

Comparative outcomes of endoscopic and radiological gastrostomy tube placement: a systematic review and meta-analysis with GRADE analysis

Divyanshoo R. Kohli^{a,b,*}, Dhruvil K Radadiya^{**}, Harsh Patel^c, Prateek Sharma^a, Madhav Desai^a

Kansas City VA Medical Center, MO; Sacred Heart Medical Center, Spokane WA; Ochsner Clinic Foundation, New Orleans, LA, USA

Abstract

Background Percutaneous endoscopic gastrostomy (PEG) and percutaneous radiological gastrostomy (PRG) are invasive interventions used for enteral access. We performed a systematic review and meta-analysis with assessment of certainty of evidence to compare the risk of adverse outcomes and technical failure between PEG and PRG.

Methods We queried PubMed, EMBASE, and Cochrane from inception through January 2022 to identify studies comparing outcomes of PEG and PRG. The primary outcome was 30-day all-cause mortality; secondary outcomes included the risk of colon perforation, peritonitis, bleeding, technical failure, peristomal infections, and tube-related complications. We performed GRADE assessment to assess the certainty of evidence and leave-one-out analysis for sensitivity analysis.

Results In the final analysis, 33 studies, including 26 high-quality studies, provided data on 275,117 patients undergoing PEG and 192,691 patients undergoing PRG. Data from high quality studies demonstrated that, compared to PRG, PEG had significantly lower odds of selected outcomes, including 30-day all-cause mortality (odds ratio [OR] 0.75, 95% confidence interval [CI] 0.60-0.95; $P=0.02$), colon perforation (OR 0.61, 95%CI 0.49-0.75; $P<0.001$), and peritonitis (OR 0.71, 95%CI 0.63-0.81; $P<0.001$). There was no significant difference between PEG and PRG in terms of technical failure, bleeding, peristomal infections or mechanical complications. The certainty of the evidence was rated moderate for colon perforation and low for all other outcomes.

Conclusions PEG is associated with a significantly lower risk of 30-day all-cause mortality, colon perforation, and peritonitis compared to PRG, while having a comparable technical failure rate. PEG should be considered as the first-line technique for enteral access.

Keywords Gastrostomy, adverse events, peritonitis, meta-analysis

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^aDepartment of Gastroenterology and Hepatology, Kansas City VA Medical Center, MO (Divyanshoo R. Kohli, Dhruvil K Radadiya, Prateek Sharma, Madhav Desai); ^bPancreas and Liver Clinic, Sacred Heart Medical Center, Spokane WA (Divyanshoo R. Kohli); ^cDepartment of Internal Medicine, Ochsner Clinic Foundation, New Orleans, LA, (Harsh Patel), USA

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*Shared first authorship

Correspondence to: Divyanshoo R Kohli, MD, 105 W 8th Ave, Spokane, WA 99204, USA, e-mail: kohli015@gmail.com

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Introduction

Enteral access through a gastrostomy tube is often required in patients unable to maintain adequate volitional intake of food. The most common techniques for performing a gastrostomy include percutaneous endoscopic gastrostomy (PEG) and percutaneous radiological gastrostomy (PRG) [1]. PEG is often performed by gastroenterologists and surgeons using an endoscope placed within the stomach [2]. PRG, on the other hand, is typically performed by radiologists using fluoroscopy and administration of oral contrast. Both techniques are considered safe and effective [3]. However, in general, gastrostomy tube placement is associated with a significant risk of adverse outcomes, including perforation, infections, peritonitis, and death.

There are conflicting data regarding the comparative safety of PEG and PRG. Most of the data are restricted to single-center retrospective analyses that were underpowered to conclusively determine the comparative outcomes and adverse events [4]. Hence, the preferred technique for safely performing a gastrostomy remains undetermined.

A prior systematic review and meta-analysis by Strijbos *et al* was limited to 16 studies reporting data on only 934 PEG and 1093 PRG procedures [4]. The authors noted no difference for 30-day mortality or infectious complications, whereas tube-related complications were higher in the PRG group. However, recent studies from large, nationally representative databases encompassing multiple hospitals nationwide have reported a statistically significantly greater risk of 30-day mortality for PRG compared to PEG [1,5]. Given the significant discrepancy in the results and the availability of newer high-quality studies, we performed this systematic review and meta-analysis to compare the risk of adverse outcomes between PEG and PRG. In addition, we performed a Grading of Recommendations, Assessment, and Evaluation (GRADE) analysis to assess the certainty of evidence.

Materials and methods

This systemic review and meta-analysis were performed in accordance with the Preferred Reporting Items for Systemic Reviews and Meta-Analyses (PRISMA) Statement [6].

Data sources and literature search

A comprehensive search strategy was developed to search for appropriate studies for this systemic review and meta-analysis. We queried PubMed, EMBASE and Cochrane from inception through 21st January 2022 to identify citations comparing outcomes of PEG and PRG. Detailed search queries for individual databases are delineated in Supplementary Table 1.

Study selection and data extraction

Randomized controlled trials, cohort studies (retrospective or prospective), and case-control studies comparing PEG with PRG were identified. We excluded duplicate studies, conference abstracts, editorials, short research letters, studies in other languages than English, and studies assessing outcomes of percutaneous endoscopic jejunostomy, PEG with jejunal extension [7] or PRG with jejunal extension. Two reviewers (DR and DK) independently performed an eligibility assessment. Any disagreement was resolved through consultation with a third author (PS).

A standard data extraction excel sheet was created using Microsoft Excel, and data were independently extracted by 2 reviewers (DR and DK). Extracted items included first author, study year, study design, patients in each arm, indication for procedure, number of study centers, country, type of PEG (pull, direct, push), antibiotic prophylaxis, mean age or median age of patients with standard deviation or range, percentages of males in each group, and outcomes of interests.

Quality assessment

The modified Newcastle-Ottawa Scale (NOS) and Jadad quality scale were used for observational studies and randomized clinical trials, respectively [4,8,9], to assess the quality of eligible studies identified after initial extraction. Quality assessment was performed individually for each study. Studies with NOS scores of less than seven and Jadad scores of less than 4 were deemed low-quality studies.

The certainty of the evidence was assessed using the GRADE approach [10]. Two independent researchers (DK and MD) graded the risk of bias, indirectness, inconsistency, imprecision, and publication bias [11]. A “Summary of Findings” table was created and the certainty of evidence for the systematic review of interventions was graded as “high”, “moderate”, “low” or “very low”, in compliance with the Cochrane Handbook, as well as the GRADE guidelines, using GRADEPro (McMaster University, 2015; developed by Evidence Prime, Inc.).

Primary and secondary outcomes

The primary outcome of interest was the 30-day mortality rate associated with PEG and PRG. Our secondary outcomes included the following: colon perforation, peritonitis, post-procedural bleeding, technical failure of the procedure, infectious complications (peristomal infections or aspiration pneumonia), tube-related complications (such as dislocation, leak, obstruction, or breakdown), readmissions, cost of the procedure, procedure times, and tumor seeding. The all-cause 30-day mortality, colon perforation and peritonitis were considered outcomes of critical importance during the GRADE analysis.

Statistical analysis

Pooled effect sizes were analyzed to examine the impact of PEG vs. PRG for primary and secondary outcomes. We examined heterogeneity among the outcomes via a sensitivity analysis. A subgroup analysis assessing high-quality studies was performed to examine the impact of high-quality evidence. We also performed a “leave-one-out” meta-analysis as a sensitivity analysis to identify outlier studies affecting outcomes. Meta-analyses were only performed if 2 or more studies were available for each outcome. Continuous variables were analyzed using the mean difference, while the odds ratio (OR) was calculated for dichotomous variables. Under the prior assumption that studies from different populations worldwide would be heterogenous, we used a random-effects model with the Mantel-Haenszel method to calculate the OR. Prediction intervals are reported along with pooled effect sizes to reflect the uncertainty expected in the summary effect. Studies with zero in both the intervention and control arms were not included in pooled effect size per standard meta-analysis practice, because such studies do not indicate either the direction or the magnitude of the relative treatment effect. Statistical

heterogeneity among different studies was determined using the I^2 statistic. The threshold of I^2 statistics being more than 50% was used to define substantial heterogeneity among the studies. Funnel plot visualization and the test of funnel plot asymmetry (i.e., Egger's test) were used to assess the presence of publication bias [12]. We did not assess publication bias if the number of studies for any outcome was less than 10, as the test of funnel-plot asymmetry would lack the statistical power to detect bias in the setting of a small number of studies [13]. "Leave-one-out" meta-analysis and test of publication bias were performed on high-quality studies. If publication bias was detected, Rucker's limit meta-analysis method was used to assess for significant effects on pooled analysis. This method builds meta-analysis models explicitly accounting for bias due to small-study effects [14]. P-values <0.05 were considered statistically significant for the meta-analysis and Egger's test. Statistical analysis was performed using "R" software.

Results

Literature search

Four hundred sixteen citations were identified on the initial literature search. After exclusion of studies based on the

selection criteria defined above, 46 studies were reviewed in detail and 33 were included in the final analysis (Fig. 1).

Population and study characteristics

Of 467,808 patients included in the analysis, 275,117 underwent a PEG procedure (59.6% male; mean age 62.6±2.6 years), whereas 192,691 patients underwent a PRG procedure (58.9% male; mean age 63.9±2.1 years). There were no differences in the sex ratio or mean age between groups.

Indications for percutaneous gastrostomy (PEG or PRG) varied among different studies. Seven studies reported outcomes among patients with motor neuron disease, 3 reported data for patients with head and neck malignancies, and the rest reported a mix of indications. Of 33 studies, 11 were from the USA and 8 from the UK (Table 1). Twenty-five studies were single-center, 6 were multicenter, and 2 studies were based on nationwide administrative databases. Twenty-seven studies were retrospective studies, 5 were prospective nonrandomized cohort studies, and only 1 study was a randomized controlled trial, specifically performed in children. Of 33 studies, 26 were deemed high-quality studies based on quality assessment. A study quality assessment using the modified NOS and Jadad score is provided in Supplementary Table 2.

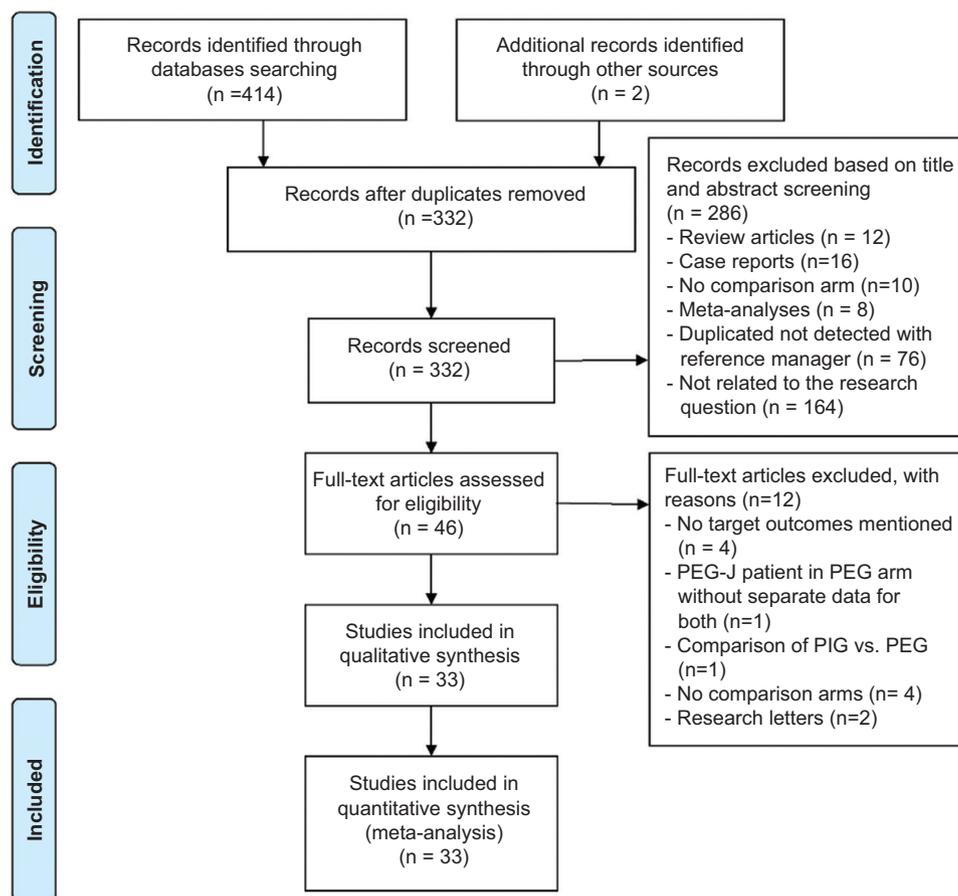


Figure 1 PRISMA diagram

PEG, percutaneous endoscopic gastrostomy; PEG-J, percutaneous endoscopic transgastric jejunostomy; PIG, per-oral image-guided gastrostomy

Table 1 Study and population characteristics

| Study [ref.] year | Country | Design | Indication | N of patients | | PEG type | Mean age (SD) | | Male (%) | | Antibiotic prophylaxis (%) | |
|-------------------------|-----------|---------------|--------------|---------------|--------|-------------------|---------------|-------------|----------|------|----------------------------------|-----|
| | | | | PEG | PRG | | PEG | PRG | PEG | PRG | PEG | PRG |
| Allen [15] 2013 | USA | Retrospective | MND | 57 | 51 | push & pull | 61.7 (11.3) | 61.2 (10.4) | 61.4 | 56.9 | NA | NA |
| Barkmeier [46] 1998 | USA | Retrospective | Various | 45 | 42 | NA | 63 (17) | 56 (16) | 53 | 76 | NA | NA |
| Blondet [16] 2010 | France | Retrospective | MND | 21 | 22 | pull | 66.2 (11.2) | 66 (12) | 33.3 | 50 | 100 | NA |
| Cherian [17] 2019 | Australia | Retrospective | Various | 307 | 95 | NA | 58.3 (21) | 63.5 (15.6) | 61 | 16 | 100 | 100 |
| Chio [18] 2004 | Italy | Retrospective | MND | 20 | 25 | NA | 65.1 (10.3) | 68.9 (9.5) | 52 | 48 | 0 | NA |
| Clayton [35] 2019 | USA | Retrospective | Various | 147 | 150 | pull | 65.8(17.3) | 61.7(16.4) | 61 | 54 | 100 | NA |
| Cosentini [39] 1998 | Austria | Retrospective | Various | 24 | 44 | pull | 52.5 (23) | 54.5 (18.4) | 50 | 63 | NA | 0 |
| Desport [19] 2005 | France | Retrospective | MND | 30 | 20 | pull | 65.7 (10.3) | 66.1 (9.70) | 70 | 25 | 100 | 100 |
| Elliot [20] 1996 | UK | Prospective | Various | 33 | 45 | pull | NA | NA | NA | NA | NA | NA |
| Galaski [21] 2009 | Canada | Retrospective | Various | 30 | 44 | NA | 55 (21) | 65 (19) | 63.3 | 70.5 | 50 | 6.8 |
| Grant [36] 2009 | UK | Prospective | HN cancer | 121 | 52 | pull | 61 | 65 | 65 | 77 | NA | NA |
| Kohli [34] 2022 | USA | Prospective | Various | 47 | 45 | push | 68.3 (7.1) | 68.6 (8.2) | 100 | 100 | 100 | 22 |
| Kohli [5] 2021 | USA | Retrospective | Various | 16384 | 154007 | Mix | 53.7 (29) | 67.2 (17.5) | 54 | 56 | NA | NA |
| Kohli [1] 2021 | USA | Retrospective | Various | 23566 | 9715 | Mix | 70.7 (10.2) | 69.6 (9.7) | 97.6 | 97.1 | NA | NA |
| La Nauze [22] 2012 | Australia | Retrospective | Various | 80 | 97 | pull | 58 (22.5) | 58 (22) | 66 | 71 | 100 | 87 |
| Laasch [41] 2003 | UK | Prospective | Various | 50 | 50 | NA | 65.3 (22.2) | 62.3 (17) | NA | NA | NA | NA |
| Laskaratos [23] 2013 | UK | Retrospective | Various | 53 | 40 | pull | 69.4 (20.7) | 76.2 (13) | 45 | 50 | 100 | 0 |
| Maasarani [37] 2021 | USA | Retrospective | Various | 232164 | 26477 | Mix | NA | NA | 47.8 | 54.4 | NA | NA |
| Maclean [45] 2007 | USA | Retrospective | Various | 268 | 110 | pull | 51 (21) | 57 (19) | 42 | 67 | NA | NA |
| Mcallistor [24] 2013 | UK | Retrospective | HN cancer | 21 | 89 | pull | NA | NA | NA | NA | 0 | 0 |
| Mcdermott [25] 2015 | UK | Prospective | MND | 163 | 121 | NA | 64.2 (11.7) | 63.6 (9.8) | 55 | 51 | NA | NA |
| Moller [26] 1999 | Sweden | Retrospective | Various | 12 | 94 | pull | 49.5 (12.7) | 60 (20.7) | 50 | 50 | NA | NA |

(Contd...)

Table 1 (Continued)

| Study [ref.] year | Country | Design | Indication | N of patients | | PEG type | Mean age (SD) | | Male (%) | | Antibiotic prophylaxis (%) | |
|-----------------------|----------------|------------------------------|--------------|---------------|-----|-------------|---------------|-------------|----------|------|----------------------------------|------|
| | | | | PEG | PRG | | PEG | PRG | PEG | PRG | PEG | PRG |
| Neeff [40] 2003 | New Zealand | Retrospective | HN cancer | 56 | 18 | NA | 65 (10.5) | 66 (12) | 77 | 72 | 100 | 100 |
| Park [43] 2019 | South Korea | Retrospective | Various | 324 | 94 | Mix | 66.7 (14.8) | 66.2 (13.3) | 72.2 | 61.7 | 89.5 | 86.2 |
| Pruthi [27] 2010 | Canada | Retrospective | Various | 376 | 42 | Mix | NA | NA | NA | NA | 89 | 38 |
| Righetti [44] 2021 | USA | Retrospective | Various | 174 | 519 | NA | 65.6 (13.9) | 64.1 (12.6) | 50.6 | 65.6 | NA | NA |
| Rio [28] 2010 | UK | Retrospective | MND | 21 | 121 | pull | NA | NA | NA | NA | NA | NA |
| Rustom [29] 2006 | UK | Retrospective | Various | 40 | 28 | NA | 63.6 | 64.8 | 31 | 19 | 100 | 100 |
| Silas [30] 2005 | USA | Retrospective | Various | 177 | 193 | pull | 68 (15) | 63 (14) | 56.5 | 59.1 | 100 | 0 |
| Singh [38] 2017 | Canada | Randomized clinical trial | Various | 97 | 96 | pull | NA | NA | NA | NA | 100 | 100 |
| Thornton [42] 2002 | Ireland | Retrospective | MND | 11 | 25 | pull | NA | NA | NA | NA | NA | NA |
| Vidhya [31] 2018 | Australia | Retrospective | Various | 85 | 52 | pull | 65 | 64 | 63.5 | 65.4 | 59 | 3.8 |
| Wollman [32] 1997 | USA | Retrospective | Various | 108 | 68 | NA | 55 (23.6) | 54 (21.3) | 62 | 56 | NA | NA |

PEG, percutaneous endoscopic gastrostomy; PRG, percutaneous radiological gastrostomy; MND, motor neuron disease; HN, head and neck; SD, standard deviation; NA, not available; single digits without SD in mean age column are median age reported in studies

Primary outcome: 30-day all-cause mortality

Twenty-two studies reported the all-cause 30-day mortality rate [1,5,15-34]. The pooled incidence of 30-day mortality was 7.8% in PEG (3279/41,663) and 8% in PRG patients (13,163/165,010). Patients undergoing PEG had 27% lower odds of 30-day mortality compared to PRG patients (OR 0.73, 95% confidence interval [CI] 0.58-0.93; $P=0.012$; $I^2=50\%$, Table 2).

Data from 18 high-quality studies showed a similar pooled incidence of 30-day mortality of 7.87% (3262/41,450) in the PEG vs. 7.97% (13,135/164,774) in the PRG group, with 25% lower odds of 30-day mortality in the PEG group (OR 0.75, 95%CI 0.60-0.95; $P=0.02$; $I^2=51\%$; Fig. 2A). “Leave-one-out” meta-analysis did not demonstrate any significant impact on the pooled OR. No publication bias was observed on the funnel plot, and the test of funnel plot asymmetry was non-significant (Egger’s test $P=0.223$).

Secondary outcomes

Colon perforation

Ten studies reported the incidence of colon perforation with PEG and PRG [1,5,17,26,28,34-38]. Pooled incidence

rates were 0.11% (310/272,866) in the PEG group and 0.20% (390/190,851) in the PRG group. Patients undergoing PEG had 37% lower odds of colon perforation compared to PRG patients (OR 0.63, 95%CI 0.47-0.86; $P=0.008$; $I^2=17\%$, Fig. 3).

Data from 8 high quality studies showed similar results, with 39% lower odds of colon perforation with PEG vs. PRG (OR 0.61, 95%CI 0.41-0.75; $P=0.009$; $I^2=0\%$, Fig. 2B). “Leave-one-out” meta-analysis did not demonstrate any significant impact on the pooled OR.

Peritonitis

Twelve studies reported the incidence of peritonitis with PEG and PRG [1,17,20-22,26,29,31,32,36,39,40]. Pooled incidence of peritonitis was 1.9% (462/24,462) in the PEG group and 2.7% (277/10351) in the PRG group. Pooled OR showed 29% lower odds of peritonitis with the PEG procedure compared to PRG (OR 0.71, 95%CI 0.62-0.81; $P<0.001$; $I^2=0\%$, Fig. 3).

Data from 9 high-quality studies showed a similar 29% lower incidence of peritonitis with PEG compared to PRG (OR 0.71, 95%CI 0.63-0.81; $P<0.001$; $I^2=0\%$; Fig. 2C). “Leave-one-out” meta-analysis showed that excluding a study by Kohli *et al* led to a statistically non-significant OR. However, Kohli *et al* was the largest study in the analysis [1].

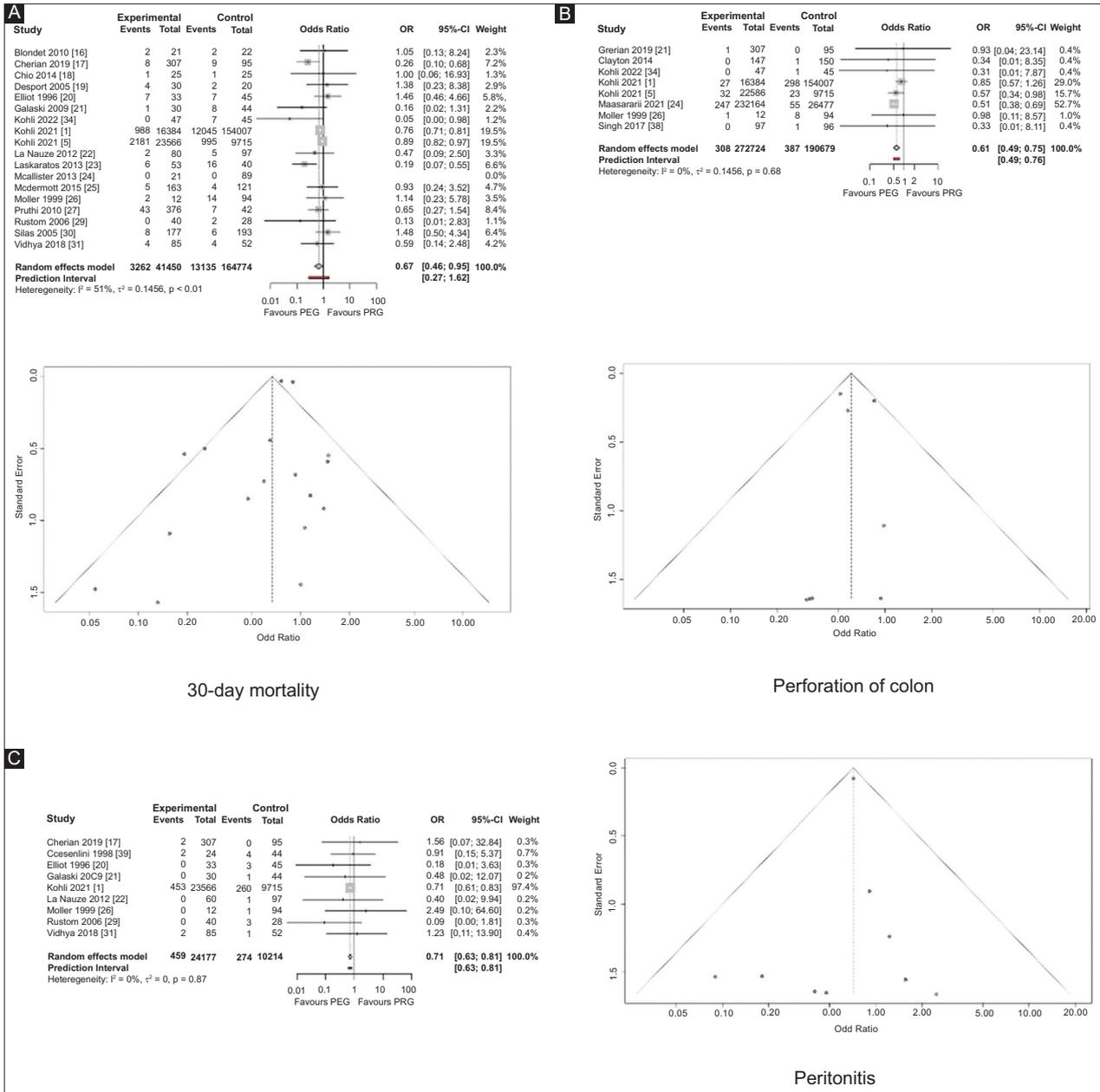


Figure 2 Forest plots and funnel plots for 30-day all-cause mortality, colon perforation, and peritonitis

Post-procedural bleeding

Sixteen studies reported bleeding as an outcome after procedures [1,5,17,19,21,22,25-27,31,35-37,39-41]. Pooled incidence rates of bleeding were 0.3% (955/273,645) and 0.4% (782/191,118) in the PEG and PRG groups, respectively. Pooled OR did not show any difference in bleeding rate between the PEG and PRG groups (OR 0.77, 95%CI 0.48-1.23; P=0.241; I²=80%).

Technical failure

Thirteen studies reported technical success or failure rates [15,16,18,25,27,31,32,34,38-42]. The pooled incidence of

procedure failure rates from all studies were 6.1% (73/1196) and 2.5% (18/705) in the PEG and PRG groups, respectively. Pooled OR did not show any difference in the technical failure rate of PEG and PRG (OR 2.52, 95%CI 0.92-6.89; P=0.068; I²=61%).

Peristomal infection

Twenty-three studies reported the incidence of infections at the gastrostomy site [1,5,19-22,25-32,35-37,39-41,43-45]. Pooled incidence of peristomal infection was 1.2% (3310/274399) and 1.2% (2281/192,135) in the PEG and PRG groups, respectively. Pooled OR was 0.87 (95%CI 0.67-1.13; P=0.268; I²=47%).

Table 2 Odds ratios for outcomes with percutaneous endoscopic gastrostomy compared to percutaneous radiological gastrostomy

| Outcome | All studies | | | | | High quality studies | | | | | Egger's test (P-value) | Quality of evidence |
|----------------------------|-------------|------|-----------|---------|--------------------|----------------------|------|-----------|---------|--------------------|------------------------|---------------------|
| | N | OR | 95%CI | P-value | I ² (%) | N | OR | 95%CI | P-value | I ² (%) | | |
| 30-day all-cause mortality | 22 | 0.73 | 0.58-0.93 | 0.012 | 50 | 18 | 0.75 | 0.60-0.95 | 0.02 | 51 | 0.223 | Low (++) |
| Colon perforation | 10 | 0.63 | 0.47-0.86 | 0.008 | 17 | 8 | 0.61 | 0.49-0.75 | <0.001 | 0 | NA | Moderate (+++) |
| Peritonitis | 12 | 0.71 | 0.62-0.81 | <0.001 | 0 | 9 | 0.71 | 0.63-0.81 | <0.001 | 0 | NA | Low (++) |
| Bleeding | 16 | 0.77 | 0.48-1.23 | 0.241 | 80 | 15 | 0.75 | 0.45-1.26 | 0.247 | 83 | 0.667 | Low (++) |
| Technical failure | 13 | 2.52 | 0.92-6.89 | 0.068 | 61 | 9 | 1.05 | 0.33-3.34 | 0.917 | 50 | NA | Low (++) |
| Peristomal infection | 23 | 0.87 | 0.67-1.13 | 0.268 | 47 | 19 | 0.93 | 0.68-1.27 | 0.625 | 54 | 0.03* | Low (++) |
| Aspiration pneumonia | 8 | 0.58 | 0.28-1.21 | 0.114 | 0 | 6 | 0.86 | 0.48-1.54 | 0.46 | 92 | NA | Low (++) |
| Tube related complications | 22 | 0.56 | 0.33-0.95 | 0.032 | 95 | 19 | 0.60 | 0.35-1.06 | 0.073 | 96 | 0.758 | Low (++) |

*Rucker's limit meta-analysis showed non-significant changes in OR

OR, odds ratio; CI, confidence interval

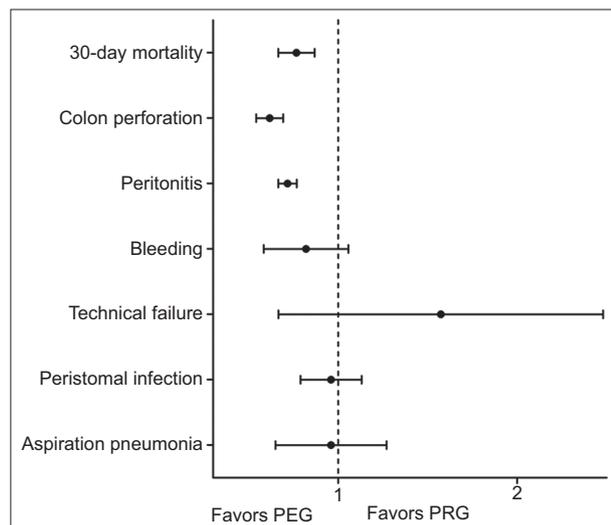


Figure 3 Forest plot for all outcomes PEG, percutaneous endoscopic gastrostomy; PRG percutaneous radiological gastrostomy

Data from 19 high-quality studies demonstrated an OR of 0.93 (95%CI 0.68-1.27; $P=0.625$; $I^2=54\%$). Publication bias was observed on the funnel plot, and the test of funnel plot asymmetry was significant ($P=0.03$). Rucker's limit meta-analysis showed non-significant changes in adjusted (OR 0.73, 95%CI 0.50-1.08; $P=0.114$) and unadjusted (OR 0.93, 95%CI 0.68-1.27; $P=0.625$) OR for small-study effects. "Leave-one-out" meta-analysis did not demonstrate any significant impact on the pooled OR.

Aspiration pneumonia

Eight studies reported aspiration pneumonia as an outcome [21,22,25,27,31,32,34,36]. Pooled incidence rates of aspiration pneumonia were 1.2% (12/976) and 3.4% (17/495)

in the PEG and PRG groups, respectively. Pooled OR did not show any difference in aspiration pneumonia rate between the 2 procedures (OR 0.58, 95%CI 0.28-1.21; $P=0.114$; $I^2=0\%$).

Tube-related complications

Twenty-two studies reported tube-related complication as an outcome [1,5,17-22,24,29-32,35-37,39-41,43-45]. Pooled incidence rates were 2.8% (7705/274,214) and 3.5% (6791/191,991) in the PEG and PRG groups, respectively. Pooled OR was 0.56 (95%CI 0.33-0.95; $P=0.032$; $I^2=95\%$).

Data from 19 high-quality studies demonstrated an OR of 0.60 (95%CI 0.35-1.09, $P=0.07$; $I^2=96\%$). No publication bias was observed on the funnel plot, and the test of funnel plot asymmetry was non-significant ($P=0.758$). "Leave-one-out" meta-analysis demonstrated that omission of studies by Cherian *et al* [17] or Desport *et al* [19] led to a statistically lower OR of complications with PEG. Both studies reported a statistically significantly greater incidence of tube-related complications with PEG on univariate analysis. However, on a subsequent multivariate analysis, Cherian *et al* [24] reported an OR of 5.4 for tube dislodgement with PRG compared to PEG, and noted that the method of gastrostomy insertion was the only predictor for dislodgement. Multivariate analysis was not performed in a study by Desport *et al* [26]. Exclusion of both studies from the meta-analysis resulted in statistically significantly fewer tube-related adverse events with PEG (OR 0.46, 95%CI 0.29-0.74; $P=0.003$; $I^2=95\%$).

30-day all-cause readmission

Two high-quality studies reported 30-day readmission rates after the procedures [5,34]. Pooled 30-day readmission rates were 17% (2817/16,431) and 19% (29,649/154,052) in the PEG and PRG groups, respectively. Pooled OR did not show any

difference in 30-day readmission rate between the 2 arms (OR 14.8, 95%CI 0.006-76.82; $P=0.480$; $I^2=63.7\%$).

Cost

Three studies reported the cost of procedures [17,21,46]. Because of differences in currencies, pooled analyses could not be performed. One low-quality study reported \$1861 as the cost for PEG and \$1985 for PRG [46]. The 2 high-quality studies reported the following mean cost: Australian dollars (AUD) 1200 for PEG vs. 1366 for PRG, Canadian dollar (CAD) 591 CAD for PEG vs. 407 for PRG [17,21].

Procedure times

Three studies, including 2 high-quality studies, reported the procedure time [32,34,43]. Only 2 studies reported procedure times with mean and standard deviation. Pooled analysis did not demonstrate any difference in procedure time (mean difference: -0.07 min, 95%CI -10.5-9.1; $P=0.882$; $I^2=99.7\%$).

Tumor seeding

Only one study reported tumor seeding events as an outcome. This low-quality study reported 0 events in both groups [40].

Assessment of certainty of evidence by GRADE

The certainty of the evidence was assessed for each outcome using the GRADE methodology (Table 2). Most of the studies were retrospective cohort studies. More than 75% of the studies were high-quality based on the NOS, without any definite selection or attrition bias. Outcomes such as all-cause 30-day mortality, colon perforation, peritonitis, and technical failure of procedure were considered to have uniform definitions across different studies. However, mechanical complications of the feeding tube were not defined uniformly across the various studies.

The certainty of the evidence was downgraded due to serious imprecision noted in the outcome of peritonitis, since one study [1] demonstrated significantly higher odds of peritonitis with PRG, while the other studies did not (Table 3). The certainty

Table 3 GRADE analysis for certainty

| Outcomes | GRADE analysis for certainty of evidence | | | | |
|----------------------------|--|-----------------------------|----------------------------|--------------------------------------|---|
| | Anticipated absolute effects* (95%CI) | | Relative effect (95%CI) | № of participants (studies) | Certainty of the evidence (GRADE) |
| | Risk with PRG | Risk with PEG | | | |
| All cause 30-day mortality | 80 per 1,000 | 60 per 1,000 (48 to 75) | OR 0.73 (0.58 to 0.93) | 206673 (22 observational studies) | ⊕⊕○○ Low |
| Colon perforation | 2 per 1,000 | 1 per 1,000 (1 to 2) | OR 0.63 (0.47 to 0.86) | 463717 (10 observational studies) | ⊕⊕⊕○ Moderate |
| Peritonitis | 27 per 1,000 | 19 per 1,000 (17 to 22) | OR 0.71 (0.62 to 0.81) | 34813 (12 observational studies) | ⊕⊕○○ Low |
| Bleeding | 4 per 1,000 | 3 per 1,000 (2 to 5) | OR 0.77 (0.48 to 1.23) | 464763 (16 observational studies) | ⊕⊕○○ Low |
| Technical failure | 26 per 1,000 | 62 per 1,000 (24 to 153) | OR 2.52 (0.92 to 6.89) | 1901 (14 observational studies) | ⊕⊕○○ Low |
| Peristomal infection | 12 per 1,000 | 10 per 1,000 (8 to 13) | OR 0.87 (0.67 to 1.13) | 466534 (23 observational studies) | ⊕⊕○○ Low |
| Tube-related complications | 35 per 1,000 | 20 per 1,000 (12 to 34) | OR 0.56 (0.33 to 0.95) | 466205 (22 observational studies) | ⊕⊕○○ Low |
| Aspiration pneumonia | 34 per 1,000 | 20 per 1,000 (10 to 41) | OR 0.58 (0.28 to 1.21) | 1471 (8 observational studies) | ⊕⊕○○ Low |

*The risk in the intervention group (and its 95% confidence interval) is based on the assumed risk in the comparison group and the relative effect of the intervention (and its 95%CI)

GRADE Working Group grades of evidence

High certainty: we are very confident that the true effect lies close to that of the estimate of the effect

Moderate certainty: we are moderately confident in the effect estimate: the true effect is likely to be close to the estimate of the effect, but there is a possibility that it is substantially different

Low certainty: our confidence in the effect estimate is limited: the true effect may be substantially different from the estimate of the effect

Very low certainty: we have very little confidence in the effect estimate: the true effect is likely to be substantially different from the estimate of effect

PEG, percutaneous endoscopic gastrostomy; PRG, percutaneous radiological gastrostomy; CI, confidence interval; OR, odds ratio

of the evidence was upgraded in colon perforation and peritonitis because of a large effect from individual studies. Since peritonitis and colon perforation are relatively uncommon serious adverse events, small single-center studies are likely to be underpowered to detect a significant difference in the incidence. In the outcome of peritonitis, 97% of the weightage can be ascribed to a single, large multicenter study [1] with adequate power to detect differences in outcomes. Similarly, 3 large studies [1,5,37], which together provide 97% of the total weightage, report a higher OR of perforation with PRG. Overall, the certainty of the evidence was considered “low” for all outcomes except colon perforation, for which the certainty was considered “moderate”.

Discussion

A percutaneous gastrostomy for a feeding tube is a frequently performed procedure [1,5]. There are endoscopic, radiological, and surgical techniques for performing a gastrostomy, but the surgical technique is used less frequently [5]. However, endoscopic and radiological techniques are widely used, and data regarding comparative outcomes have recently been published. While PEG and PRG are complementary techniques [1], significant differences in outcomes need to be considered when a particular technique is chosen. This systematic review and meta-analysis of 33 studies, including more than 450,000 patients, demonstrated that PEG was associated with a lower risk of 30-day all-cause mortality, colon perforation and peritonitis, compared to PRG. Notably, the 2 techniques have comparable rates of technical failure.

Different studies have variously demonstrated a higher technical success rate for either PEG [27] or PRG [15], or no significant difference [34]. However, the significant heterogeneity in these primarily retrospective studies limited the quality of the evidence. Further, in some studies, it is unclear if PEG or PRG was selected after the failure of the other technique [5]. This meta-analysis demonstrates that PEG and PRG have comparable technical failure/success rates. Notably, the most widely used technique for performing a PEG is the peroral “pull” technique which necessitates the passage of the feeding tube through the mouth and esophagus [47]. This technique may not be feasible in patients with stenotic malignancies and those at risk of implantation metastasis [48], thus contributing to the failure of the PEG technique. Additionally, PEG requires significantly higher doses of sedatives and analgesics than PRG [34]. These limitations may possibly be overcome using a direct PEG technique [44] and propofol-based sedation.

This study demonstrates that PEG is associated with lower 30-day all-cause mortality compared to PRG. This may possibly be explained, in part, by a higher incidence of colon perforation and peritonitis with PRG [1,37]. However, there is also a possible selection bias, whereby sicker patients with probably shorter life expectancy are preferentially referred for a PRG. Indeed, recent studies have demonstrated a statistically significant preference for PRG in patients with malignant causes of dysphagia, such as malignancies of the head and

neck. In contrast, PEG is preferentially used in benign causes of dysphagia such as stroke [1]. However, 2 recent, large multicenter studies, with over 160,000 patients, have demonstrated higher odds of 30-day all-cause mortality with PEG after incorporating the presence of malignancy and the Charlson comorbidity index scores [1,5]. Despite the impact of presumed selection bias, high 30-day mortality highlights the dilemma in selecting patients likely to benefit from a feeding tube.

This meta-analysis demonstrated a lower risk for colon perforation and peritonitis with PEG than PRG. The lower risk of colon perforation and peritonitis with PEG has been ascribed to safe endoscopic techniques, such as transillumination, finger indentation, and the “safe-tract” method of using the introducer needle [5]. PRG also uses techniques such as contrast administration to delineate the gastric rugae vs. the colon, but further interventions may be needed to decrease the risk of colon perforation and peritonitis.

It has previously been suggested that patients undergoing a PEG may be at a higher risk for bleeding, since PEG is preferentially undertaken in patients with a stroke typically on dual antiplatelet medications [1]. This meta-analysis, however, demonstrated a relatively low risk of bleeding with a gastrostomy, without a statistically significant difference between PRG and PEG. Notably, it is unclear how many patients who bled were on antiplatelet and/or anticoagulant medications.

Peristomal infection is a common adverse outcome of a gastrostomy. Therefore, the American Society for Gastrointestinal Endoscopy recommends administering periprocedural antibiotics during the procedure [49]. However, the Society for Interventional Radiology until recently recommended prophylactic antibiotics only for the “pull” gastrostomy, but did not have a recommendation for antibiotics for the transabdominal “push” gastrostomy [3]. This may have led some physicians to not administer antibiotics during a PRG [34]. The recent 2018 guidelines, however, recommend prophylactic antibiotics for both types of gastrostomy techniques [50]. Our study did not demonstrate a significant difference in the odds of infection. The source studies did not explicitly state whether antibiotics were administered or not.

Notably, stratification of data based on the administration of antibiotics, type of technique, and extent of follow up was not feasible. Similarly, this meta-analysis did not demonstrate a statistically significant difference in the incidence of mechanical complications of a PEG and PRG. However, there was significant variation in the types of feeding tubes and definitions of complications used by individual investigators.

The strengths of this study include a large dataset from multiple sites, use of a validated quality assessment tool, utilization of “leave-one-out” meta-analysis to assess for outliers, and application of the GRADE process to evaluate the strength of our analysis. Indeed, a recent meta-analysis on this subject reported data on 2027 patients and demonstrated no difference in mortality [4]. However, this current meta-analysis reports the data of 467,808 patients from 33 studies. The study was limited by the retrospective study design of most individual studies, lack of uniform definitions across different studies, and

an over-representation of 2 large nationwide studies recently published by our group [1,5]. The analysis was also limited by a lack of ancillary data relevant for specific outcomes, such as the use of antibiotics in relation to the incidence of peristomal infections. Finally, “pull” and direct/“push” gastrostomy techniques were analyzed as a single group, since very few studies reported data on direct/“push” gastrostomies. Notably, despite the low certainty of the evidence for most outcomes, these data represent the best available evidence comparing the risks of PEG and PRG.

In conclusion, this systematic review and meta-analysis demonstrated that PEG was associated with a significantly lower risk of 30-day all-cause mortality, colon perforation and peritonitis, compared to PRG, while having a comparable technical failure rate. Therefore, PEG should be considered the first-line technique for obtaining enteral access in appropriate patients.

Summary Box

What is already known:

- Percutaneous endoscopic (PEG) and radiological (PRG) gastrostomy are complementary procedures performed for enteral access

What the new finding is:

- In our systematic review and meta-analysis of 33 studies, PEG was associated with significantly lower odds of colon perforation, peritonitis, and all-cause mortality at 30 days compared to PRG

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Supplementary material

Supplementary Table 1 Literature search strategy

| Database | Search strategy | Number of citations |
|----------|--|---------------------|
| PubMed | ("PEG"[Title/Abstract] OR "percutaneous endoscopic gastrostomy"[Title/Abstract] OR ("endoscopic"[Title/Abstract] AND ("gastrostomy"[MeSH Terms] OR "gastrostomy"[Title/Abstract]))) AND (((("radiologic"[Title/Abstract] OR "fluoroscopic"[Title/Abstract] OR "radiological"[Title/Abstract]) AND ("gastrostomy"[MeSH Terms] OR "gastrostomy"[Title/Abstract])) OR ("percutaneous radiologic gastrostomy"[Title/Abstract] OR "PRG"[Title/Abstract] OR "radiologically inserted gastrostomy"[Title/Abstract] OR "RIG"[Title/Abstract])) AND ("complication*" [Title/Abstract] OR "adverse event*" [Title/Abstract] OR "adverse effect*" [Title/Abstract] OR "mortality"[Title/Abstract] OR "outcome*" [Title/Abstract] OR "mortality"[MeSH Terms] OR "mortality"[Title/Abstract]) | 218 |
| EMBASE | #1. 'percutaneous endoscopic gastrostomy'/exp OR 'percutaneous endoscopic gastrostomy' OR 'percutaneous endoscopic gastrostomy':ti,ab OR 'peg':ti,ab #2. 'percutaneous radiologic gastrostomy':ti,ab OR 'prg':ti,ab OR 'radiologically inserted gastrostomy':ti,ab OR 'rig':ti,ab OR 'fluoroscopically placed gastrostomy':ti,ab OR 'fpg':ti,ab #3. 'complication'/exp OR 'complication' OR 'adverse event'/exp OR 'adverse event' OR 'adverse outcome'/exp OR 'adverse outcome' OR 'mortality'/exp OR 'mortality' OR 'complication*':ti,ab OR 'adverse event*':ti,ab OR 'adverse effect*':ti,ab #4. #1 AND #2 AND #3 | 187 |
| Cochrane | #1 MeSH descriptor: [Gastrostomy] explode all trees #2 "endoscopic":ti,ab #3 #1 AND #2 #4 "percutaneous endoscopic gastrostomy":ti,ab OR "peg":ti,ab #5 #3 OR #4 #6 "radiologic":ti,ab OR "fluroscopic":ti,ab OR "radiological":ti,ab 9692 #7 #6 AND #1 #8 "percutaneous radiologic gastrostomy":ti,ab OR "prg":ti,ab OR "radiologically inserted gastrostomy":ti,ab OR "rig":ti,ab OR "fluoroscopically placed gastrostomy":ti,ab OR "fpg":ti,ab #9 #7 OR #8 #10 "complication*":ti,ab OR "adverse event*":ti,ab OR "adverse effect*":ti,ab #11 MeSH descriptor: [Mortality] explode all trees #12 #10 OR #11 #13 #5 AND #9 AND #12 | 9 |

Supplementary Table 2 Modified Newcastle-Ottawa scale (NOS) and JADAD quality scale

| Study [ref.] year | Selection | | | | Comparability | | Outcome | | Total score |
|----------------------|------------|------------|------------|------------|---------------|------------|------------|------------|-------------|
| | Question 1 | Question 2 | Question 3 | Question 4 | Question 1 | Question 1 | Question 2 | Question 3 | |
| Allen 2013 [15] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 0 | 6 |
| Barkmeier 1998 [46] | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 5 |
| Blondet 2010 [16] | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Cherian 2019 [17] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Chio 2004 [18] | 1 | 0 | 1 | 1 | 1 | 1 | 1 | 1 | 7 |
| Clayton 2019 [14] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Cosentini 1998 [39] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Desport 2005 [19] | 1 | 0 | 1 | 1 | 2 | 1 | 1 | 1 | 8 |
| Elliot 1996 [20] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Galaski 2009 | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Grant 2009 [21] | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Kohli 2021 [5] | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Kohli 2021 [1] | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Kohli 2022 [34] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| La Nauze 2012 [22] | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 0 | 8 |
| Laasch 2003 [41] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Laskaratos 2013 [23] | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Maasarani 2021 [37] | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Macleane 2007 [45] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Mcallistor 2013 [24] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Mcdermott 2015 [25] | 1 | 1 | 1 | 1 | 2 | 0 | 1 | 1 | 8 |
| Moller 1999 [26] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Neeff 2003 [40] | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 6 |
| Park 2019 [43] | 1 | 1 | 1 | 1 | 2 | 0 | 1 | 1 | 8 |
| Pruthi 2010 [27] | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Righetti 2021 [44] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Rio 2010 [28] | 1 | 0 | 1 | 1 | 0 | 1 | 1 | 1 | 6 |
| Rustom 2006 [29] | 1 | 1 | 1 | 1 | 0 | 1 | 1 | 1 | 7 |
| Silas 2005 [30] | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Throntron 2002 [42] | 1 | 0 | 1 | 1 | 0 | 0 | 1 | 1 | 5 |
| Vidhya 2018 [31] | 1 | 1 | 1 | 1 | 2 | 1 | 1 | 1 | 9 |
| Wollman 1997 [32] | 1 | 1 | 1 | 1 | 0 | 0 | 1 | 1 | 6 |

| JADAD quality score | | | |
|---------------------|---------------|----------|-------------|
| | Randomization | Blinding | Withdrawals |
| Singh 2017 [38] | 2 | 2 | 1 |