Review Article

Nasogastric tube versus postpyloric tube feeding for critical illness: A systematic review and meta-analysis

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Background and Objectives: Gastric tube feeding and postpyloric tube feeding are two common forms of enteral nutrition in critically ill patients. This study aimed to compare the efficacy and safety of gastric tube feeding with that of postpyloric tube feeding in critically ill patients. **Methods and Study Design:** PubMed, Embase, and Cochrane Library were systematically searched for eligible trials from their inception until March 2023. Relative risks (RRs) or weighted mean differences (WMDs) with 95% confidence intervals (CIs) were used to estimate categorical and continuous outcomes using the random-effects model. **Results:** Sixteen trials involving 1,329 critically ill patients were selected for the final meta-analysis. Overall, we noted that gastric tube feeding showed no significant difference from post-pyloric tube feeding in mortality (p = 0.891), whereas the risk of pneumonia was significantly increased in patients who received gastric tube feeding (RR: 1.45; p = 0.021). Furthermore, we noted that gastric tube feeding was associated with a shorter time required to start feeding (WMD: -11.05; p = 0.007). **Conclusions:** This research revealed that initiating feeding through the gastric tube required less time compared to postpyloric tube feeding. However, it was also associated with a heightened risk of pneumonia among critically ill patients.

Key Words: enteral nutrition, nutritional support, pneumonia, critical illness, systematic review

INTRODUCTION

Patients with critical illnesses, including severe acute illnesses such as sepsis, severe trauma, or major surgery, are admitted to the intensive care unit (ICU). The characteristics of critical illnesses result in malnutrition and are complicated by other diseases or dysfunctions. Moreover, the generalized inflammatory response could caused by this situation owing to the release of endogenous stress hormones and cytokines.[1] Unmet nutritional needs are significantly associated with energy-protein malnutrition and the breakdown of muscle mass.[1,2] Although clinical practice guidelines have addressed the importance of nutritional support for critically ill patients, only 40–60% of patients meet the recommended nutritional goals.[3,4] Studies have already found that malnutrition is associated with an increased risk of nosocomial infection and mortality in critically ill patients and that patients should receive enteral feeding as long as gastrointestinal function permits.[5-7]

Enteral nutrition (EN) is considered the preferred means of nutritional support owing to its enhancement of gut immune function, lower cost, and lower risk of septic complications.[8,9] The EN could be provided via various methods, and the two common forms are gastric tube feeding and small intestinal feeding.[10,11] The use of gastric tube feeding showed that slow gastric emptying could increase the residual gastric volume; in addition, the risk of bacterial colonization and aspiration pneumonia increased in critically ill patients. One study found that the use of a postpyloric tube could overcome the shortcomings of gastric tube feeding and was associated with high absorptive capacity.[12] The nutritional status of ICU patients is significantly associated with the clinical prognosis. However, whether the use of postpyloric tube feeding was associated with better prognosis for critically illness than gastric tube feeding postpyloric tube feeding remained unclear.

Several systematic reviews and meta-analyses have compared the efficacy and safety of gastric tubes with those of postpyloric tube feeding in critically ill patients.[13-15] Zhang et al.[13] identified 17 randomized controlled trials (RCTs) and found that postpyloric tube feeding was associated with higher proportions of estimated energy requirements and reduced residual gastric volume, whereas no significant differences were found between groups for the risk of mortality, new-onset pneumonia,

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and aspiration. Based on a Cochrane review,[14] RCTs were identified. The review indicated that postpyloric tube feeding was linked to a reduced risk of pneumonia and an enhanced delivery of nutrition.14 In another study by Liu et al.,[15] involving 41 investigations, post-pyloric tube feeding demonstrated an association with diminished risks of pulmonary aspiration, gastric reflux, pneumonia, or gastrointestinal complications, along with more optimal gastrointestinal nutrition. Nevertheless, it's important to highlight several limitations in prior research, including errors in study inclusion, data extraction, failure to include the latest relevant studies meeting the inclusion criteria, and lack of exploratory analysis results. Therefore, the current study was performed to update the efficacy and safety of gastric tube versus post-pyloric tube feeding in critically ill patients.

METHODS

Search strategy and selection criteria

The Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA) guidelines were used to guide the study and report this systematic review and meta-analysis.[16] Our study was retrospective registered in INPLASY platform and the registered number was INPLASY202380104. This meta-analysis included RCTs designed to compare the effectiveness and safety of gastric tube feeding with postpyloric tube feeding in critically ill patients. The publication language was restricted to English, while the publication status was not restricted. We systematically searched the PubMed, Embase, and Cochrane Library databases to identify eligible RCTs from their inception until March 2023 using the core search terms, “enteral nutrition” and “critically ill”. Details of the search strategy in each database are provided in the Supplementary Table 1. The websites of ClinicalTrials.gov (US NIH) were searched to identify unpublished trials that had already been completed but had not yet been published. We also manually searched the reference lists of relevant reviews and original articles to identify new eligible trials.

Two reviewers independently performed the literature search and study selection, and inconsistent results were resolved by mutual discussion until a consensus was reached. Studies that met the following inclusion criteria were included: (1) Patients: all patients with critical illness and admitted to the ICU; (2) Intervention and control: gastric tube feeding and postpyloric tube feeding; (3) Outcomes: the primary endpoints were mortality and pneumonia, while the secondary endpoints included abdominal distension, diarrhea, vomiting, bacteremia, constipation, gastrointestinal bleeding, high gastric residual volume, pulmonary aspiration, percentage of total nutrition delivered to the participant, time required to achieve the full nutritional target, time required to start feeding, length of ICU stay, length of hospital stay, and length of mechanical ventilation; and (4) Study design: the study had to have RCT design.

Data collection and quality assessment

The abstracted data were independently analyzed by two reviewers, and the collected information included the first author’s name, publication year, country, sample size, mean age, proportion of male participants, disease status, Acute Physiology and Chronic Health Evaluation, intervention, control, enteral feeding protocol, and investigated outcomes. The two reviewers independently assessed the methodological quality of the included trials using the risk of bias described by the Cochrane Collaboration, which was based on random sequence generation, allocation concealment, blinding of participants and personnel, blinding of outcome assessment, incomplete outcome data, selective reporting, and other bias.[17] Any disagreement between the reviewers regarding data collection and quality assessment was resolved by referring to the full text of the article.

Statistical analysis

The investigated outcomes were divided into categorical and continuous outcomes. The categorical outcomes were assessed using events/sample size per group, while the mean, standard deviation, and sample size per group were applied to assess continuous outcomes. The pooled relative risk (RR) or weighted mean difference (WMD) with 95% confidence intervals (CI) was calculated using a random-effects model, which considered the underlying variations across the included trials.[18,19] Heterogeneity among the included trials was assessed using I^2 and Q statistics, and significant heterogeneity was defined as $I^2 \geq 50.0\%$ or $p < 0.10$.[20,21] The robustness of the pooled conclusions for mortality and pneumonia was assessed using sensitivity analysis through the sequential removal of a single trial.[22] Subgroup analyses for mortality and pneumonia were performed according to country, age, the proportion of male participants, and postpyloric tube, and differences between subgroups were assessed using the interaction t-test.[23] Publication bias for mortality and pneumonia was assessed using funnel plots and Egger and Begg tests.[24,25] The reported *p* value for the pooled effect estimates was two-sided, and the inspection level was 0.05. The analyses in this study were performed using STATA software (version 14.0; Stata Corporation, College Station, TX, USA).

RESULTS

Literature search and study selection

The initial electronic search yielded 1,524 studies, of which 553 articles were removed because of duplicate titles. A total of 927 studies were removed because they reported irrelevant articles, and the remaining 44 studies were retrieved for full-text evaluation. Reviewing the reference lists of relevant studies yielded 13 studies, and detailed evaluations were performed for 57 studies; of these, 38 studies were removed owing to a lack of appropriate controls (n = 17), insufficient data (n = 16), and reviews (n = 5) (Supplementary Table 2). The remaining 16 RCTs were selected for meta-analysis,26-41 and the study selection process is presented in Figure 1.

Study characteristics

The baseline characteristics of the identified trials and the patients involved are summarized in Table 1. A total of 1,329 critically ill patients from 16 RCTs were identified, and the sample sizes ranged from 25 to 180. The mean age of the included patients ranged from 34.2 to 82.0

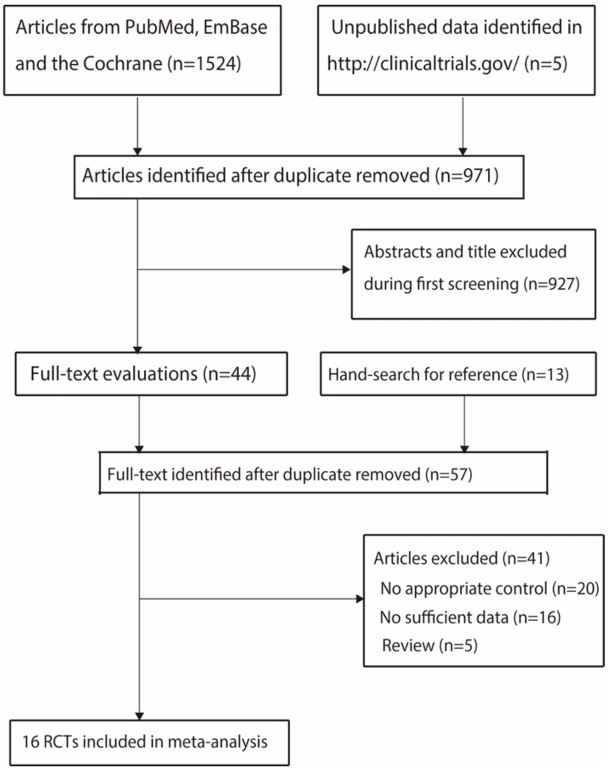

Figure 1. Details of the literature search and trial selection processes.

years, and the proportion of male participants ranged from 48.7% to 77.5%. Among the trials included, three employed a duodenal tube, eight utilized a jejunal tube, and the remaining five opted for a smaller intestinal tube for postpyloric tube feeding. The methodological quality of the included trials is presented in the Supplementary Table 3. Overall, the included trials reported a low risk of bias for random sequence generation, allocation concealment, incomplete outcome data, selective reporting, and other biases, whereas there was a high risk of bias for the blinding of participants, personnel, and outcome assessment.

Primary endpoints

Thirteen trials reported the effects of gastric tube versus postpyloric tube feeding on the risk of mortality. There was no significant difference between gastric tube and postpyloric tube feeding for the risk of mortality (RR: 0.99; 95% CI: 0.83–1.17; p = 0.891; Figure 2), and no evidence of heterogeneity across included trials was observed (I^2 = 0.0%; p = 0.872). Sensitivity analysis indicated that the pooled conclusion was stable after the sequential removal of individual trials (Supplementary Figure 1). The results of subgroup analyses were consistent with those of the overall analysis of all subsets (Table 2). No evidence of publication bias for mortality was observed (p value for Egger: 0.087; p value for Begg: 1.000; Supplementary Figure 2).

Twelve trials reported the effect of gastric tube feeding versus postpyloric tube feeding on the risk of pneumonia. The summary of the results indicated that gastric tube feeding was associated with an increased risk of pneumonia as compared with postpyloric tube feeding (RR: 1.45; 95% CI: 1.06–1.99; p = 0.021; Figure 3), and unimportant heterogeneity was observed among included trials (I^2 = 22.5%; p = 0.223). Considering the lower limit of 95%CI was approximately 1.00, the pooled conclusion was not stable after the sequential removal of a single trial (Supplementary Figure 3). Subgroup analyses found that gastric tube versus postpyloric tube feeding showed an elevated risk of pneumonia if patients' age was ≥ 55.0 years, the proportion of male participants was ≥ 70.0%, and used duodenal tube feeding as the control group. No other significant difference was observed between gastric tube versus postpyloric tube feeding for the risk of pneumonia in subgroup analyses (Table 2). There was no significant publication bias for pneumonia (p value for Egger: 0.059; p value for Begg: 0.150; Supplementary Figure 4).

Secondary endpoints

The breakdown of the number of trials reporting the effects of gastric tube versus postpyloric tube feeding on the risk of abdominal distension, diarrhea, and vomiting was 5, 11, and 7 trials, respectively (Figure 4). Overall, gastric tube feeding has no significant effects on the risk of abdominal distension (RR: 1.36; 95% CI: 0.99–1.88; p = 0.061), diarrhea (RR: 0.93; 95% CI: 0.74–1.18; p = 0.571), and vomiting (RR: 1.34; 95% CI: 0.85–2.12; p = 0.210). There was no evidence of heterogeneity for abdominal distension (I^2 = 0.0%; p = 0.478) or diarrhea (I^2 = 0.0%; p = 0.912), whereas significant heterogeneity was observed for vomiting (I^2 = 47.3%; p = 0.077).

The breakdown of the number of trials reporting the effects of gastric tube versus postpyloric tube feeding on the risk of bacteremia, constipation, gastrointestinal bleeding, high gastric residual volume, and pulmonary aspiration was three, two, four, two, and four trials, respectively (Figure 5). There were no significant differences between gastric tube and postpyloric tube feeding for the risk of bacteremia (RR: 0.94; 95% CI: 0.45–1.97;

Table 1. The baseline characteristics of included studies and involved patients

Study	Country	Sample size	Age (years)	Male (%)	Disease status	APACHE	Intervention	Control
Montecalvo 1992[26]	USA	38 (19/19)	47.7 (44.8/50.5)	60.5	Critical patients	II: 16.9	Gastric	Jejunal
Kortbeek 1999[27]	Canada	80 (43/37)	34.2 (34.7/33.6)	77.5	Ventilated blunt trauma	II: 18.0	Gastric	Duodenal
Kearns 2000[28]	USA	44 (23/21)	54.4 (49.0/54.0)	68.2	Critical patients	II: 21.0	Gastric	Small intestinal
Day 2001[29]	USA	25 (11/14)	56.7 (60.6/53.6)	56.0	Neurological disease	III: 47.7	Gastric	Duodenal
Montejo 2002[30]	Spain	101 (51/50)	58.0 (59.0/57.0)	70.3	Critical patients	II: 18.0	Gastric	Jejunal
Davies 2002[31]	Australia	73 (39/34)	54.5 (53.5/55.7)	68.5	Critical patients	II: 18.2	Gastric	Jejunal
Neumann 2002[32]	USA	60 (30/30)	58.9 (58.1/59.6)	50.0	Critical patients	NA	Gastric	Small intestinal
Eatock 2005[33]	Scotland	49 (27/22)	60.8 (64.0/58.0)	53.1	Severe acute pancreatitis	NA	Gastric	Jejunal
White 2009[34]	Australia	104 (54/50)	52.1 (54.0/50.0)	50.0	Critical patients	II: 27.1	Gastric	Small intestinal
Hsu 2009[35]	China	121 (62/59)	68.9 (62/59)	70.2	Critical patients	II: 20.4	Gastric	Duodenal
Davies 2012[36]	Australia	180 (89/91)	52.5 (54.0/51.0)	73.9	Critical patients	II: 20.0	Gastric	Jejunal
Singh 2012[37]	India	78 (39/39)	39.4 (39.1/39.7)	67.9	Severe acute pancreatitis	II: 8.3	Gastric	Jejunal
Friedman 2015[38]	Brazil	115 (61/54)	61.4 (60.0/63.0)	48.7	Critical patients	II: 22.0	Gastric	Jejunal
Wan 2015[39]	China	70 (35/35)	52.4 (52.0/52.7)	68.6	Critical patients	NA	Gastric	Jejunal
Taylor 2016[40]	UK	50 (25/25)	52.0 (51.0/53.0)	76.0	Critical patients	II: 19.0	Gastric	Small intestinal
Zhu 2018[41]	China	141 (71/70)	82.0 (82.0/82.0)	62.4	Critical patients	II: 27.9	Gastric	Small intestinal

Study	Enteral feeding protocol	Follow-up duration
Montecalvo 1992[26]	Began at 25 mL/h/d for the first 24 h and then were increased by 24 mL/h/d until the protein/caloric intake goals were reached	42.0 days
Kortbeek 1999[27]	Starting at 25 mL/h and increasing the rate by 25 mL/h every 4 h until the volume required to meet caloric support was achieved	28.0 days
Kearns 2000[28]	Infusion was stopped for residuals >150 mL, and once the residual was < 150 mL, feeding resumed	42.0 days
Day 2001[29]	The Harris Benedict equation with activity and stress factors were used to calculate the total energy and protein requirement	10.0 days
Montejo 2002[30]	Feedings were started in the first 36 h after admission and delivered continuously to achieve half of the estimated caloric needs in 24 h	16.0 days
Davies 2002[31]	At a rate of 20 mL/hr and increased by 20 mL/h every 4 hrs until the target nutrition rate was reached	12.0 days
Neumann 2002[32]	Starting at 30 mL/h, then advanced to a patient-specific goal rate by 10 mL/h every 6 h	14.0 days
Eatock 2005[33]	Rate of 30 mL/h increasing to 100 mL/h over 24-48 h. The caloric target was 2,000 kcal per day	16.0 days
White 2009[34]	Enteral feeds were commenced at 40 mL/h. The nasogastric tube was aspirated every 4 h. If the gastric residual was less than 200 mL after 4 h, the rate was increased to the recommended target rate	5.0 days
Hsu 2009[35]	starting at 20 mL/h. The rate was increased by 20 mL/h every 4 h until the patient's goal rate was achieved	34.0 days
Davies 2012[36]	The initial commencement rate and advancement rate toward the hourly target were determined by each hospital's standard practice, but the aim was to meet estimated energy requirements as soon as possible by following a locally developed evidence-based algorithm	22.0 days
Singh 2012[37]	Nutrient goal (25 kcal/kg per day) in 3 to 4 days	18.0 days
Friedman 2015[38]	The individual energy needs and the formulation of enteral nutrition were determined by clinical staff (doctors and nutritionists)	28.0 days
Wan 2015[39]	Rate of 30 mL/h increasing to 100 mL/h over 24-72 h, the caloric target was set at 25 kcal/kg of ideal bodyweight/day for women and 30 kcal/kg of ideal bodyweight/day for men	14.0 days
Taylor 2016[40]	Increased from 40 mL feed/h or current rate to full rate whenever tolerated	5.0 days
Zhu 2018[41]	Energy goals were set at 25 kcal per kg of ideal body weight per day, and the protein target was 1.2-2.0 g per kg of ideal body weight per day	7.0 days

APACHE II: Acute Physiology and Chronic Health Evaluation II; NA: not available

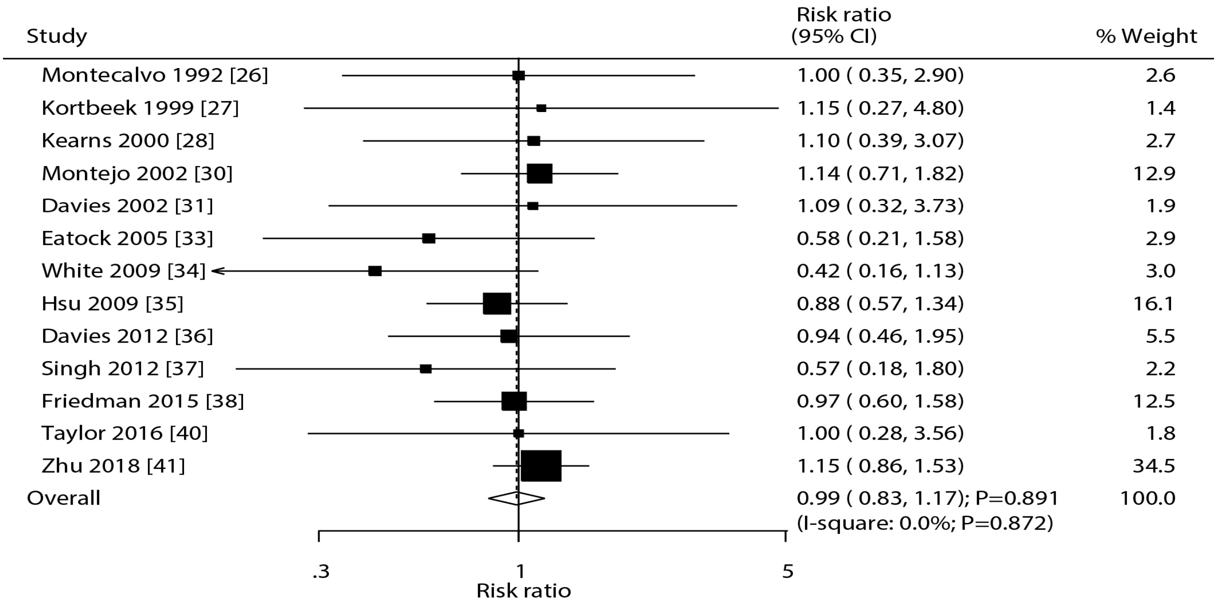

Figure 2. Gastric tube feeding versus postpyloric tube feeding on the risk of mortality.

Table 2. Subgroup analyses for mortality and pneumonia

Outcomes, factors and subgroup	No of trials	RR and 95%CI	*p* value	I^2 (%)	Q statistic	*p* value between subgroups
Mortality						
Country						0.608
Eastern	3	1.02 (0.79-1.31)	0.903	7.8	0.338	
Western	10	0.95 (0.74-1.21)	0.668	0.0	0.887	
Age (years)						0.320
≥ 55.0	5	1.03 (0.85-1.25)	0.761	0.0	0.633	
< 55.0	8	0.85 (0.58-1.23)	0.376	0.0	0.864	
Male (%)						1.000
≥ 70.0	5	0.99 (0.75-1.30)	0.916	0.0	0.954	
< 70.0	8	0.99 (0.80-1.23)	0.928	0.0	0.511	
Postpyloric tube						0.809
Duodenal	2	0.90 (0.60-1.35)	0.604	0.0	0.723	
Jejunal	7	0.96 (0.73-1.25)	0.765	0.0	0.890	
Small intestinal	4	0.97 (0.64-1.47)	0.875	23.6	0.270	
Pneumonia						
Country						0.391
Eastern	4	2.07 (0.84-5.06)	0.113	68.8	0.022	
Western	8	1.28 (0.94-1.75)	0.113	0.0	0.800	
Age (years)						0.195
≥ 55.0	4	1.83 (1.11-3.02)	0.017	25.1	0.261	
< 55.0	8	1.23 (0.82-1.85)	0.311	17.6	0.291	
Male (%)						1.000
≥ 70.0	5	1.39 (1.02-1.89)	0.036	0.0	0.474	
< 70.0	7	1.70 (0.79-3.64)	0.173	45.3	0.089	
Postpyloric tube						0.190
Duodenal	3	1.94 (1.16-3.27)	0.012	0.0	0.407	
Jejunal	6	1.19 (0.76-1.86)	0.450	27.3	0.230	
Small intestinal	3	1.69 (0.87-3.28)	0.125	8.4	0.336	

p = 0.871), constipation (RR: 1.39; 95% CI: 0.70–2.78; p = 0.349), gastrointestinal bleeding (RR: 0.67; 95% CI: 0.33–1.36; p = 0.269), high gastric residual volume (RR: 3.77; 95% CI: 0.07–215.21; p = 0.520), and pulmonary aspiration (RR: 0.91; 95% CI: 0.44–1.88; p = 0.792). No significant heterogeneity was observed for bacteremia (I2 = 0.0%; p = 0.636), constipation (I^2 = 0.0%; p = 0.946), gastrointestinal bleeding (I^2 = 36.9%; p = 0.190), and pulmonary aspiration (I^2 = 0.0%; p = 0.498), while substantial heterogeneity was observed for high gastric residual volume (I^2 = 92.1%; p <0.001).

The breakdown of the number of trials reporting the effects of gastric tube versus postpyloric tube feeding on the percentage of total nutrition delivered to the participant, time required to achieve the full nutritional target, and time required to start feeding was six, four, and five trials, respectively (Figure 6). There were no significant differences between gastric tube and postpyloric tube feeding for a percentage of total nutrition delivered to the

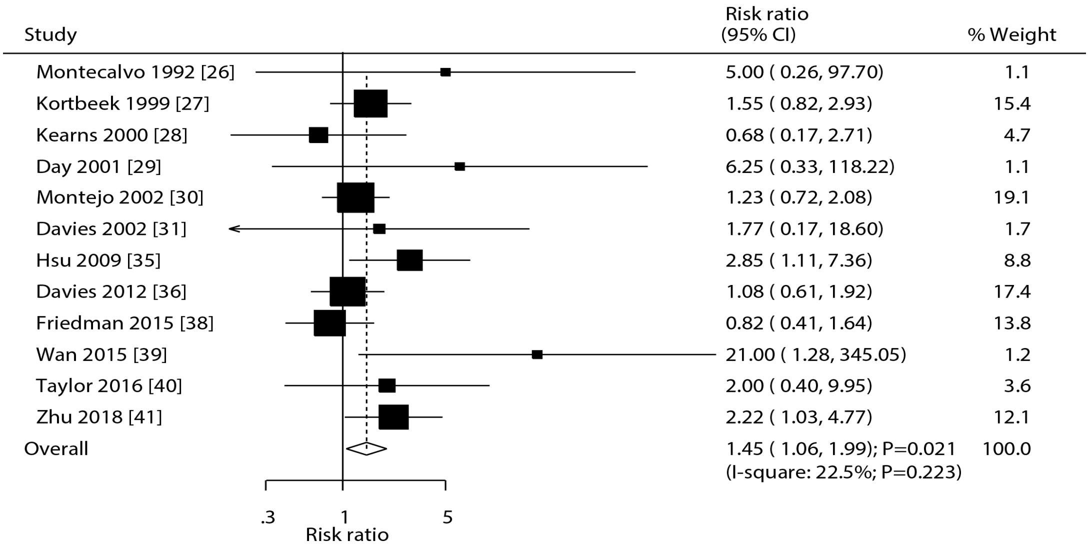

Figure 3. Gastric tube feeding versus postpyloric tube feeding on the risk of pneumonia.

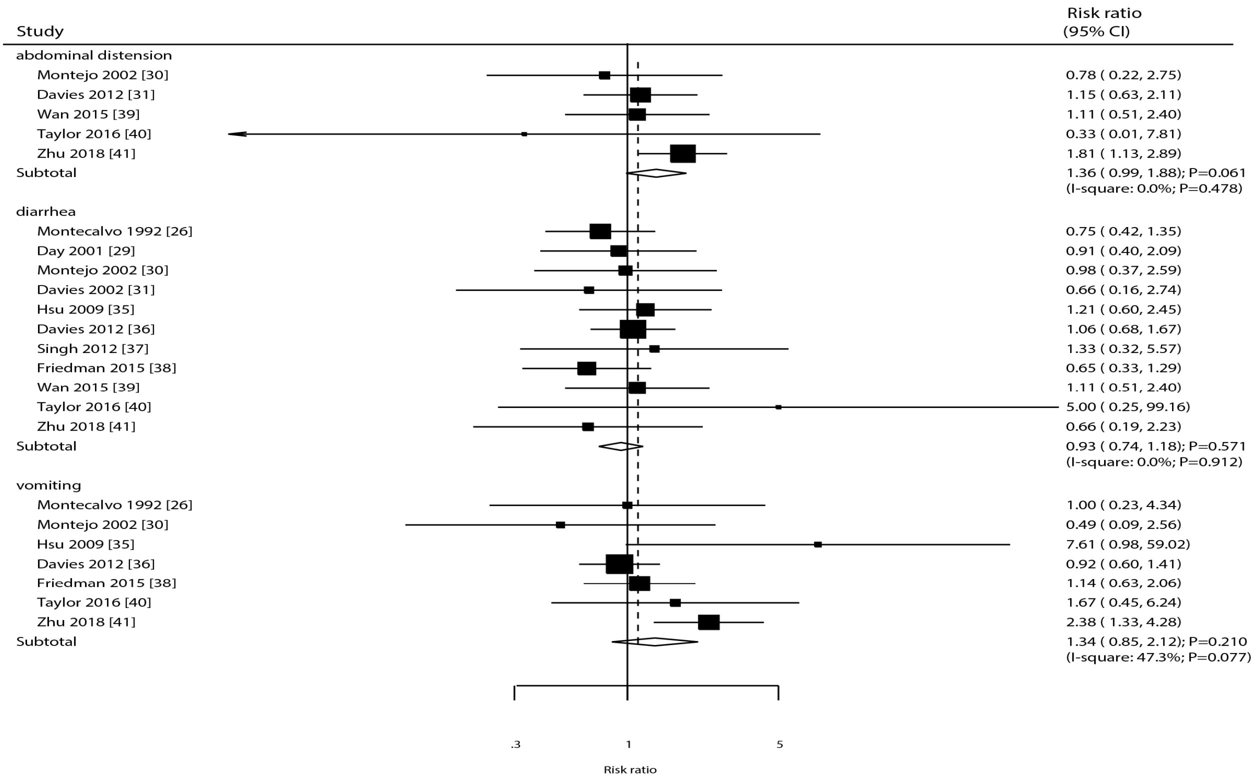

Figure 4. Gastric tube feeding versus postpyloric tube feeding on the risk of abdominal distension, diarrhea, and vomiting.

participant (WMD: –7.62; 95% CI: –15.49–0.26; *p* = 0.058), and time required to achieve the full nutritional target (WMD: –1.28; 95% CI: –6.51–3.95; *p* = 0.631), while gastric tube feeding was associated with shorter time required to start feeding as compared with postpyloric tube feeding (WMD: –11.05; 95% CI: –19.05 to –3.05; *p* = 0.007). We noted substantial heterogeneity across the included trials in the percentage of total nutrition delivered to the participants (I^2 = 91.5%; *p* <0.001), the time required to achieve the full nutritional target (I^2 = 85.1%; *p* <0.001), and the time required to start feeding (I^2 = 90.0%; *p* <0.001).

The breakdown of the number of trials reporting the effects of gastric tube versus postpyloric tube feeding on the length of ICU stay, length of hospital stay, and length of mechanical ventilation was 10, 7, and 8 trials, respectively (Figure 7). No significant differences between gastric tube and postpyloric tube feeding for length of ICU stay (WMD: 0.66; 95% CI: -0.96–2.28; *p* = 0.423), length of hospital stay (WMD: 1.63; 95% CI: -0.65–3.91; *p* = 0.162), and length of mechanical ventilation (WMD: 1.01; 95% CI: -0.89–2.91; *p* = 0.296) were observed.

DISCUSSION

The use of an enteral route for EN can reduce gastric motility, which is responsible for limited caloric intake and is associated with an increased risk of aspiration pneumonia. Postpyloric tube feeding, which delivers feed to the

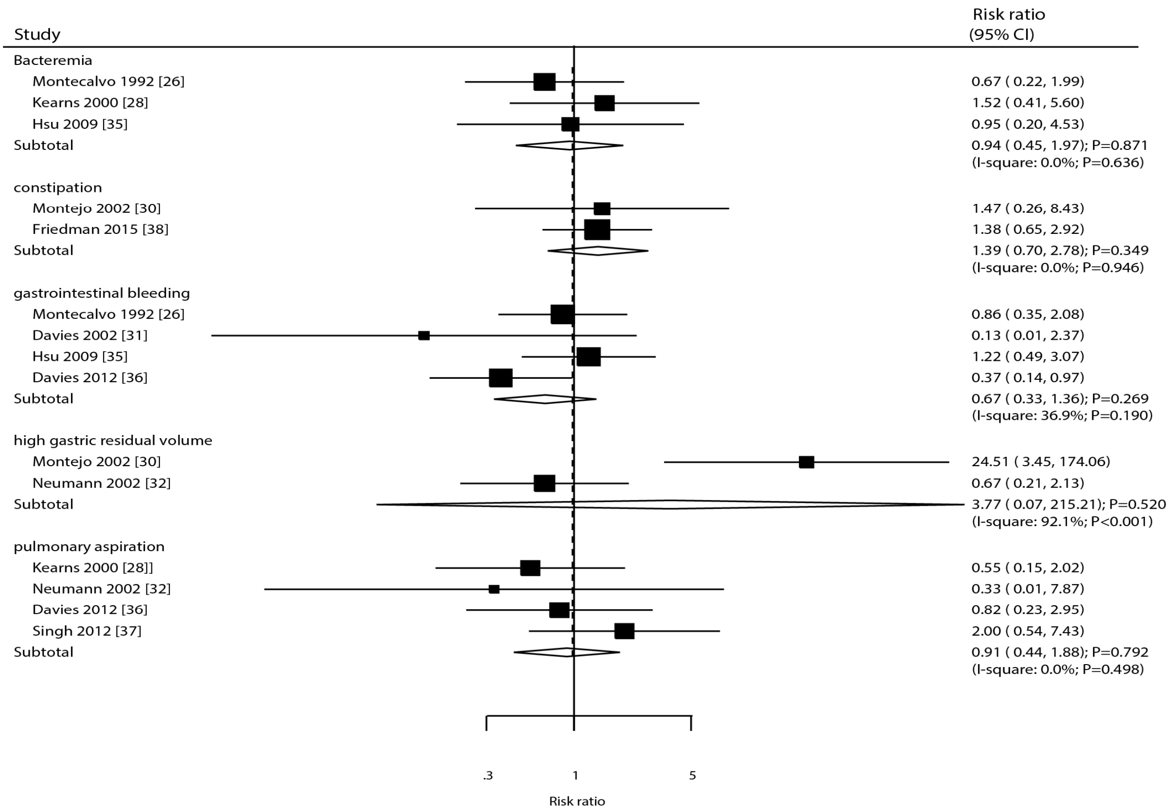

Figure 5. Gastric tube feeding versus postpyloric tube feeding on the risk of bacteremia, constipation, gastrointestinal bleeding, high gastric residual volume, and pulmonary aspiration.

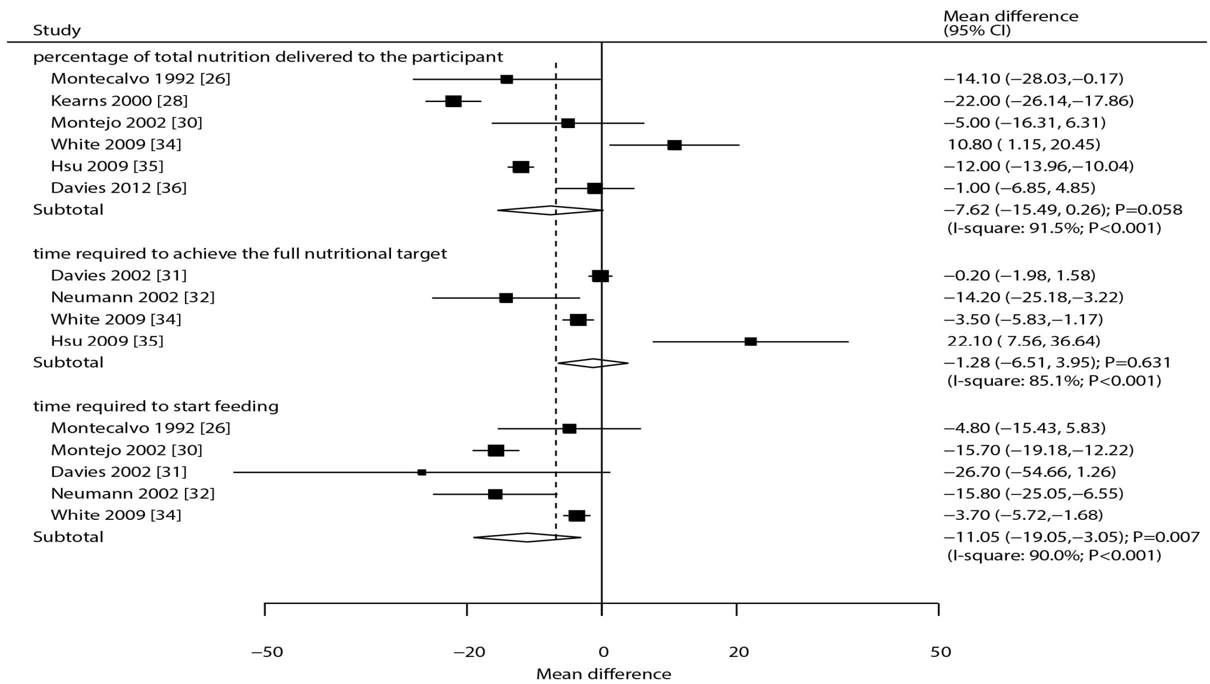

Figure 6. Gastric tube feeding versus postpyloric tube feeding on percentage of total nutrition delivered to the participant, time required to achieve the full nutritional target, and time required to start feeding.

duodenum or jejunum, could overcome these shortcomings. This comprehensive, quantitative study was performed to compare the efficacy and safety of gastric tubes with postpyloric tube feeding for critically ill patients, and a total of 1,329 critically ill patients across a broad range of patients' characteristics, especially disease status, from 16 RCTs were included. This study found that gastric tube feeding although, allowing for an earlier start time for feeding, significantly increased the risk of pneumonia compared with post-pyloric tube feeding, whereas there were no significant differences between the groups in terms of mortality, abdominal distension, diarrhea, vomiting, bacteremia, constipation, gastrointestinal bleeding, high gastric residual volume, pulmonary aspiration, percentage of total nutrition delivered to the participant, time required to achieve the full nutritional target, length

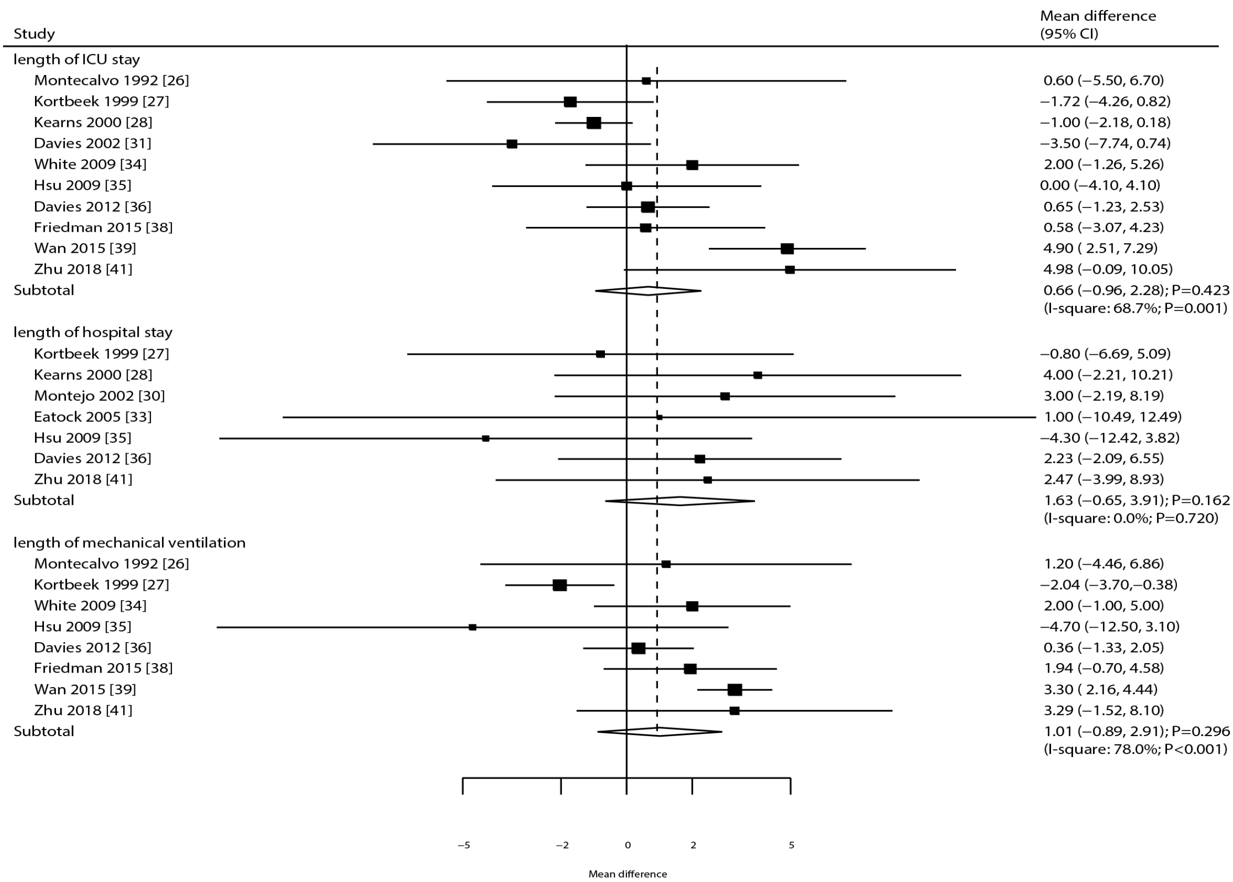

Figure 7. Gastric tube feeding versus postpyloric tube feeding on length of ICU stay, length of hospital stays, and length of mechanical ventilation. ICU, intensive care unit.

of ICU stay, length of hospital stay, and length of mechanical ventilation.

Our study reported similar effects of gastric tube and postpyloric tube feeding on the risk of mortality, which is consistent with prior meta-analyses.[13-15] Moreover, the results of the sensitivity and subgroup analyses indicated no significant difference between gastric and postpyloric tube feeding on the risk of mortality, and all included trials reported similar conclusions. The potential reason for this could be that these trials were designed with nutritional and safety outcomes as the primary outcomes, and the sample size was not sufficient to detect potential differences in the risk of mortality between groups.

Our study found that gastric tube feeding was associated with an increased risk of pneumonia compared to postpyloric tube feeding, which was consistent with previous meta-analyses.[14,15] Studies have illustrated that inhibited gastrointestinal motility, reduced gastric emptying, a pressure drop at the gastroesophageal junction, and abnormal esophageal motility are significantly associated with the progression of pneumonia.[42,43] The end of the tube in postpyloric tube feeding was placed post-pylorus, which was associated with reduced gastric residual volume and inhibition of gastrointestinal peristalsis. Moreover, postpyloric tube feeding can prevent nutrients from flowing back into the stomach, thereby reducing the risk of aspiration. Furthermore, subgroup analyses found an increased risk of pneumonia in patients receiving gastric tube feeding, when patients' age was ≥ 55.0 years, the proportion of male participants was ≥ 70.0%, and used duodenal tube feeding as control. These results suggest that differences are mainly observed in patients at high risk for pneumonia.

Our study did not find significant differences between gastric tube and postpyloric tube feeding for the risk of gastrointestinal complications, which is inconsistent with a previous study.15 The potential reasons for these differences could be explained by the following: (1) the incidence of gastrointestinal complications could be affected by the dosage, type, and dropping rate of the nutrient solution; (2) the disease status varied between gastric tube and postpyloric tube feeding and could be affected by the progression of gastrointestinal complications; and (3) the incidence of most specific gastrointestinal complications was lower, and a smaller number of trials reported these outcomes; thus, the power was not sufficient to detect potential differences between the groups. In addition, although the use of postpyloric tube feeding could provide more nutrition and reduce the risk of complications, there were no significant differences between the groups in terms of the lengths of ICU stay, hospital stay, and mechanical ventilation.

This study has several limitations. First, most of the included trials reported a high risk of bias for blinding of participants, personnel, and outcome assessment. Second, substantial heterogeneity was observed for several outcomes, particularly the continuous outcomes. Third, the severity of critically illness and disease status differed across the included trials, which could have affected the prognosis of critically ill patients. Fourth, meta-analyses based on published articles have inherent limitations, including inevitable publication bias and restricted detailed analyses.

In conclusions, our study found that gastric tube feeding required a shorter time to start feeding than postpyloric tube feeding but related to a significantly increased risk of pneumonia in critically ill patients. Therefore, post-pyloric tube feeding should be applied for critically ill patients to prevent the risk of pneumonia in clinical practice.

CONFLICT OF INTEREST AND FUNDING DISCLOSURE

The authors declare no competing interests.

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Supplementary Tables and Figures

Supplementary Table 1. Search strategy in PubMed, EmBase, and the Cochrane Library

Search strategy in PubMed

#1: (enteral nutrition OR duodenostomy OR gastrostomy OR jejunostomy OR intubation, gastrointestinal) [MeSH]

#2: (duodenostom* OR gastrostom* OR PEJ OR PEG OR jejunostom* OR jtube* OR g-tube* OR ng-tube* OR nj-tube*):[ab,ti,kw] OR ((nutrition* OR feed* OR fed OR tube* OR intub*)

#3: #1 OR #2

#4: (nasogastr* OR duoden* OR gastr* OR nasoduoden* OR jejun* OR nasojejun* OR post-pylor* OR bowel* OR trans-pylor* OR intestine* OR gavage OR orogastric OR stomach OR nasoenter*):[ab, ti, kw]).

#5: #3 AND #4

#6: (intensive care OR critical care OR critical illness OR pneumonia OR burn OR respiratory failure OR craniocerebral trauma OR burns OR pancreatitis)

#7: (intensive care OR ICU OR critical* ill* OR critical patients OR critical* care OR pneumonia OR burn OR pancreatitis OR trauma OR injur*):[ab, ti, kw].

#8: #6 AND #7

#9: #5 AND #8

Search strategy in EmBase

1. enteric feeding/ or artificial feeding/ or nose feeding/ or nasogastric tube/ or stomach tube/ or stomach intubation/ or gastrostomy/ or percutaneous endoscopic gastrostomy/ or duodenum intubation/ or duodenostomy/ or jejunostomy/ or (g-tube* or ng-tube* or gastrostom* or PEG or duodenostom* or jejunostom* or PEJ or j-tube* or nj-tube*).ti,ab. or ((nutrition* or fed or feed* or tube* or intub*) adj5 (gastr* or nasogastr* or stomach or duoden* or nasoduoden* or jejun* or nasojejun* or bowel* or intestine* or post?pylor* or trans? pylor* or nasoenter* or orogastric or gavage)).ab,ti.

2. exp pancreatitis/ or injury/ or burn/ or "head and neck injury"/ or multiple trauma/ or critical illness/ or intensive care/ or intensive care unit/ or pneumonia/ or aspiration pneumonia/ or (pneumonia* or critical* ill* or critical* care or intensive care or ICU or burn* or trauma* or head injur* or pancreatitis).ab,ti.

3. 1 and 2

4. (infant* or child* or adolescent*).af.

5. (adult* or aged).af.

6. 3 not (4 not (5 and 4))

7. (placebo.sh. or controlled study.ab. or random*.ti,ab. or trial*.ti,ab.) not (animals not (humans and animals)).sh.

8. 6 and 7

Search strategy in Cochrane library

#1 MeSH descriptor Enteral Nutrition explode all trees

#2 MeSH descriptor Gastrostomy explode all trees

#3 MeSH descriptor Duodenostomy explode all trees

#4 MeSH descriptor Jejunostomy explode all trees

#5 MeSH descriptor Intubation, Gastrointestinal explode all trees

#6 (gastrostom* or duodenostom* or jejunostom* or PEG or g-tube* or ng-tube* or j-tube* or nj-tube* or PEJ):ab,ti

#7 ((nutrition* or fed or feed* or tube* or intub*) near (gastr* or nasogastr* or stomach or duoden* or nasoduoden* or jejun* or nasojejun* or bowel* or intestine* or post?pylor* or trans?pylor* or nasoenter* or orogastric or gavage)):ab,ti

#8 (#1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7)

#9 MeSH descriptor Pneumonia explode all trees

#10 MeSH descriptor Pneumonia, Aspiration explode all trees

#11 MeSH descriptor Intensive Care Units explode all trees

#12 MeSH descriptor Burn Units explode all trees

#13 MeSH descriptor Respiratory Care Units explode all trees

#14 MeSH descriptor Critical Care explode all trees

#15 MeSH descriptor Intensive Care explode all trees

#16 MeSH descriptor Critical Illness explode all trees

#17 MeSH descriptor Craniocerebral Trauma explode all trees

#18 MeSH descriptor Burns explode all trees

Supplementary Table 1. Search strategy in PubMed, EmBase, and the Cochrane Library (cont.)

Search strategy in Cochrane library
#19 MeSH descriptor Wounds and Injuries explode all trees
#20 MeSH descriptor Pancreatitis explode all trees
#21 (pneumonia* or critical* ill* or critical* care or intensive care or ICU or burn* or trauma* or head injur* or pancreatitis):ti,ab
#22 (#9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17 OR #18 OR #19 OR #20 OR #21)
#23 (#8 AND #22)
#24 (infant* or child* or adolescent*)
#25 (adult* or aged)
#26 (#24 AND NOT (#25 AND #24))
#27 (#23 AND NOT #26)

Supplementary Table 2. The full bibliography list of the 38 excluded articles

Lack of appropriate controls

1. Landais, M., Nay, M. A., Auchabie, J., Hubert, N., Frerou, A., Yehia, A. et al.Continued enteral nutrition until extubation compared with fasting before extubation in patients in the intensive care unit: an open-label, cluster-randomised, parallel-group, non-inferiority trial. Lancet Respir Med. 2023;11:319-28. doi: 10.1016/S2213-2600(22)00413-1.

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Supplementary Table 2. The full bibliography list of the 38 excluded articles (cont.)

Insufficient data

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Reviews

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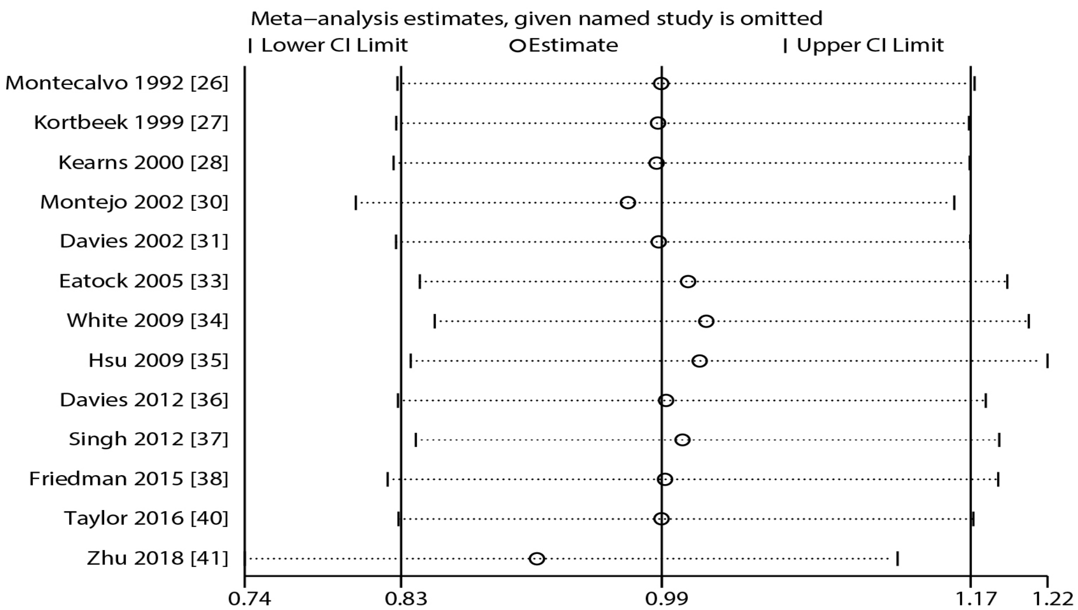
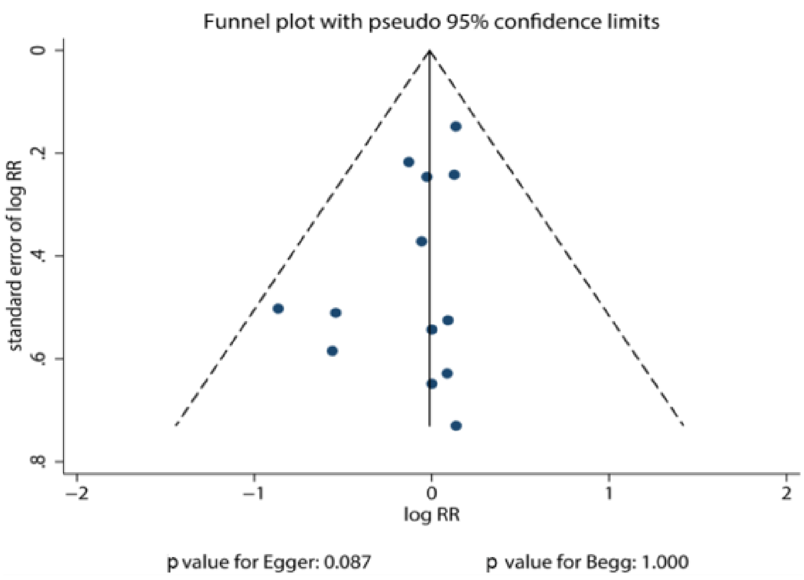
Supplementary Table 3. Quality assessment of included trials

Study	Random sequence generation	Allocation concealment	Blinding of participants and personnel	Blinding of outcome assessment
Montecalvo 1992[26]	Low	Unclear	High	Low
Kortbeek 1999[27]	Low	Low	High	High
Kearns 2000[28]	Low	Low	Low	Low
Day 2001[29]	Low	Low	High	Low
Montejo 2002[30]	Low	Unclear	High	High
Davies 2002[31]	Unclear	Low	High	High
Neumann 2002[32]	Low	Low	High	Low
Eatock 2005[33]	Low	Low	High	Unclear
White 2009[34]	Low	Low	High	High
Hsu 2009[35]	Low	Low	Low	Low
Davies 2012[36]	Low	Low	High	High
Singh 2012[37]	Low	Low	High	Low
Friedman 2015[38]	Unclear	Low	Unclear	Unclear
Wan 2015[39]	Low	Low	High	Unclear
Taylor 2016[40]	Low	Low	High	High
Zhu 2018[41]	Low	Low	High	Low

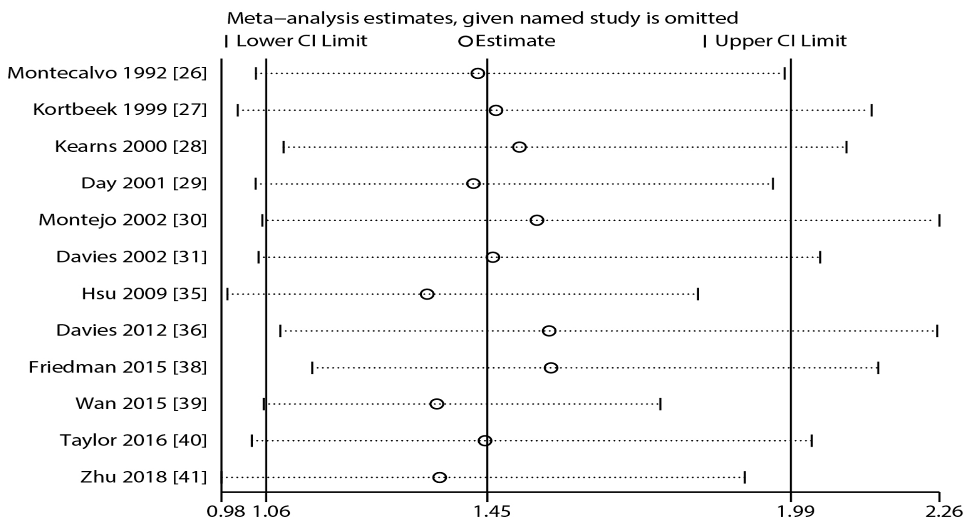
Study	Incomplete outcome data	Selective reporting	Other bias
Montecalvo 1992[26]	Low	Low	Unclear
Kortbeek 1999[27]	Low	Low	Low
Kearns 2000[28]	Low	Low	Low
Day 2001[29]	Low	Low	Low
Montejo 2002[30]	Low	Low	Low
Davies 2002[31]	Low	Low	Low
Neumann 2002[32]	Low	Low	Low
Eatock 2005[33]	High	Low	Low
White 2009[34]	Low	Low	Unclear
Hsu 2009[35]	Low	Low	Low
Davies 2012[36]	Low	Low	Low
Singh 2012[37]	Low	Low	Low
Friedman 2015[38]	Low	Low	Unclear
Wan 2015[39]	Low	Low	Low
Taylor 2016[40]	Low	Low	Low
Zhu 2018[41]	Low	Low	Unclear



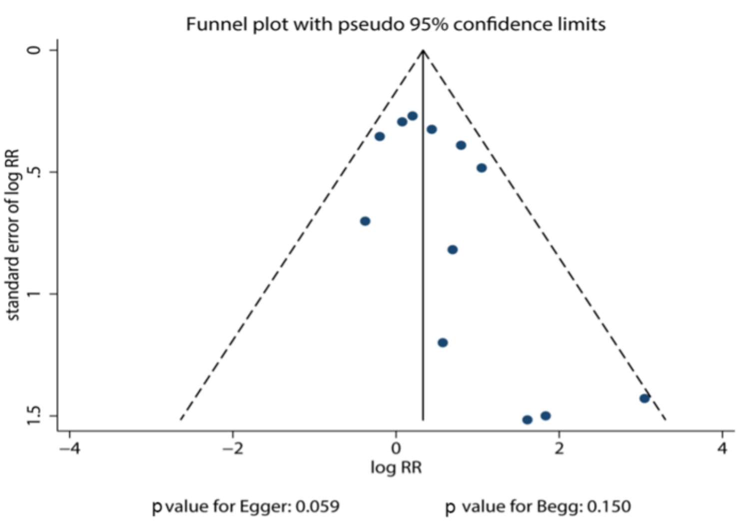
Supplementary Figure 1. Sensitivity analysis for the effect of gastric-tube feeding versus postpyloric tube feeding on the risk of mortality.



Supplementary Figure 2. Funnel plot for the effect of gastric-tube feeding versus postpyloric tube feeding on the risk of mortality.



Supplementary Figure 3. Sensitivity analysis for the effect of gastric-tube feeding versus postpyloric tube feeding on the risk of pneumonia.



Supplementary Figure 4. Funnel plot for the effect of gastric-tube feeding versus postpyloric tube feeding on the risk of pneumonia