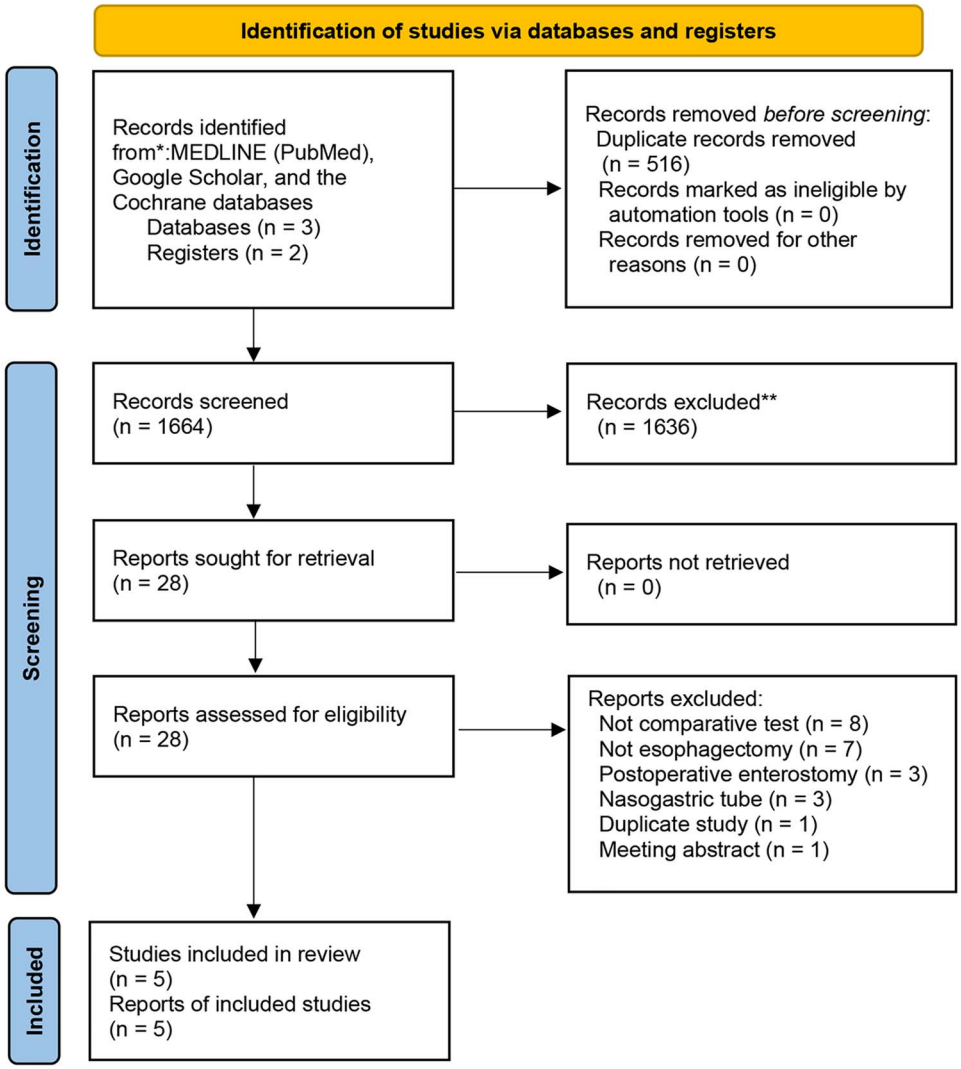

Fig. 1 Flow diagram of study selection (PRISMA 2020).

wall through the round ligament into the gastric tube or duodenum, respectively (Figure 2). Because the intestinal tract is not fixed to the abdominal wall with either, the risk of small bowel obstruction is potentially lower.[9] Although several recent retrospective cohort studies of feeding enterostomy have been reported, definitive conclusions cannot be drawn owing to their small sample sizes.[10–14] Therefore, we conducted this meta-analysis to evaluate the short-term safety and efficacy of FG and FD using the round ligament and compare them with FJ.

METHODS

Study design

This meta-analysis was designed according to the 2020 Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[15] Two investigators (TY and AM) independently conducted searches of the PubMed, Google Scholar and Cochrane databases to identify relevant studies published prior to May 2022 using the following search terms: ('Esophagectomy' OR 'Esophageal Neoplasms') AND ('Gastric Tube' OR 'Duodenum' OR 'Jejunum') AND ('Enterostomy' OR 'Gastrostomy' OR 'Duodenostomy' OR 'Jejunostomy' OR 'Feeding') (Figure 1). Reference lists of all relevant publications were manually searched for additional studies that may have been overlooked.

Eligibility

The inclusion and exclusion criteria were defined a priori. Studies that evaluated esophageal cancer patients who underwent esophagectomy combined with FG, FD or FJ and compared morbidity and mortality between FG or FD patients and FJ patients were included in the meta-analysis. We excluded duplicated studies and those in which pre-defined outcomes were not reported or the number of outcome events was unable to be extracted. Case reports, reviews, letters and meeting abstracts were also excluded.

Data extraction

The two investigators independently extracted and evaluated the following information from each

retrieved publication: name of primary author, year of publication, country in which the study was performed, number of institutions, design and duration of the study, number of included participants, participant characteristics (age, sex, surgical and reconstruction procedure details) and all available short-term outcomes. The primary endpoint was major abdominal complications such as small bowel obstruction and catheter site infection. Secondary endpoints were complications at other sites, length of post-operative hospital stay and hospital mortality. The unpublished data required for the current meta-analysis were requested through the corresponding authors of the included studies. All data were cross-checked to reach consensus and entered into a spreadsheet for analysis.

Quality assessment

The quality of each included study was assessed using the Methodological Index for Non-Randomized Studies (MINORS) score and Grading of Recommendations, Assessment, Development and Evaluation (GRADE) methodology using GRADE Pro software (McMaster University and Evidence Prime Inc., Ontario, Canada).[16,17]

Data synthesis and statistical analysis

Dichotomous variables were analyzed by calculating Odds Ratios (ORs) with 95% confidence intervals (CIs) for short-term adverse outcomes (hospital mortality and post-operative small bowel obstruction, catheter site infection, anastomotic leakage, pneumonia, recurrent nerve palsy and chylothorax). An OR < 1 favored the FG or FD group and $P < 0.05$ was considered significant if the 95% CI did not include the value 1. Pooled ORs were calculated using the Mantel–Haenszel random-effects model to combine ORs for outcomes of interest. Meta-analysis was performed using Review Manager version 5.4 for Windows (Nordic Cochrane Center, Cochrane Collaboration; Copenhagen, Denmark; http://www.cc-ims.net/RevMan). Cochran's chi square-based Q test and the I^2 statistic were used to test inter-study heterogeneity; $\chi 2$ $P < 0.05$ and $I2 \geq 50\%$ indicated heterogeneity. The random-effects model was applied for all comparisons because of the possibility that the underlying effect differed across studies, which were usually heterogeneous. Publication bias was assessed by visual analysis of funnel plot symmetry.

RESULTS

Studies and patient characteristics

The initial screening using the above search terms identified 1664 citations. After reviewing article titles and abstracts, 1636 studies were excluded. An additional 23 were excluded after full article evaluation. Finally, five studies[10–14] were included in the meta-analysis (date range of publication, 2014–2020). The characteristics of the included studies are shown in Table 1. Four studies[11–14] originated from Japan and one[10] from China. All were retrospective. Four[10–13] compared FG with FJ and one[14] compared FD with FJ. Among the 1687 patients included in the meta-analysis, 660 (39.1%) underwent FG, 111 (6.6%) underwent FD and 916 (54.3%) underwent FJ. Patient and surgical procedure characteristics are also shown in Table 1. The mean MINORS score of the included studies was 14.4 (standard deviation, 1.5), indicating a fair quality of evidence for non-randomized studies.[17] A comprehensive presentation of the MINORS assessment of the included studies is shown in Table 2. According to the GRADE criteria, the overall quality of evidence was very low for anastomotic leakage, pneumonia, chylothorax, recurrent laryngeal nerve palsy, and length of hospital stay and low for catheter site infection and small bowel obstruction (Table 3).

Effect of feeding method on abdominal complications

The incidence of small bowel obstruction was zero in the FG/FD group and 3.8% (35/916) in the FJ group (OR 0.09; 95% CI, 0.02–0.33). Heterogeneity testing indicated $\chi 2 = 0.9$ and $I^2 = 0\%$, which indicated study homogeneity (Figure 3A). The funnel plot was roughly symmetrical, suggesting a low risk of publication bias (Figure 3B). The incidence of catheter site infection was 0.9% (7/771) in the FG/FD group and 5.8% (53/916) in the FJ group (OR 0.18; 95% CI, 0.06–0.51). Heterogeneity testing indicated $\chi 2 = 5.66$ and $I^2 = 29\%$, which indicated study homogeneity (Figure 3C). The funnel plot was roughly symmetrical, suggesting a low risk of publication bias (Figure 3D). Therefore, the meta-analysis demonstrated that incidence rates of both small bowel obstruction and catheter site infection were lower in esophagectomy patients who underwent FG/FD than in those who underwent FJ.

Effect of feeding method on post-operative complications at other sites

The incidence of anastomotic leakage was 7.1% (55/771) in the FG/FD group and 11.1% (102/916) in the FJ group (OR 0.53, 95% CI, 0.32–0.89) without statistical heterogeneity (Figure 4A). Incidence rates and ORs for pneumonia, recurrent laryngeal nerve palsy and chylothorax did not significantly differ between the FG/FD and FJ groups (Figure 4B–D).

Post-operative stay and hospital mortality

The mean length of hospital stay was significantly shorter in the FG/FD group than in the FJ group

Table 1 Characteristics of included studies and patients

Characteristics of included studies

Author	Design	Group	Number	Period of enrollment	Age	Sex (M/F)	BMI (kg/m^2)	Location (Ce + Ut/Mt/Lt + Ae)	Stage (0-I/II-IV)	Neoadjuvant (yes/no)
Huang 2014	Retrospective	FG	121	2008–2012	61.5 ± 6.5	103/18			20/101	
		FJ	153	2008–2012	61.8 ± 7.2	129/24			38/115	
Oya 2015	Retrospective	FD	111	2009–2012	65.2 ± 7.6	90/21		130/60/35	24/87	73/38
		FJ	267	1998–2011	61.9 ± 7.9	214/53		41/132/94	52/215	108/159
Kawai 2017	Retrospective	FG	206	2008–2015	64	175/31	21.5 ± 3.1	35/113/58	13/193	192/14
		FJ	214	2005–2007	61	181/33	21.2 ± 3.0	34/105/75	40/174	125/89
Konishi 2018	Retrospective	FG	133	2011–2016	66.9 ± 9.2	112/21	21.3 ± 3.1	29/68/36	42/73	87/46
		FJ	82	2010–2011	65.4 ± 8.7	68/14	20.8 ± 2.8	18/42/22	24/56	57/25
Otake 2020	Retrospective	FG	200	2013–2016	64	165/35	21.6	32/87/81	81/119	123/77
		FJ	200	2011–2012	65	165/35	22.1	**29/98/73**	81/119	123/77

Characteristics of included studies

Author	Group	Procedure (transhiatal/-transthoracic)	Chest Approach (open/minimally invasive)	Abdominal approach (open/laparo)	Lymph node resection (2FLD/3FLD)	Reconstruction root (posterior/retrosternal/anterior)	Site of feeding catheter
Huang 2014	FG			121/0		0/121/0	10–25 cm from incision
	FJ			153/0		0/153/0	40–45 cm from Treitz ligament
Oya 2015	FD			111/0			40 cm from Treitz ligament
	FJ			267/0			50 cm from Treitz ligament
Kawai 2017	FG	0/206	206/0	206/0	26/180	5/195/6	20 cm from Treitz ligament
	FJ	0/214	214/0	214/0	44/170	78/117/19	40 cm from Treitz ligament
Konishi 2018	FG	83/50	40/93	133/0	113/20	0/133/0	30 cm from Treitz ligament
	FJ	6/76	68/14	82/0	57/25	0/82/0	30 cm from Treitz ligament
Otake 2020	FG	0/200	31/169	47/153	86/114	52/148/0	Third portion of duodenum
	FJ	0/200	115/85	186/14	85/115	185/14/1	15–30 cm from Treitz ligament

Table 2 MINORS assessment

MINORS assessment

Author	A clearly stated aim	Inclusion of consecutive patients	Prospective collection of data	End points appropriate to the aims of the study		Unbiased assessment of the study endpoint	Follow-up period appropriate to the aim of the study	
Huang 2014	2	2	0	1		0	1	
Oya 2015	2	2	0	1		0	1	
Kawai 2017	2	2	0	1		0	1	
Konishi 2018	2	2	0	1		0	1	
Otake 2020	2	2	0	1		0	2	
Author	Loss to follow-up less than 5%	Prospective calculation of the study size		An adequated control group	Contemporary groups	Baseline equivalence of groups	Adequate statistical analyses	Total
Huang 2014	2	0		2	2	2	2	16
Oya 2015	2	0		2	0	1	2	13
Kawai 2017	2	0		2	0	1	2	13
Konishi 2018	2	0		2	2	2	2	16
Otake 2020	2	0		2	0	1	2	14

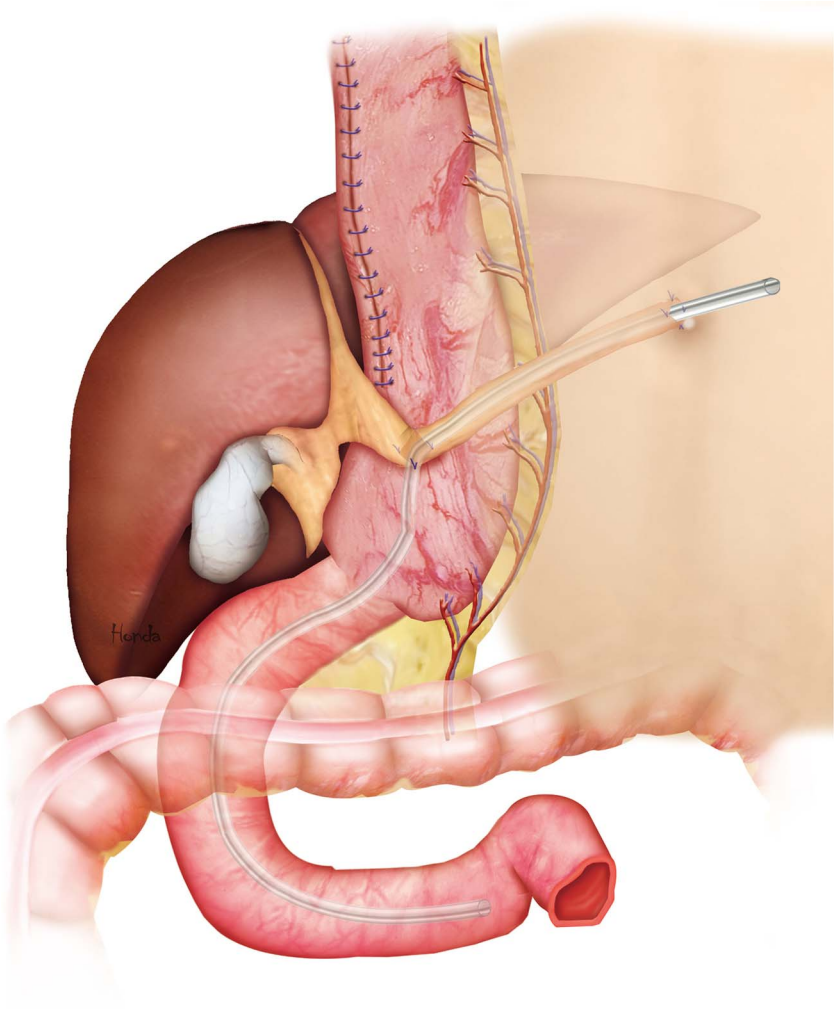

Fig. 2 Schematic presentation of FG. A feeding tube was placed from the abdominal wall through the round ligament into the antrum of the gastric tube. The tip is placed in the third portion of the duodenum or jejunum around the Treitz ligament.

Table 3 GRADE evidence profile

Outcome	GRADE										
	No. of studies	No. of patients	Quality assessment								
			Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Publication bias	Other considerations (for upgrading)	Overall quality of evidence	Importance
Small bowel obstruction	5	1687	5RS	Serious	Not serious	Not serious	Serious	Not serious	Large magnitude	Low	Critical
Catheter site infection	5	1687	5RS	Serious	Not serious	Not serious	Serious	Not serious	None	Low	Critical
Anastomotic leakage	5	1687	5RS	Serious	Not serious	Not serious	Serious	Not serious	None	Very low	Critical
Recurrent nerve palsy	4	1413	4RS	Serious	Serious	Not serious	Very serious	Not serious	None	Very low	Critical
Chylothorax	4	1309	4RS	Serious	Not serious	Not serious	Very serious	Not serious	None	Very low	Critical
Pneumonia	5	1687	5RS	Serious	Serious	Very serious	Very serious	Not serious	None	Very low	Critical
Post-operative hospital stay	4	1413	4RS	Serious	Serious	Not serious	Serious	Not serious	None	Very low	Important
Hospital mortality	4	1413	4RS	Serious	Serious	Not serious	Serious	Not serious	None	Very low	Critical

(mean difference, −10.83 days; 95% CI, −18.55 to −3.11); however, the studies were heterogeneous (Figure 5A). Hospital mortality did not significantly differ between the groups (Figure 5B).

DISCUSSION

This systematic review and meta-analysis of five studies included 1687 patients who underwent esophagectomy for esophageal cancer combined with feeding enterostomy in the gastric tube (FG), duodenum (FD) or jejunum (FJ). Our aim was to compare short-term outcomes of feeding enterostomy using the round ligament of the liver (FG and FD), which does not involve fixing the jejunum to the abdominal wall, with those of FJ, which does involve jejunal fixation. Our most important finding was that both incidence and odds of small bowel obstruction, catheter site infection and anastomotic leakage were lower in patients who underwent FG or FD compared with FJ.

Watanabe et al. first reported feeding enterostomy in which a feeding tube is inserted into the gastric tube or duodenum through the round ligament of the liver.[9] During esophagectomy, the round ligament is dissected from the abdominal wall and cut just above the umbilicus after the esophagus is removed. Then, a feeding tube is inserted from the umbilical side and passed through the ligament just above the gastric antrum. The feeding tube is then inserted from the gastric antrum or duodenum and the tip is placed in the third portion of the duodenum or jejunum around the Treitz ligament. The procedure is completed by suturing and covering both sides of the ligament with the gastroduodenal and abdominal wall at four points.[9,14] Importantly, all these procedures can be conducted under direct vision not only from upper abdominal midline incision, but also from an approximately 5-cm incision in the upper abdomen where the gastric tube is constructed.[13] Therefore, these can be performed in minimally invasive surgery and require no more time than an enterostomy to jejunum.[11,13]

Both FG and FD theoretically have a very low chance of causing small bowel obstruction because the tube is placed in less mobile gut and the jejunum is not fixed to the abdominal wall. Our findings confirmed this theory. In contrast, conventional FJ reportedly causes bowel obstruction in 1.7–6.9% of patients over the short term.[18,19] Small bowel obstruction occurs in 12% of thoracoscopic esophagectomy patients who undergo FJ within the first 5 years after surgery[20] and has been associated with increased risk of serious surgical complications such as intestinal necrosis and sepsis. Furthermore, intestinal obstruction can recur over time, which can interrupt cancer treatment and worsen long-term outcome.[21]

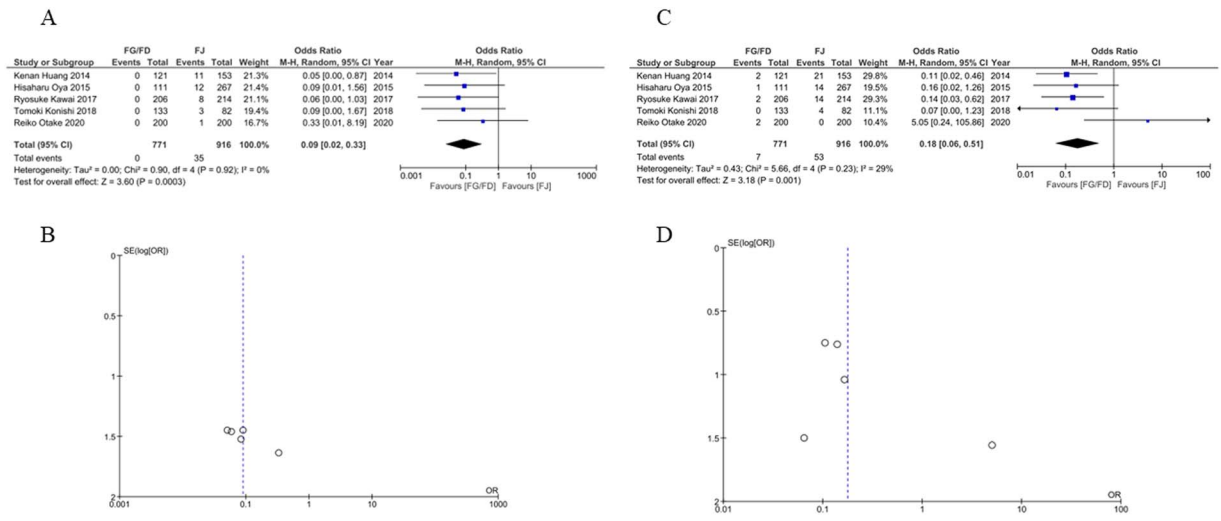

Fig. 3 Forest plot showing effective of FG/FD on small bowel obstruction (A) and catheter site infection (C) during post-operative hospitalization. Funnel plot depicting the distribution of risk ratio for the studies on small bowel obstruction (B) and catheter site infection (D).

A

Study or Subgroup	FG/FD Events	FG/FD Total	FJ Events	FJ Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Kenan Huang 2014	5	121	10	153	15.3%	0.62 [0.20, 1.85]	2014
Hisaharu Oya 2015	1	111	19	267	5.7%	0.12 [0.02, 0.90]	2015
Ryosuke Kawai 2017	18	206	31	214	29.7%	0.57 [0.31, 1.05]	2017
Tomoki Konishi 2018	19	133	11	82	22.9%	1.08 [0.48, 2.39]	2018
Reiko Otake 2020	12	200	31	200	26.4%	0.35 [0.17, 0.70]	2020
Total (95% CI)		**771**		**916**	**100.0%**	**0.53 [0.32, 0.89]**	
Total events	55		102				

Heterogeneity: Tau² = 0.13; Chi² = 6.72, df = 4 (P = 0.15); I² = 40%
Test for overall effect: Z = 2.40 (P = 0.02)

B

Study or Subgroup	FG/FD Events	FG/FD Total	FJ Events	FJ Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Kenan Huang 2014	14	121	40	153	20.3%	0.37 [0.19, 0.72]	2014
Hisaharu Oya 2015	7	111	16	267	17.0%	1.06 [0.42, 2.64]	2015
Ryosuke Kawai 2017	27	206	19	214	20.8%	1.55 [0.83, 2.88]	2017
Tomoki Konishi 2018	12	133	26	82	19.1%	0.21 [0.10, 0.45]	2018
Reiko Otake 2020	43	200	66	200	22.9%	0.56 [0.36, 0.87]	2020
Total (95% CI)		**771**		**916**	**100.0%**	**0.59 [0.31, 1.13]**	
Total events	103		167				

Heterogeneity: Tau² = 0.43; Chi² = 19.77, df = 4 (P = 0.0006); I² = 80%
Test for overall effect: Z = 1.60 (P = 0.11)

C

Study or Subgroup	FG/FD Events	FG/FD Total	FJ Events	FJ Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Hisaharu Oya 2015	3	111	19	267	13.0%	0.36 [0.11, 1.25]	2015
Ryosuke Kawai 2017	20	206	11	214	23.5%	1.98 [0.93, 4.25]	2017
Tomoki Konishi 2018	45	133	34	82	30.1%	0.72 [0.41, 1.27]	2018
Reiko Otake 2020	39	200	46	200	33.4%	0.81 [0.50, 1.31]	2020
Total (95% CI)		**650**		**763**	**100.0%**	**0.87 [0.51, 1.47]**	
Total events	107		110				

Heterogeneity: Tau² = 0.16; Chi² = 6.92, df = 3 (P = 0.07); I² = 57%
Test for overall effect: Z = 0.52 (P = 0.60)

D

Study or Subgroup	FG/FD Events	FG/FD Total	FJ Events	FJ Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Kenan Huang 2014	2	121	3	153	18.1%	0.84 [0.14, 5.11]	2014
Ryosuke Kawai 2017	12	206	14	214	57.1%	0.88 [0.40, 1.96]	2017
Tomoki Konishi 2018	1	133	2	82	10.8%	0.30 [0.03, 3.40]	2018
Reiko Otake 2020	1	200	8	200	14.0%	0.12 [0.01, 0.97]	2020
Total (95% CI)		**660**		**649**	**100.0%**	**0.59 [0.26, 1.36]**	
Total events	16		27				

Heterogeneity: Tau² = 0.15; Chi² = 3.65, df = 3 (P = 0.30); I² = 18%
Test for overall effect: Z = 1.24 (P = 0.21)

Fig. 4 Forest plot showing no significant difference in pneumonia (B), recurrentnerve palsy (C) and chylothorax (D) except for anastomotic leakage (A) by FG/FDin postoperative complication of remote site.

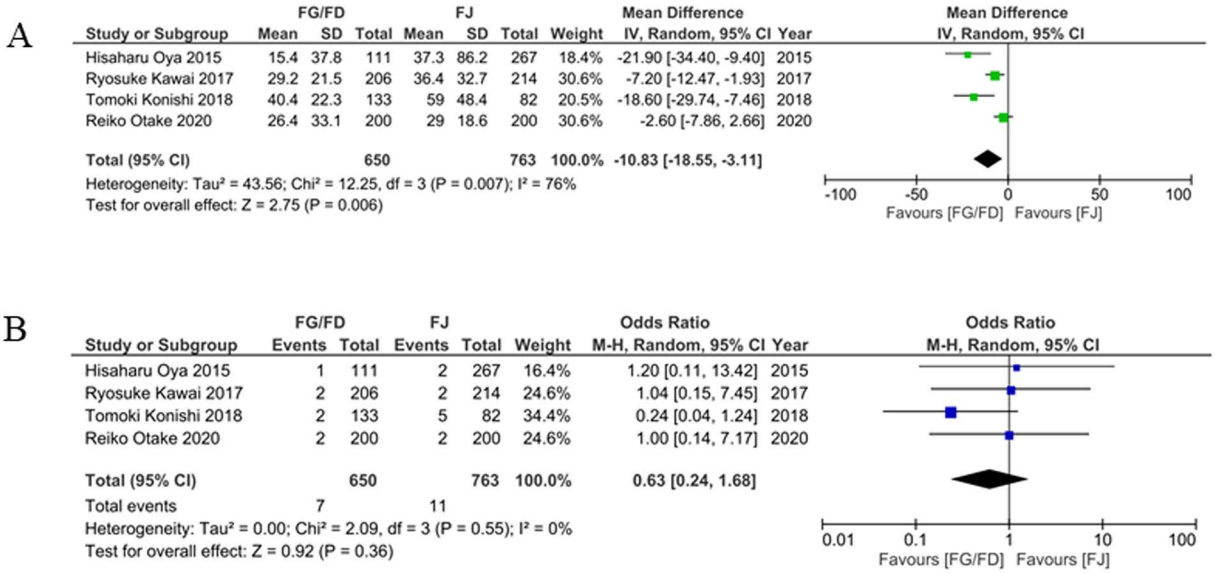

Fig. 5 Forest plot showing significant reduction of post-operative hospital stay (A) in FG/FD and no significant difference in post-operative mortality (B) in the two groups.

Despite the concern for leakage of digestive fluids from the feeding tube at the insertion site, FG/FD was associated with lower incidence and odds of catheter site infection. The round ligament can be used to cover the ends of the gastroduodenal and hepatic arteries after pancreatoduodenectomy to protect against pancreatic juice leakage. With FG/FD, the round ligament can also be used in the same fashion to prevent digestive juice leakage into the abdominal cavity after esophagectomy. In addition, after esophagectomy, gut activity and digestive fluid secretion are lower in the stomach and duodenum than in the small intestine; therefore, the risk of insertion site inflammation and infection is lower with an FG/FD insertion site.[22]

Compared with FJ, FG/FD was also associated with fewer post-operative infectious complications, including anastomotic leakage and post-operative pneumonia. In addition, FG/FD is more physiologic. Jejunal feeding is not physiologic and is associated with poor digestion and absorption as well as dumping syndrome and hyperglycemia.[6–8,23,24] Hyperglycemia, in particular, can lead to serious complications and anastomotic leakage after gastrointestinal surgery.[25] Moreover, incidence rates of reflux and gastric drainage after esophagectomy are lower in FG/FD patients than FJ patients.[10] FG/FD stimulates physiologic peristalsis of the intestinal tract via secretion of gastrointestinal hormones, whereas FJ results in abnormal peristalsis and regurgitation because the jejunum is fixed to the abdominal wall.[26] These physiologic advantages of FG/FD may have contributed to the observed lower incidence and odds of post-operative infectious complications.

This meta-analysis had several limitations. The main limitation is the lack of a comorbidity score to be compared in the complication rates. Although the primary endpoints are set to post-operative bowel obstruction and catheter site infection, which is largely related with physical effects by feeding enterostomy, major complications are connected to preoperative comorbidities.[27] The comorbidity score unavailable in this study may have influenced the results. And none of the analyzed studies were randomized or controlled studies; therefore, our findings may have been affected by various biases. However, conducting a randomized study would be unethical because of the clear discrepancy in incidence of small bowel obstruction between the FJ and FG/FD groups. Furthermore, time-related bias almost certainly was a factor in our meta-analysis owing to the various advances in perioperative management and surgical techniques that occurred over the periods the analyzed studies were conducted. FG/FD was more frequently performed in the later years of each study and the widespread adoption of Enhanced Recovery After Surgery protocols after 2010[28] probably had a significant effect on the incidence of post-operative pneumonia and the length of hospital stay. Future studies comparing long- and short-term outcomes of feeding methods after esophagectomy, including nasogastric feeding, are warranted.

In conclusion, FG and FD using the round ligament of the liver are associated with lower incidence and odds of small bowel obstruction, catheter site infection and anastomotic leakage than FJ in esophageal cancer patients undergoing esophagectomy. Although a previous meta-analysis compared FJ and nasogastric tube feeding,[29] to the best of our knowledge, ours is the first to compare FG and FD with FJ. Our findings suggest that esophagectomy should be performed in combination with FG or FD using the round ligament rather than FJ.

ACKNOWLEDGMENTS

The authors would like to extend their deep appreciation to Tetsuya Abe,[11] Atsushi Shiozaki,[12] Reiko Otake[13] and Akihiko Okamura[11] for providing the unpublished data. We also thank Edanz (https://jp.edanz.com/ac) for editing a draft of this manuscript.

DATA AVAILABILITY STATEMENT

The raw data supporting the conclusions of this article will be made available by the authors, without undue reservation.

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