Duodenal versus gastric feeding in patients with traumatic brain injury: a systematic review and meta-analysis

Keywords
nursing, traumatic brain injury, care, enteral nutrition, duodenal feeding, gastric feeding

Abstract
Introduction
Enteral nutrition support is very important to improve the prognosis of patients with traumatic brain injury (TBI). We aimed to assess the role of duodenal versus gastric feeding in TBI patients, to provide insights into the clinical practice and nursing care.

Material and methods
We searched PubMed and other databases for RCTs on the role of duodenal versus gastric feeding in TBI patients up to Dec 15, 2021. Cochrane Collaborations risk of bias tool was used to assess the methodological quality and risk of bias of included studies. The RevMan 5.3 software was used for data analysis, risk rate (RR) or mean differences (MDs) with 95% confidence interval (CI) were calculated, and publication bias were evaluated by funnel plots.

Results
A total of 16 RCTs were included in this meta-analysis. Synthesized outcomes indicated that compared with gastric feeding, duodenal feeding is beneficial to reduce the incidence of pneumonia [RR =0.46, 95% CI (0.38, 0.57)], aspiration [RR =0.30, 95% CI (0.14, 0.63)], reflux esophagitis [RR =0.25, 95% CI (0.17, 0.38)], diarrhea [RR =0.58, 95% CI (0.44, 0.77)], abdominal distension [RR =0.41, 95% CI (0.25, 0.68)], no significant difference in the mortality [RR =0.85, 95% CI (0.50, 1.47), P=0.57] was found. Egger regression test indicated that there were no publication biases in the synthesized outcomes (all p>0.05).

Conclusions
Duodenal feeding may be superior to gastric feeding in the treatment and nursing care of TBI patients with less complications. Future studies with larger sample size and rigorous design are needed to further elucidate the effects and safety of duodenal versus gastric feeding.

Explanation letter
Dear editor:
Manuscript AMS-13922-2022-01R2 entitled "Duodenal versus gastric feeding in patients with traumatic brain injury: a systematic review and meta-analysis", which we submitted to Archives of Medical Science, has now been revised and resubmitted, the responses to the comments of the reviewers are organized one by one at the bottom of this letter.
We sincerely thank you for your tireless patience and reviewer’s wise comments on our manuscript, we have cited papers related to this topic published in the Archives of Medical Science in last 2-3 years(Ref 29, 33,38). Besides, we have marked our responses in red color to distinct from the reviewers’ suggestion, and marked the revised parts in the manuscript with red color, sincerely hope this will simplify your work.
If you have any questions, please do not hesitate to contact us.
Best regards,
Xu
Review 1:
I have reviewed the revised version of the manuscript "Duodenal versus gastric feeding in patients with traumatic brain injury: a meta-analysis and systematic review".

The manuscript has improved substantially and is almost ready for publication. I have only a couple of observations:

1. Since the first step to perform a meta-analysis is the literature review, it would be better a title like "Duodenal versus gastric feeding in patients with traumatic brain injury: a systematic review and meta-analysis".

   Thank you for your kind suggestions, we have revised the title to "Duodenal versus gastric feeding in patients with traumatic brain injury: systematic review and meta-analysis" as you kindly suggested.

2. The sentence "We searched PubMed et al databases for RCTs..." is not appropriate, since "et al." (the abbreviation of et alii) refers mostly to colleagues or persons. I would recommend change to "We searched PubMed and other databases for RCTs..."

   Thank you for your kind suggestion, we have revised it as you kindly suggested. Please see the revised abstract section.

Review 2:
Dear author
This study is a meta-analysis study of randomized controlled trials. It is a very good quality work, but there is an error in the conclusion. You have made most of the suggested fixes. However, the discussion of the study is definitely not suitable for a meta-analysis study. This study has the highest level of evidence, however, the discussion section was reported using low quality studies. A few meta-analysis studies were added due to the recommendations. The majority of studies used in the discussion are low-quality studies (such as cohort study, incomplete pilot RCT, another RCT not included in the study). Other meta-analysis studies should be reviewed and a discussion section should be rewritten.

Thank you for your discreet consideration and kind suggestions, we have reviewed the associated meta-analysis studies and revised the discussion section as you kindly suggested, please see the revised discussion section.

response_letter.docx
Title: Duodenal versus gastric feeding in patients with traumatic brain injury: a systematic review and meta-analysis

Running title: feeding care & TBI

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Abstract

Introduction: Enteral nutrition support is very important to improve the prognosis of patients with traumatic brain injury (TBI). We aimed to assess the role of duodenal versus gastric feeding in TBI patients, to provide insights into the clinical practice and nursing care.

Methods: We searched PubMed and other databases for RCTs on the role of duodenal versus gastric feeding in TBI patients up to Dec 15, 2021. Cochrane Collaborations risk of bias tool was used to assess the methodological quality and risk of bias of included studies. The RevMan 5.3 software was used for data analysis, risk rate (RR) or mean differences (MDs) with 95% confidence interval (CI) were calculated, and publication bias were evaluated by funnel plots.

Results: A total of 16 RCTs were included in this meta-analysis. Synthesized outcomes indicated that compared with gastric feeding, duodenal feeding is beneficial to reduce the incidence of pneumonia [RR =0.46, 95% CI (0.38, 0.57)], aspiration [RR =0.30, 95% CI (0.14, 0.63)], reflux esophagitis [RR =0.25, 95% CI (0.17, 0.38)], diarrhea [RR =0.58, 95% CI (0.44, 0.77)], abdominal distension [RR =0.41, 95% CI (0.25, 0.68)], no significant difference in the mortality [RR =0.85, 95% CI (0.50, 1.47), P=0.57] was found. Egger regression test indicated that there were no publication biases in the synthesized outcomes (all p>0.05).

Conclusions: Duodenal feeding may be superior to gastric feeding in the treatment and nursing care of TBI patients with less complications. Future studies with larger sample size and rigorous design are needed to further elucidate the effects and safety of duodenal versus gastric feeding.
**Keywords:** traumatic brain injury; duodenal feeding; gastric feeding; enteral nutrition; care; nursing

**Background**

Patients with traumatic brain injury (TBI) are in a state of high decomposition and high metabolism due to traumatic stress response, resulting in an imbalance of the body's nitrogen metabolism[1, 2]. The clinical manifestations include malnutrition, immune function damage, and eventually pulmonary infection[3]. Proper nutritional support can improve the nutritional status of patients with TBI, strengthen the immune function, and reduce the concurrent pulmonary infections[4]. Clinically, enteral nutrition support and parenteral nutrition support can be used, but parenteral nutrition support is not conducive to the maintenance of the physiological functions of the digestive tract, and the nutrients are relatively single[5]. Therefore, the nutritional support and care of TBI patients are of great significance to the prognosis of patients.

Enteral nutrition support has gradually become a common clinical nutritional support method. The clinical applications of enteral nutrition are mainly gastric and duodenal feeding. Previous studies[6, 7] have shown that patients treated by nasogastric tube are prone to gastric retention and gastroesophageal reflux, aspiration, pneumonia and many other complications, but its operation is relatively simple, the cost is relatively economical, and it is widely used in clinical practice[8]. Duodenal feeding has been reported to more safer yet it is more expensive[9]. Previous several studies[10-12] have focused on the use of duodenal versus gastric feeding for enteral nutrition support. However, the related results remain inconsistent. Understanding the advantages and disadvantages of duodenal versus gastric feeding is beneficial to provide evidence for the clinical nursing care and treatment of enteral nutrition. Therefore, we aimed to conduct a meta-analysis to
evaluate the risk ratio of complications associated with duodenal versus gastric feeding in TBI patients, to provide insights to the clinical management and nursing care of TBI.

**Methods**

We conducted and reported this systematic review and meta-analysis based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)[13].

**Literature search strategy**

Two authors independently searched PubMed, OVID, Cochrane Library, Clinical trials, China national knowledge infrastructure(CNKI) and Wanfang databases for RCTs on the role of duodenal versus gastric feeding for enteral nutrition support. The search time limit was from the establishment of the databases to Dec 15, 2021. The search terms used were as following: (“traumatic brain injury” OR “severe brain injury” OR “brain injury” OR “TBI”) AND (“enteral nutrition” OR “nasogastric tube” OR “nasal-intestinal tube” OR “duodenal feeding” OR “gastric feeding”).

**Inclusion and exclusion criteria**

The inclusion criteria for this study were as following: Study type: Randomized controlled trials (RCTs) on the effects and safety of duodenal versus gastric feeding in TBI patients. Research patients: TBI patients with Glasgow coma score (GCS) ≤ 8; Intervention measures: the comparison of duodenal versus gastric feeding in TBI patients. The intervention duration and frequency of enteral nutrition were not limited. Outcome indicators: The article reports related outcome indicators for complications including incidence of pneumonia, reflux esophagitis, aspiration, abdominal distension, diarrhea. We excluded duplicate publications and low-quality literature reports.

**Literature screening and data extraction**
Two researchers developed standardized data extraction tables based on inclusion, exclusion criteria, and literature content, and conducted literature screening. The data extracted by this meta-analysis included the study population (inclusion criteria and exclusion criteria, grouping methods and processes, sample size), sampling methods, intervention methods (intervention context, duration, and frequency), outcome indicators. In case of disagreement, it was solved through discussion or arbitration by the third researcher.

Quality evaluation

We adopted the Cochrane Collaborations risk of bias tool to assess the methodological quality and risk of bias of included studies. Any disagreements in the quality evaluation were solved by further discussion and consensus. The tool assessed seven specific domains including sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective outcome reporting and other issues. Every domain could be classified as low risk of bias, high risk of bias or unclear risk of bias in compliance with the judgment criteria.

Statistical analysis

All the statistical analyses were conducted with RevMan 5.3 software. All the collected data were double-checked by two authors. Data syntheses and interpretations were also conducted by two authors to ensure the accuracy of the results. All the binary outcomes were presented as Mantel–Haenszel risk rate (RR) with 95% confidence interval (CI). Continuous outcomes were showed as mean differences (MDs). We applied the fixed-effect model in the cases of homogeneity (P value of $\chi^2$ test > 0.10 and $I^2$ ≤ 50%), and we used random-effect model in the cases of obvious heterogeneity (P value of $\chi^2$ test > 0.10 and $I^2$ ≥ 50%). Publication bias were evaluated by funnel plots, and asymmetry
was assessed by conducting Egger regression test. \( P < 0.05 \) indicated that the differences were statistically different.

**Results**

**Search outcome**

The process for study inclusion is showed in Figure 1. The first search identified 179 potentially relevant studies. Of these identified reports, 18 studies were excluded as duplicates. After viewing the titles and abstracts of the 161 remaining studies, the full texts of 38 RCTs were retrieved. Among them, 22 studies were excluded with failure to meet the inclusion criteria. Finally, 16 RCTs\[10-12, 14-26\] were included in this meta-analysis.

![Figure 1 PRISMA flow diagram of RCT selection](image)

The characteristics and quality of included RCTs

Of the included 16 RCTs\[10-12, 14-26\], a total of 1294 TBI patients received enteral nutrition, specifically 641 patients accepted the gastric feeding and 653 patients accepted the duodena feeding.

The countries of included studies differed from Spain, USA, Canada, UK to China. The numbers of included participants among studies differed from 27 to 246. The detailed characteristics of included RCTs are presented in Table 1.

| Table 1 The characteristics of included RCTs |

The risk of bias graph of included RCTs is presented in Figure 2 and 3. All the included RCTs mentioned randomization, two RCTs\[14, 26\] did not provide a detailed description of the methods used to produce a random sequence. Only two studies\[19, 20\] reported the allocation blinding, and
all the other included RCTs did not report allocation blinding or the personnel blinding. No study reported the blinding of outcome assessment. No other selective reporting or other significant biases amongst the 16 included RCTs were found.

Figure 2 Risk of bias graph

Figure 3 Risk of bias summary

Primary outcome

**Incidence of pneumonia** 11 studies[10, 12, 14-17, 20, 22, 24-26] reported the incidence of pneumonia in the two groups of patients. There was no significant heterogeneity between the studies ($I^2=42\%, P=0.07$). We used a fixed-effect model for meta-analysis. The synthesized results showed that the incidence of pneumonia in TBI patients with duodena feeding was significantly lower than that of gastric feeding [$RR =0.46, 95\% CI (0.38, 0.57), P<0.001$, Figure 4A].

**Incidence of aspiration** 7 studies[10, 12, 18, 19, 23-25] reported the incidence of aspiration in the two groups of patients. There was no significant heterogeneity between the studies ($I^2= 0\%, P = 1.00$). We used a fixed-effect model for meta-analysis. The synthesized results showed that the incidence of aspiration in TBI patients with duodena feeding was significantly lower than that of gastric feeding [$RR =0.30, 95\% CI (0.14, 0.63), P=0.002$, Figure 4B].

**Incidence of reflux esophagitis** 9 studies[10, 12, 18, 19, 23-25] reported the incidence of reflux esophagitis in the two groups of patients. There was no significant heterogeneity between the studies
(I^2= 0%, P = 0.88). We used a fixed-effect model for meta-analysis. The synthesized results showed that the incidence of reflux esophagitis in TBI patients with duodena feeding was significantly lower than that of gastric feeding [RR =0.25, 95% CI (0.17, 0.38), P<0.001, Figure 4C].

Figure 4 The forest plots for synthesized outcomes

The incidence of diarrhea 6 studies[17, 20, 21, 23, 24, 26] reported the incidence of diarrhea in the two groups of patients. There was no significant heterogeneity between the studies (I^2= 0%, P = 0.98). We used a fixed-effect model for meta-analysis. The synthesized results showed that the incidence of diarrhea in TBI patients with duodena feeding was significantly lower than that of gastric feeding [RR =0.58, 95% CI (0.44, 0.77), P<0.001, Figure 5A].

The incidence of abdominal distension 7 studies[10, 11, 18, 19, 21, 23, 25] reported the incidence of abdominal distension in the two groups of patients. There was no significant heterogeneity between the studies (I^2= 0%, P = 0.75). We used a fixed-effect model for meta-analysis. The synthesized results showed that the incidence of abdominal distension in TBI patients with duodena feeding was significantly lower than that of gastric feeding [RR =0.41, 95% CI (0.25, 0.68), P<0.001, Figure 5B].

Mortality 9 studies[11, 12, 17-21, 23, 24, 26] reported the mortality in the two groups of patients. There was no significant heterogeneity between the studies (I^2= 0%, P = 1.00). We used a fixed-effect model for meta-analysis. The synthesized results showed that there was no significant difference in the mortality between two groups [RR =0.85, 95% CI (0.50, 1.47), P=0.57, Figure 5C].

Figure 5 The forest plots for synthesized outcomes
The funnel plots of synthesized outcomes were indicated in Figure 6, the dots were evenly distributed in the funnel plots, and Egger regression test indicated that there were no significant differences in the synthesized outcomes (all p>0.05).

![Figure 6 The funnel plots for synthesized outcomes](image)

Sensitivity analyses, which investigate the influence of one study on the overall risk estimate by removing one study in each turn, suggested that the overall risk estimates were not substantially changed by any single RCT.

**Discussion**

The acute stage of TBI is a critical stage for various secondary pathological changes. In this stage, patients cannot eat for a long time and their metabolic rate is significantly higher than that of normal status, which is likely to cause malnutrition, low immunity, and infection[27-29]. Therefore, reasonable nutritional support plays an important role in patients with TBI. Metabolic support is divided into enteral nutrition and parenteral nutrition. Most patients with TBI have impaired gastrointestinal function, and enteral nutrition is often used for nutrition support[30]. The path of enteral nutrition includes nasogastric tube, nasointestinal tube, pharyngostomy tube, and stomach fistula placement. Different enteral nutrition methods can produce different complications related to catheterization, such as reflux, vomiting and aspiration pneumonia, etc[31-33]. The results of this meta-analysis have found that duodena feeding is advantageous over gastric feeding for TBI patients with regards to that it reduces the incidence of pneumonia, aspiration, reflux esophagitis, abdominal
In various clinical diagnosis and treatment, gastric tube has been placed for the gastrointestinal pressure reduction, enteral nutrition support, and drug administration[34]. Swallowing dysfunction is very common in TBI patients[35]. It’s been reported that the long-term placement of gastric tube will have the risk of vocal paralysis. The emergence of nasal-intestinal tubes is to make up for the limitations of nasal stomach tubes. In the past, many studies have pointed out in some critical diseases that cannot withstand their stomach nutritional support or high reflux risk, such as esophageal fistula, gastric oysters, etc[36-38]. Besides, the naso-intestinal feeding would be beneficial on the aspect of pain relieving and patient comfort[39, 40]. Previous meta-analyses[36, 41] have showed that duodena feeding is beneficial to increase the quality of life for TBI patients, and it is an effective way to make nutritional support, which is consistent with our findings.

TBI lead to intracranial high pressure and hypothalamus autonomic nerve dysfunction, which is easy to cause gastrointestinal motility dysfunction, mainly manifested as the stomach and proximal duodenal dysfunction. With the amount of gastric retention increases, the gastric emptying time is prolonged, this is an important reason for the complications including reflux, and abdominal distention[42, 43]. The distal duodenal and null intestines are different from near-end duodenal and stomach, and the function is relatively small[44]. For critically ill patients, the pulmonary infection is associated with the refractive flow of the stomach contents[45]. Besides, it’s been reported that the nasal tube placement can increase the absorption of intestinal mucosal nutrients. Inhibit the reproduction of pathogens, and effectively avoid the occurrence of intestinal infections and flora shifts, is beneficial to the prevention of pulmonary infections[46].

Previous studies[47, 48] have shown that both duodenal and gastric feeding are beneficial to
improve the nutritional status of TBI patients, but the improvement effect of duodena feeding is better. Its main reasons may be that due to major traumatic stress, TBI patients always are in high metabolism, the body storage energy is reduced, the energy supplement is required, and the intestinal nutrient liquid used in clinical use is nutrients that can be directly absorbed, but the gastric feeding is injected into the stomach, and the stomach digestion is needed, which may damage some of the nutrients due to gastric acid damage[49]. Besides, the stomach nutrients also need to pass the nutrient solution to the small intestine by gastrointestinal creep[41, 50]. This process may lose some nutrients. The duodenal feeding directly slightly passes the stomach, directly absorb nutrients via the small intestine, avoiding the loss of nutrients, thereby having better effects for nutrition support[51].

Many limitations in this present meta-analysis must be considered. Firstly, there are differences in the timing of placement and the enteral nutrition support plans, and the sample sizes of included RCTs are not large. Secondly, there are some heterogeneity of synthesized outcomes, limited by sample size and collected data, we cannot perform the subgroup analysis. Thirdly, no included RCT has reported the blinding of outcome assessment. Therefore, large samples and multi-center RCTs in the future are needed to further evaluate the role of gastric and duodenal feeding in enteral nutrition, to provide reliable evidence to the clinical management and nursing care of TBI.

Conclusion

In conclusion, this present meta-analysis has found that compared with gastric feeding, duodenal feeding is more beneficial to reduce the incidence of pneumonia, aspiration, reflux esophagitis, abdominal distension and diarrhea, and no effect difference on the mortality has been found. However, at present, the naso-intestinal tube is less used in the clinical practice, the main reason is
that the success rate of naso-intestinal tube placement is much less than that of gastric tube[52].

Exploration should be strengthened and improve the insertion success of naso-intestinal tube.

List of abbreviations

TBI: traumatic brain injury
PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses
CNKI: China national knowledge infrastructure
GCS: Glasgow coma score
RR: risk rate
MD: mean difference

Declarations

Ethics approval and consent to participate
In this study, all methods were performed in accordance with the relevant guidelines and regulations.
Ethics approval and consent to participate is not necessary since our study is a systematic review.

Consent for publication
Not applicable.

Availability of data and materials
All data generated or analyzed during this study are included in this published article.

Competing interests
The authors declare that they have no competing interests.

Funding
This study has been founded by the Suzhou Medical Key Supporting Discipline Project (approval number: SZFCXK202109). The funder had no role in study design, data collection and analysis,
decision to publish, or preparation of the manuscript.

Author contributions

X Y, L S, Y X designed research; X Y, L S, L Z, M X, X Z, X M, Y X conducted research; X Y, L S, L Z analyzed data; X Y, L S, L Z wrote the first draft of manuscript; Y X had primary responsibility for final content. All authors read and approved the final manuscript.

Acknowledgments

None.

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**Figure legend**

- Figure 1 PRISMA flow diagram of RCT selection
- Figure 2 Risk of bias graph
- Figure 3 Risk of bias summary
- Figure 4 The forest plots for synthesized outcomes
- Figure 5 The forest plots for synthesized outcomes
- Figure 6 The funnel plots for synthesized outcomes
# Table 1 The characteristics of included RCTs

| Study ID         | Country | Sample size | Feeding intervention |
|------------------|---------|-------------|----------------------|
| Acosta-Escribano 2010[10] | Spain   | 50  54      | Inserted within 24 hours after admission. Both groups received 105 kJ/ (kg d) calories, 0.2 g N/ (kg d) |
| Chen 2013[20]     | China   | 90  85      | Inserted within 48 hours after admission. Enteral nutrition was given on the second and third day based on 60% and 80% of the calorie requirement, and after the fourth day, enteral nutrition was given 80% body needs. |
| Cheng 2007[23]    | China   | 16  18      | Inserted within 24 hours after TBI, gradually transition from 500mL/d on the first day to 1500mL/d, and the instillation time was not less than 16h per day |
| Graham 1989[14]   | USA     | 17  15      | Inserted within 36 hours after admission, infused at a rate of 70-100 mL/h |
| Hsu 2009[15]      | China   | 59  62      | The initial rate was 20mL/h, and the rate was increased by 20mL/h every 4h until the rate was stable after meeting the calorie demand of the body |
| Kortbeek 1999[16] | Canada  | 37  43      | Inserted within 72 hours after admission, the initial rate was 25mL/h, and the rate was increased by 25mL/h every 4h, until meet the body's calorie demand. |
| Li 2010[24]       | China   | 27  30      | Inserted within 24 hours after TBI, 500 mL feeding was given on the first day, gradually increasing to 1500 mL on the 3rd day, and maintained at 1500 mL/d. |
| Liu 2020[17]      | China   | 123 123     | Inserted within 48 hours after TBI, gave 1/3 of the required amount on the 1st day, 2/3 within 24 hours on the 2nd day, and give all the physiological requirements from the 4th day |
| Minard 2000[18]   | USA     | 12  15      | Inserted within 72 hours after admission, and both groups received 88kJ/(kg·d) calorie. |
| Mu 2010[12]       | China   | 30  30      | Inserted within 24 hours after TBI, 500 mL feeding was given on the first day, gradually increasing to 1500 mL on the 3rd day, and maintained at 1500 mL/d. |
| Tang 2017[26]     | China   | 45  45      | Inserted within 48 hours after TBI, and 50% of the total calories were started to increase by 1/4 daily to 100%. |
| Taylor 1999[22]   | UK      | 41  41      | Inserted within 72 hours after TBI, and both groups received 63kJ/h calories and gradually increased to the specified maximum rate. |
| Wang 2015[11]     | China   | 30  30      | Inserted within 24 hours after admission, the speed on the first day was 20mL/h, and the daily increase was 20mL/h to 100mL/h. |
| Zeng 2016[25]     | China   | 40  38      | Inserted within 24 hours after TBI, 20 mL/h on the first day, increasing by 20 mL/h every day to a stable rate. |
| Zhao             | China   | 24  24      | Inserted within 4 days after admission, instilled |
| Year   | Author | Country | Reference | Methodology |
|--------|--------|---------|-----------|-------------|
| 2007   | Zhao   | China   | 25 26     | Inserted within 24 hours after TBI. The actual daily supply of calories was basal energy metabolism ×1.3, and the ratio of non-protein calories to nitrogen was 130:1. On the first day, the supply of 1/3 of the total amount of the day would gradually increase, and the transition to total enteral nutrition would be within 3 to 5 days. |
| 2010   | Zhao   | China   | 19        | continuously at a rate of 40 to 60 mL/h, increasing by 25 mL/h every 8 hours until it reached 100 to 125 mL/h. |
Figure 1 PRISMA flow diagram of RCT selection
Figure 2 Risk of bias graph
Figure 3 Risk of bias summary
Figure 4 The forest plots for synthesized outcomes

A Forest plot for the incidence of pneumonia

| Study or Subgroup | Duodenal feeding Events | Gastric feeding Events | Total Events | Total | Weight | Risk Ratio M-H. Fixed, 95% CI |
|-------------------|-------------------------|------------------------|-------------|-------|--------|-------------------------------|
| Acosta-Escobano 2010 | 18 | 50 | 31 | 54 | 15.3% | 0.63 [0.41, 0.97] |
| Chen 2013 | 7 | 90 | 15 | 85 | 7.9% | 0.44 [0.19, 1.03] |
| Graham 1994 | 2 | 17 | 3 | 20 | 15.1% | 0.59 [0.11, 2.56] |
| Hsu 2009 | 3 | 59 | 3 | 62 | 15.5% | 1.00 [0.22, 5.00] |
| Korbseh 1999 | 10 | 37 | 18 | 43 | 8.5% | 0.83 [0.34, 2.02] |
| Li 2010 | 1 | 27 | 2 | 30 | 1.0% | 0.56 [0.05, 6.79] |
| Liu 2020 | 13 | 123 | 63 | 186 | 32.3% | 0.21 [0.12, 0.36] |
| Mu 2010 | 1 | 30 | 2 | 32 | 1.0% | 0.50 [0.05, 5.22] |
| Tang 2017 | 14 | 45 | 26 | 41 | 13.3% | 0.54 [0.33, 0.89] |
| Taylor 1999 | 18 | 41 | 26 | 44 | 13.9% | 0.60 [0.46, 1.05] |
| Zeng 2016 | 2 | 40 | 8 | 38 | 4.2% | 0.24 [0.05, 1.05] |

Total events 89 197

Heterogeneity: Chi² = 17.37, df = 10 (P = 0.07), I² = 42%
Test for overall effect: Z = 7.27 (P < 0.00001)

B Forest plot for the incidence of aspiration

| Study or Subgroup | Duodenal feeding Events | Gastric feeding Events | Total Events | Total | Weight | Risk Ratio M-H. Fixed, 95% CI |
|-------------------|-------------------------|------------------------|-------------|-------|--------|-------------------------------|
| Acosta-Escobano 2010 | 0 | 50 | 2 | 54 | 8.8% | 0.22 [0.01, 4.36] |
| Cheng 2007 | 0 | 16 | 2 | 18 | 8.6% | 0.22 [0.01, 4.34] |
| Li 2010 | 2 | 27 | 5 | 30 | 17.3% | 0.44 [0.09, 2.16] |
| Minard 2000 | 0 | 12 | 2 | 15 | 8.2% | 0.25 [0.01, 5.69] |
| Mu 2010 | 0 | 30 | 5 | 35 | 18.2% | 0.40 [0.08, 1.92] |
| Zeng 2010 | 2 | 40 | 6 | 38 | 29.9% | 0.24 [0.05, 1.06] |
| Zeng 2015 | 2 | 25 | 2 | 27 | 9.0% | 0.21 [0.01, 4.12] |

Total events 6 26

Heterogeneity: Chi² = 0.63, df = 6 (P = 1.00), I² = 0%
Test for overall effect: Z = 3.14 (P = 0.002)

C Forest plot for the incidence of reflux esophagitis

| Study or Subgroup | Duodenal feeding Events | Gastric feeding Events | Total Events | Total | Weight | Risk Ratio M-H. Fixed, 95% CI |
|-------------------|-------------------------|------------------------|-------------|-------|--------|-------------------------------|
| Chen 2013 | 7 | 90 | 16 | 106 | 16.0% | 0.41 [0.18, 0.95] |
| Cheng 2007 | 0 | 16 | 4 | 18 | 4.1% | 0.12 [0.01, 1.24] |
| Hsu 2009 | 1 | 59 | 8 | 67 | 7.8% | 0.13 [0.02, 1.02] |
| Li 2010 | 1 | 27 | 10 | 37 | 9.2% | 0.33 [0.10, 1.09] |
| Liu 2020 | 6 | 123 | 36 | 165 | 35.0% | 0.17 [0.07, 0.38] |
| Minard 2000 | 1 | 12 | 3 | 15 | 2.5% | 0.42 [0.05, 3.51] |
| Mu 2010 | 3 | 30 | 10 | 43 | 9.7% | 0.30 [0.06, 1.46] |
| Wang 2015 | 3 | 30 | 10 | 33 | 9.7% | 0.30 [0.09, 0.98] |
| Zeng 2016 | 1 | 40 | 6 | 46 | 6.0% | 0.16 [0.02, 1.25] |

Total events 25 103

Heterogeneity: Chi² = 3.75, df = 8 (P = 0.88), I² = 0%
Test for overall effect: Z = 6.64 (P < 0.00001)
Figure 5 The forest plots for synthesized outcomes
Figure 6 The funnel plots for synthesized outcomes