

## Original Article

# Nasoenteric tube versus jejunostomy for enteral nutrition feeding following major upper gastrointestinal operations: a meta-analysis

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**Background and Objectives:** Following major upper gastrointestinal surgical procedures, early enteral nutrition to the jejunum is strongly recommended, either through a nasoenteric tube or a percutaneous transperitoneal jejunal feeding tube (jejunostomy). However, to date there has been no consensus as to the best enteral feeding strategy. Our aim was to determine the safest and most efficacious early enteral nutrition supplement strategy following major upper gastrointestinal operations. **Methods and Study Design:** PubMed, Embase and Cochrane Library databases were systematically searched for comparison of trials. The primary outcome analyzed was length of postoperative hospital stay, and secondary outcomes were: duration of enteral nutrition, time to resumption of normal oral intake, and tube dislodgement, tube leakage and tube obstruction complications. Weighted mean differences (WMDs) and risk ratios (RRs) were calculated with 95% confidence intervals (CI). **Results:** A total of 5 studies were included with 420 patients in all. The length of hospital stay, duration of enteral nutrition and the time to resumption of normal oral intake were all significantly shorter in the nasoenteric group ( $p < 0.05$ ). There was no increase or reduction in the RR of tube obstruction between the nasoenteric and jejunostomy groups ( $p = 0.5$ ). The RR of tube dislodgement was increased in the nasoenteric group ( $p < 0.05$ ) while the RR of tube leakage was increased in the jejunostomy group ( $p < 0.05$ ). **Conclusions:** A nasoenteric tube is more likely to be effective in early postoperative enteral feeding following major upper gastrointestinal operations.

**Key Words:** nasoenteric tube, jejunostomy, enteral nutrition, upper gastrointestinal operations, meta-analysis

## INTRODUCTION

The upper gastrointestinal tract is the segment of the gastrointestinal (GI) tract that includes the esophagus, the stomach and the duodenum. Major upper GI tract operations for carcinomas include esophagectomy, gastrectomy, and pancreaticoduodenectomy (PD). They all are complex procedures with a high morbidity and mortality rate. In malnourished patients in particular, there is a high rate of postoperative complications.<sup>1-3</sup> Postoperative nutritional supplementation can clearly reduce the incidence of postoperative complications and therefore is strongly recommended. Enteral feeding is not only more physiologically compatible and safer than parenteral nutrition, but is also cheaper and results in less morbidity.<sup>4,5</sup> Indeed, the current guidelines of the European Society for Parenteral and Enteral Nutrition (ESPEN) recommend routine early enteral nutrition following major GI operations.<sup>6</sup> Enteral nutrition is usually administered via a tube placed in the jejunum (proximal small intestine). Enteral nutrition to the jejunum is generally achieved through one of two routes; either through a nasoenteric tube or through a percutaneous transperitoneal jejunal feeding tube (jejunostomy).<sup>7</sup> However, there is currently no consensus as to which is the best approach following major upper GI operations, and in practice the choice of enteral feeding route is determined by the individual surgeon's preferen-

ce.<sup>8</sup> One systematic review has compared the routes for early enteral nutrition after esophagectomy,<sup>9</sup> and another systematic review has compared different feeding routes after PD.<sup>10</sup> But no meta-analysis has yet been published undertaking a comparative analysis of the nasoenteric tube with the jejunostomy approach following major upper GI operations. Our meta-analysis evaluates the most recent studies to date and investigates the efficacy of the two different feeding routes and the tube-related complications to determine the safest and most efficacious strategy for early enteral nutrition supplement following major upper GI operations.

## MATERIALS AND METHODS

### Literature search

The PubMed, Embase and Cochrane Library databases

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were searched systematically for studies published up to January 2015. The search terms were ‘enteral nutrition,’ ‘enteral feeding,’ ‘enteral intake,’ ‘enteral support,’ ‘enteral supplement,’ ‘nasoenteric tube,’ ‘nasoduodenal tube,’ ‘nasojejunal tube,’ and ‘jejunostomy,’ which were searched in all fields. No filters or limits were applied. In order to make sure that no clinical trials were omitted, additional manual searches were made using the reference lists of identified articles and reviews. Titles, abstracts and full texts were independently reviewed by 2 reviewers (Lidong Wang and Zhong Tian) according to the inclusion and exclusion criteria. Disagreements were resolved by discussion between the reviewers.

### ***Inclusion criteria and exclusion criteria***

To these potentially eligible articles, the following inclusion criteria were applied: (1) human, not animal, trials of patients  $\geq 18$  years of age undergoing major upper GI surgical operations (esophagectomy, gastrectomy, or PD); (2) the intervention was the two different methods for early enteral feeding (nasoesenteric tube versus jejunostomy); (3) articles needed to report at least one of the outcomes mentioned below; (4) when more than one version of the same study or similar study from the same author was discovered, only the highest quality article was included; and (5) only articles with the full text available in English were included.

Exclusion criteria were: (1) abstracts, review articles, letters, opinion papers, case reports, fundamental research or animal research; (2) studies not reporting the results of the two different methods separately; (3) studies reporting on only one route of enteral feeding (nasoesenteric tube or jejunostomy) or only comparing the difference between enteral nutrition and parenteral nutrition; (4) studies with no patients undergoing major upper GI operations and (5) lack of suitable data for this meta-analysis.

### ***Assessment of methodological quality***

Two authors (Lidong Wang and Zhong Tian) independently evaluated the methodological quality of these studies. Randomized, controlled clinical trials (RCTs) were qualitatively analyzed using the Jadad scale scoring system which included randomization, blinding, and withdrawals or dropouts of studies.<sup>11</sup> A score of greater than 3 in the Jadad scale was considered indicative of a high-quality RCT. Non-randomized retrospective cohort studies were similarly evaluated using the Newcastle-Ottawa scoring Scale (NOS).<sup>12</sup>

### ***Data extraction and outcomes***

All eligible studies were reviewed and the data extracted by two reviewers (Lidong Wang and Zhong Tian) independently. Discrepancies were resolved through discussion among the reviewers and other authors of this paper. The following variables were recorded: author, journal, date of publication, and number of patients in each group. The primary outcome was the length of postoperative hospital stay (defined as the number of days from surgery to discharge). The secondary outcomes were duration of enteral nutrition, time to resumption of normal oral intake and tube-related complications, including tube dislodgement, tube leakage and tube obstruction.

### ***Statistical analysis***

We used the Cochrane Collaboration’s Review Manager Software 5.3 (The Nordic Cochrane Centre, The Cochrane Collaboration, 2014) to perform the meta-analysis. Continuous variables such as length of postoperative hospital stay, duration of enteral nutrition and time to resumption of normal oral intake, were expressed as weighted mean differences (WMDs) with corresponding 95% confidence intervals (CI). Some standard deviation (SD) not mentioned in articles were estimated by median (range) values using the methods reported by Hozo and colleagues.<sup>13</sup> Categorical variables like tube dislodgement complication, tube leakage complication and tube obstruction complication were expressed as risk ratios (RRs) with corresponding 95% CIs. The use of fixed-effects model or random-effects model depended on the absence or presence of significant heterogeneity.  $I^2$  values were used for the evaluation of statistical heterogeneity.<sup>14</sup> We considered substantial heterogeneity as an outcome of  $I^2 > 50\%$  following Higgins and Thompson’s classification.<sup>15</sup> The random-effects analysis was performed when the test rejected the collection of the homogeneity.<sup>16</sup> Funnel plots and Egger’s regression model were both used to help uncover potential publication bias, since the capacity of the funnel plot to evaluate bias was limited when the number of trials was small.<sup>17</sup> If the p value of the Egger’s regression model was  $< 0.1$ , we considered the asymmetry to be statistically significant.

## **RESULTS**

### ***Literature search***

Through the database search, we identified 65 potentially relevant articles but only 5 articles met the inclusion criteria. The article selection process is showed in Figure 1. Of the 5 articles included, 3 were randomized trials and 2 were retrospective non-randomized cohort studies. The characteristics of the 5 included studies are shown in Table 1.<sup>18-22</sup> Not all of the included studies reported data on the time to resumption of normal oral intake.<sup>18,20</sup> Han-Geurts et al<sup>18</sup> stated only that the median duration of hospital stay was 14 days in both groups, which could not be used to calculate the weighted mean values.

### ***Methodological quality***

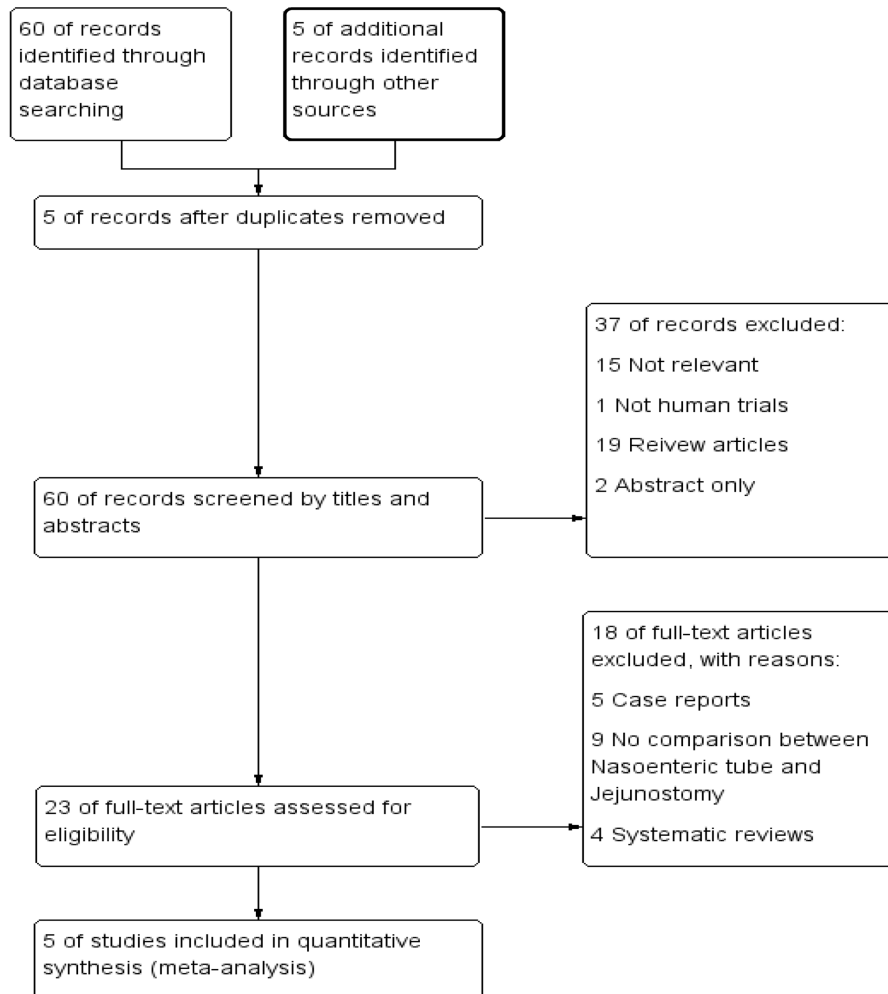
The Jadad scores of each of the 3 included RCTs are displayed in Table 2. The quality assessment outcomes of the two retrospective non-randomized cohort studies are presented in Table 3.

### ***Pooled outcomes***

#### **Primary outcome**

##### ***Length of hospital stay***

Four of the included studies reported the length of hospital stay as an outcome.<sup>19-22</sup> Han-Geurts et al stated only that the median duration of hospital stay was 14 days in both groups, with no method to pool into the total data.<sup>18</sup> The length of hospital stay was significantly shorter in the nasoesenteric group (WMD -1.88 days; 95% CI -2.81 to -0.95 days;  $p < 0.0001$ , from a fixed effects model), with almost no heterogeneity ( $\text{Chi}^2 = 3.28$ ,  $p = 0.35$ ;  $I^2 = 9\%$ ). (Figure 2)



**Figure 1.** Study flow diagram studies included in the meta-analysis

**Table 1.** Characteristics of the 5 included studies.

Reference	Year	Country	Study design	Mean-age (years)		Sample size	Male sex (%)	
				NE	Jejunostomy		NE	Jejunostomy
Han-Geurts et al <sup>18</sup>	2007	Netherland	RCT	61	61	150	56	64
Zhu X et al <sup>19</sup>	2014	China	RCT	53.5	52.6	68	16	20
Torres Júnior et al <sup>20</sup>	2014	Brail	RCT	60	65	42	13	8
Abu-Hilal et al <sup>21</sup>	2010	UK	Retrospective cohort	67	65	68 <sup>†</sup>	23	15
Gerritsen et al <sup>22</sup>	2012	Netherland	Retrospective cohort	63	65	92	26	33

NE: nasoenteric tube.

<sup>†</sup>Only the total sample size of the nasojejunal group and the jejunostomy group.

## Secondary outcomes

### *Duration of enteral nutrition*

All 5 included studies presented the duration of enteral nutrition as an outcome. The pooled outcome was that the duration of enteral nutrition was apparently shorter in the nasoenteric group (WMD -2.84 days; 95% CI -4.31 to -1.36 days;  $p=0.0002$ , from a random effects model), with some evidence of heterogeneity ( $\text{Chi}^2=11.1$ ,  $p=0.03$ ;  $I^2=64\%$ ).

### *Time to resumption of normal oral intake*

Only 3 articles reported the time to resumption of normal oral intake as an outcome which was certainly shorter in the nasoenteric group (WMD -2.98 days; 95% CI -3.85 to

-2.11 days;  $p<0.00001$ , from a fixed effects model), with no heterogeneity ( $\text{Chi}^2=0.19$ ,  $p=0.91$ ;  $I^2=0\%$ ).<sup>19,21,22</sup>

### *The tube obstruction complication*

The risk ratio of tube obstruction was not increased or reduced between the 2 groups (RR 0.81; 95% CI 0.44 to 1.50;  $p=0.5$ , from a fixed effects model), with no heterogeneity between trials ( $\text{Chi}^2=1.31$ ,  $p=0.86$ ;  $I^2=0\%$ ).

### *The tube dislodgement complication*

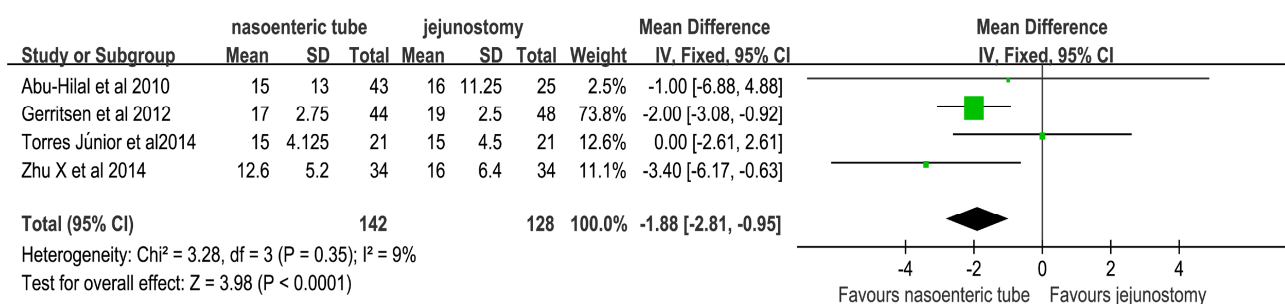
The risk ratio of tube dislodgement was increased in the nasoenteric group (RR 2.59; 95% CI 1.54 to 4.37;  $p=0.0003$ , from a fixed effects model), with no heterogeneity between articles ( $\text{Chi}^2=1.50$ ,  $p=0.83$ ;  $I^2=0\%$ ).

**Table 2.** Quality assessment of RCTs based on the Jadad scoring scale

Reference	Randomized	Appropriate randomization	Appropriately double blinded	Describe withdrawals and dropouts	Total score
Han-Geurts et al <sup>18</sup>	2	2	0	1	5
Zhu X et al <sup>19</sup>	2	0	0	1	3
Torres Júnior et al <sup>20</sup>	2	2	0	1	5

**Table 3.** Quality assessment of retrospective cohort trials based on the Newcastle-Ottawa Scale

Methods of quality assessment	Abu-Hilal et al <sup>21</sup> (star numbers)	Gerritsen et al <sup>22</sup> (star numbers)
Selection		
Representativeness of the exposed cohort	1	1
Selection of the non exposed cohort	1	1
Ascertainment of exposure	1	1
Demonstration that outcome of interest was not present at start of study	1	1
Comparability		
Comparability of cohorts on the basis of the design or analysis	1	1
Outcome		
Assessment of outcome	1	1
Was follow-up long enough for outcomes to occur	0	0
Adequacy of follow up of cohorts	0	0
Total star numbers	6	6

**Figure 2.** Forest plot comparing the nasoenteric tube with the jejunostomy for the outcome of length of hospital stay. IV: inverse variance; SD: standard deviation; CI: confidence intervals; df: degrees of freedom.

### The tube leakage complication

The risk ratio of tube leakage increased in the jejunostomy group (RR 0.16.; 95% CI 0.04 to 0.59;  $p=0.006$ , from a fixed effects model), with no heterogeneity between articles (Chi<sup>2</sup>=0.13,  $p=1.00$ ; I<sup>2</sup>=0%).

### Risk of bias

The total detailed information regarding the methodological quality of the 5 included studies is shown in Table 4. We used the Cochrane risk of bias tool to evaluate the risk of bias for each article. The blinding part of all included studies is high risk. It was not in practice possible to blind participants and study personnel. Funnel plots did not show the presence of publication bias (Figure 3). The results of the Egger test were confirmed statistically with no obvious evidence of asymmetry in any of these plots (Table 5).

## DISCUSSION

Nutritional supplementation is one of the most significant factors of concern in the management of patients following major GI operations. In many published studies, enteral nutrition has been proven to be both more helpful and safer than parenteral nutrition.<sup>4,23</sup> Enteral support

immediately following surgical operations has now become commonplace. Because of the unique nature of patients undergoing upper GI surgery and the inherent risk of upper GI anastomotic failure, post-pyloric feeding is the obvious choice for enteral feeding. However, it remains controversial as to which of the two major enteral feeding routes in common use, i.e. via nasoenteric or jejunostomy tube, is the safest and most effective. Both approaches have been reported to be associated with specific tube-related complications. The nasoenteric tube feeding method, which includes the use of nasojejunal or nasodudenal tubes, has caused patients to experience inconvenience and discomfort. In addition, there have been tube-related complications such as aspiration pneumonia and even bowel necrosis.<sup>24,25</sup> The jejunostomy route is associated with postoperative tube-related complications in up to 35 percent of all patients.<sup>18</sup> The choice of approach remains generally dependent on the surgeon's familiarity with a particular approach.

All 5 studies in this meta-analysis compared the two different enteral feeding routes. Their methodological quality and feeding-related complications were analyzed. Several relevant outcomes of patients appeared to be more favorable in the nasoenteric tube group, such as

**Table 4.** Methodological quality summary: review of authors' judgments about each methodological quality item for each included study.

Methodological quality items	Han-Geurts et al <sup>18</sup>	Zhu X et al <sup>19</sup>	Torres Júnior et al <sup>20</sup>	Abu-Hilal et al <sup>21</sup>	Gerritsen et al <sup>22</sup>
Random sequence generation (selection bias)	? <sup>†</sup>	+	+	-	-
Allocation concealment (selection bias)	+ <sup>‡</sup>	+	+	-	-
Blinding (performance bias and detection bias): participants and personnel	- <sup>§</sup>	-	+	-	-
Blinding (performance bias and detection bias): outcome assessment	-	-	-	-	-
Incomplete outcome data (attrition bias)	-	+	+	+	+
Selective reporting (reporting bias)	+	+	+	+	+
Other bias	+	+	+	-	-

<sup>†</sup>Authors' judgment is unclear risk.

<sup>‡</sup>Authors' judgment is low risk.

<sup>§</sup>Authors' judgment is high risk.

**Table 5.** Results of the Egger test

Outcome	SE	<i>t</i>	95% CI		<i>p</i> <sup>†</sup>
Length of hospital stay	1.20	0.32	-4.79	5.56	0.779
Duration of enteral nutrition	1.41	0.90	-3.21	5.73	0.437
Time to resumption of normal oral intake	0.405	-0.79	-5.47	4.83	0.574
Tube obstruction	2.18	-1.52	-10.2	3.62	0.226
Tube dislodgement	0.935	1.17	-1.88	4.07	0.326
Tube leakage	1.64	2.30	-1.44	8.96	0.105

SE: standard error; CI: confidence intervals.

<sup>†</sup>Asymmetry:  $p < 0.1$ .

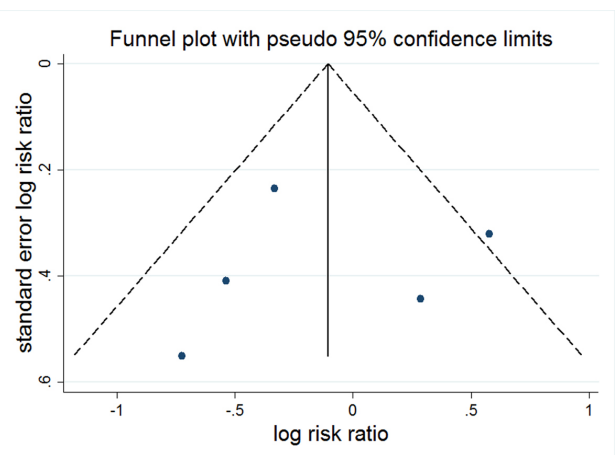
length of hospital stay, duration of enteral nutrition, and time to resumption of normal oral intake. The risk ratio of tube dislodgement was increased in the nasoenteric group while the risk ratio of tube leakage was increased in the jejunostomy group. Hence, in comparing these outcomes, there is some evidence that nasoenteric tube feeding may be considered the preferred postoperative enteral feeding route.

It may be argued that the length of hospital stay can be influenced by several factors other than postoperative nutrition, for example, variations in surgical procedures and variations in discharge policies applying in different countries. Nevertheless, length of stay was a very commonly reported outcome in the literature in this area of clinical study. In our study, outcomes specifically related to tube feeding, such as duration of enteral nutrition and time to resumption of normal oral intake, were also considered and analyzed.

In recent published studies of enteric nutrition following GI surgery, dislodgement was considered to be the main tube-related complication of nasoenteric tube feeding, with the complication rate reported as 16-36%.<sup>26-30</sup> Many new techniques to reduce the dislodgement of the nasoenteric tube have been described, however. Among these, nasal bridling can be considered to be the most effective, reducing the dislodgement rate from 63% to 18% with only a few minor adverse effects.<sup>31</sup> The nasoenteric tube also has caused discomfort to the patient, not only in the nasopharynx but also in the oropharynx which has contributed to patients pulling the tube out to relieve the discomfort.

Jejunostomy has commonly been associated with less dislodgement, as well as with less nausea and vomiting

with the main complication being leakage; other rare complications have included pain or/and peritonitis after tube removal, pain around the feeding tube, GI bleeding, infection of feeding tube and so on. One article reported that in a large series of 2002 applications the jejunostomy-related reoperation rate was 1% and life-threatening complications of torsion and bowel necrosis occurred in 0.4%.<sup>32</sup> Complications such as small bowel perforations and pneumatosis intestinalis were also reported.<sup>33</sup> A technological update from the needle catheter jejunostomy technique described by Delany in 1,973 to the jejunostomy longitudinal and transverse Witzel technique introduced into clinical practice, apparently reduced the rates of jejunostomy-related morbidity and mortality.<sup>34</sup>

**Figure 3.** Funnel plot (with pseudo 95% confidence limits) for comparing the risk ratio of the nasoenteric tube with the jejunostomy for total tube-related complications.

Stamm's jejunostomy technique, with the advantage of allowing repositioning when an obstruction happened,<sup>20</sup> was also mentioned.

Our meta-analysis has some limitations that must be taken into account, and the results may therefore be interpreted with some caution. Firstly, the relatively small number of cases may have affected the final results, possibly leading to a type II error, especially in the meta-analysis of length of hospital stay and time to resumption of normal oral intake. Secondly, the lack of blinding assessments, including double blinding (observers and patients) or single blinding (just patients) in all 5 included studies, mainly due to the ethical concerns and the nature of the interventions, increased the bias. Thirdly, some important details from the 2 retrospective cohort trials also increased the bias, setting the level of evidence at moderate. Fourthly, the discomfort experienced by patients in the nasopharynx and oropharynx caused by the nasoenteric tube may have forced surgeons to remove the tube at an early stage. The impact of this might have caused some bias but we could not properly assess it because in the majority of the studies the patient discomfort was not recorded. However, some studies stated that none of the patients reported any problems with having a tube in the nose for feeding purposes.<sup>19,21</sup>

### Conclusions

Our meta-analysis demonstrates that both routes are suitable for the provision of early postoperative enteral feeding. Each route is associated with some particular identified complications, but the tube-related complications are similar in totality in each route. Our conclusion from the meta-analysis is that, for patients undergoing major upper GI surgical procedures, a nasoenteric tube is more likely to be an effective route for early postoperative enteral feeding. However, more randomized controlled trials which are adequately powered and well-designed are required.

### AUTHOR DISCLOSURES

The authors declare that they have no conflicts of interest.

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