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A Systematic Review and Meta-Analysis on Outcomes and Complications of Percutaneous Endoscopic Versus Radiologic Gastrostomy for Enteral Feeding

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Background: The optimal technique for long-term enteral feeding has not yet been established. Both percutaneous endoscopic gastrostomy (PEG) and percutaneous radiologic gastrostomy (PRG) are widely used. Aim was to extensively review outcomes of PEG and PRG.

Materials and Methods: A systematic review using Medline, Embase, and Cochrane was performed, using standardized tools for assessing bias. Main outcomes were infectious and tube-related complications, procedure related and 30-day mortality. Pooled risk differences (RDs) with corresponding 95% confidence intervals (95% CIs) were calculated using random effects. Arcsine transformations were applied.

Results: In total, 344 studies were identified, of which 16 were included, reporting on 934 PEGs and 1093 PRGs. No differences were found for infectious complications [RD, 0.03 (−0.05 to 0.11)], procedure-related mortality [RD, 0.01 (−0.04 to 0.06)], or 30-day mortality [RD, 0.06 (−0.01 to 0.13)]. Tube-related complications were higher in PRG [RD, 0.16 (0.06-0.26)]. Subgroup analysis was performed for head and neck cancer (HNC) and motor neuron disease. In HNC, this revealed significantly lower tube-related complications and procedure-related mortality after PEG. In motor neuron disease, no differences were seen. The level of evidence appears sufficient considering the low degree of heterogeneity.

Conclusions: No differences were found with regard to mortality or infectious complications. PEG showed lower risk of tube-related complications. Subgroup analysis revealed PEG to be favorable in HNC based on lower rates of procedure-related mortality and tube-related complications. Local experience and availability should be taken into account in the decision process.

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The authors declare that they have nothing to disclose.

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Gastrostomy feeding is preferred over nasogastric tube feeding when medium and long-term enteral feeding ($\geq$4 wk) is indicated.[1] In case the gastrointestinal tract is available for digestion and absorption of nutrients, enteral nutrition has proven to be superior to parenteral nutrition: it improves nutritional outcome, reduces associated morbidity, and preserves gut function.[2] The optimal technique for long-term enteral feeding has not yet been well established. Both percutaneous endoscopic gastrostomy (PEG) and percutaneous radiologic gastrostomy (PRG) are widely used techniques. Most common indications for gastrostomy placement include head and neck cancer (HNC, often prophylactic before start of chemoradiotherapy), motor neuron disease (MND), other neurologic disorders, for example, a cerebrovascular accident, and malnutrition (eg, postsurgical recovery, mental retardation, motility disorders of the gastrointestinal tract).

Complications and mortality of both techniques have previously been reported, but separately. Consensus on which technique is more favorable has not been reached up to now. Most patients in need for a gastrostomy are vulnerable and malnourished. Therefore, when choosing between PRG and PEG, it is of utmost relevance to take into account procedure-related complication and mortality risks. It appears that 30-day mortality is relatively high both in patients undergoing PEG or PRG procedures.[3–5] This has been associated with poor patient selection. Several risk factors for 30-day mortality have previously been identified. These include higher age, lower body mass index,[6] C-reactive protein $>$21.5 g/L,[7,8] diabetes mellitus,[8] albumin $<$3 g/d,[7,9] radiotherapy, cirrhosis, cancer,[10] chronic obstructive pulmonary disease, and residing in a nursing home.[7]

Previous publications have indicated that infectious complications occur at rates of 8% to 15%[1,11] in PEG and 2% to 22% in PRG.[3,12,13] In PEG, antibiotic prophylaxis significantly reduces the risk of infectious complications, as shown in a meta-analysis by Lipp and Lusardi,[11] leading to a decrease from, 24.2% to 8.4%. The benefit of antibiotic prophylaxis in PRG is less clear.[12,14] Generally, antibiotics are not administered because the risk of peristomal infection is considered to be lower in PRG due to a lower risk of contamination as the tube

does not pass the oropharynx. Tube-related complications such as dislocation, obstruction, leak, or rupture are reported in 1.7% to 15% in PEG and 5.2% to 57% in PRG.[3,4,15]

In the past, a few systematic reviews including meta-analyses were performed comparing PEG to PRG.[12,16,17] However, these meta-analyses have certain limitations as they generally focused only on a single outcome or included studies of low quality. Conclusions of these meta-analyses should therefore be interpreted with caution. A confirmative meta-analysis based on representative data is therefore warranted.

Our aim was to perform a systematic review of the literature and meta-analyses for outcomes of PEG and PRG in order to delineate the best suitable options for specific groups of patients and also for individual patients. On the basis of previous literature, we expected to encounter higher tube-related complications for PRG, slightly higher infectious complications in PEG, and a comparable 30-day and procedure-related mortality for PEG and PRG.

MATERIALS AND METHODS

Methods and inclusion criteria were specified before the study and have been documented in a protocol (Appendix I, Supplemental Digital Content 1, http://links.lww.com/JCG/A418). The search was performed by the main and second investigator in collaboration with an experienced librarian.

Studies were identified by searching electronic databases according to the PRISMA guidelines, including hand searching of reference lists of articles and consultation with experts in the field if necessary. No limits were applied for language and foreign papers were translated. The search was applied to Medline (1966 to 2.5.2017) and adapted for Embase (1980 to 2.5.2017). Cochrane and DARE (Database of Abstracts of Reviews of Effectiveness) databases were reviewed. Details on the search strategy and methods can be found in Appendix II (Supplemental Digital Content 2, http://links.lww.com/JCG/A419).[18,28–34] Terms used were complication(s), adverse event (s) or effect(s), PEG, PRG, and their synonyms. No publication date, or publication status restrictions were imposed.

Study Selection

Types of studies included were randomized clinical trials and retrospective reviews/cohort/case-control studies. A selection list by title and abstract was made (Appendix III, Supplemental Digital Content 3, http://links.lww.com/JCG/A420). Eligibility assessment was performed independently in an unblinded standardized manner by 2 authors (D.S. and D.K.) according to PRISMA guidelines. Discrepancies between reviewers were resolved by consensus. A third reviewer was consulted in case disagreements remained (A.A. M.M.). Selection of outcomes was based on the clinical principles underlying the hypothesis. Main outcome parameters were infectious and tube-related complications ($\leq$30 d), procedure-related mortality, and 30-day mortality. Among infectious complications we included peristomal infection and peritonitis. Absolute peritonitis rates were assessed as well. Among tube-related complications we included dislocation, leak, obstruction, need for replacement, and defects (eg, rupture, break down). Secondary outcome was the occurrence of tumor seeding. Characteristics of trial participants, type of intervention, and the trial's inclusion and exclusion criteria were extracted and classified in a data extraction sheet partially based on the Cochrane Consumers and Communication Review Group's data extraction template.[19]

Assessment of Confounding

To ascertain the validity of eligible studies, standardized assessment tools [The Risk of Bias in Nonrandomized Studies (ROBINS-I)[20] and Newcastle Ottawa Scale (NOS)[21]] were applied before inclusion. This was performed for all 4 outcome levels separately and all together. Separate analysis did not change the overall result and therefore we only reported the overall result.

Statistical Methods

Because of expected low complications risks, pooled risk differences (RDs) with corresponding 95% confidence intervals (CIs) were calculated. Random effects models with DerSimonian-Laird estimator to cover both within and between study heterogeneity were used. To correct for low complication rates an Arcsine transformation was applied, to stabilize variance in order to make the pooled outcome more reliable.[22] The results were translated to the original scale and presented in Forest plots. Heterogeneity among studies was measured with the inconsistency index (I^2), where a value of minimal 50% was considered as substantial heterogeneity between studies.[23] Possible publication bias was studied using Funnel plots with Egger's test for asymmetry.[24] Two-sided P-values of ≤ 0.05 were considered significant. We used the Metafor package version 1.9[25] in R statistical program version 3.2.2[26] to process all the collected data. The effect of single studies with different methodology was tested by sensitivity analyses in which pooled rates with and without this study were compared.[26,27] Subgroup analysis was planned for studies including only MND or HNC patients, and studies including a various population.

RESULTS

In total, 455 citations were found (Fig. 1, PRISMA diagram), with 344 unique citations. Criteria for eligibility were assessed by screening on title, reasons for exclusion are specified in Appendix III (Supplemental Digital Content 3, http://links.lww.com/JCG/A420) (exclusion by title). No relevant articles in other languages than English or unpublished ongoing studies were found. Most articles were no head-to-head comparison, case reports, reviews, or not relevant. In total, 68 articles were found eligible. Inclusion for qualitative assessment was based on abstract, reasons for exclusion are stated in the PRISMA diagram (Fig. 1) and are specified in Appendix III (Supplemental Digital Content 3, http://links.lww.com/JCG/A420) (exclusion by abstract).

A total of 16 studies were included in the quantitative meta-analysis (4 prospective nonrandomized, 12 retrospective studies), reporting on 934 PEGs (placed using the pull method[1]) and 1093 PRGs.[3–5,12,13,15,35–45] Study characteristics and the risk of bias are stated in Tables 1 and 2, respectively, including risk per domain (as stated in the ROBINS-I scale).

Overall Results

In the overall population, no differences were found between PEG and PRG for procedure-related mortality [RD, 0.01 (95% CI, −0.04 to 0.06); Fig. 2], or 30-day mortality [RD, 0.06 (−0.01 to 0.13); Fig. 3], nor infectious complications [RD, 0.03 (−0.05 to 0.11); Fig. 4]. Tube-related complications (including dislocation, obstruction, leak and tube defects) were significantly lower in PEG [RD, 0.16 (0.06-0.26); Fig. 5].

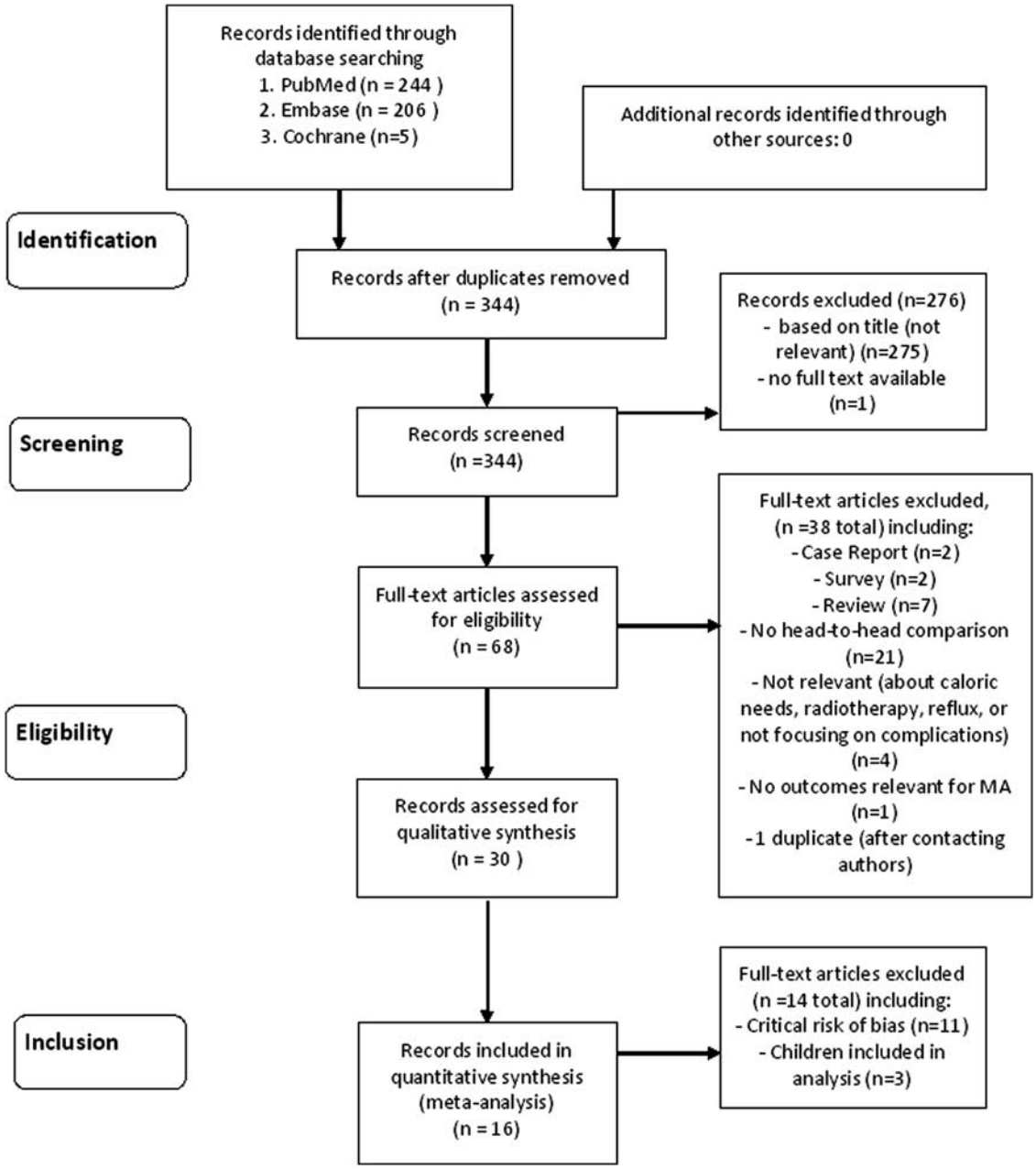

FIGURE 1. PRISMA diagram.

Funnel plots are shown in Figures 6–9, absolute complication rates are stated in Table 3. Absolute peritonitis rates are stated in Table 4.

Mean follow-up of all studies was 10 months (range, 1 to 36 mo). In the 3 studies including only HNC patients, mean follow-up was 8 months (range, 1 to 18 mo). In six studies including only MND patients, mean follow-up was 16.5 months (range, 6 to 36 mo).

Subgroup Analysis

Subgroup analysis was performed in patients with HNC (349 patients) as well as MND (529 patients). Results are shown in combined Forest plots (Figs. 2–5). In HNC patients, this revealed a significantly lower incidence in patients with PEG versus PRG with respect to tube-related complications [RD, 0.15 (0.04-0.27)], as well as procedure-related mortality [RD, 0.14 (0.005-0.27)] (borderline significant). In MND, no differences were seen.

Sensitivity Testing

Sensitivity testing for infectious complications in HNC was performed, thereby excluding the study by McAllister et al[41] because the authors expected underreporting by patients, nurses, and medical staff. RD for HNC increased from a nonsignificant 0.11 (−0.06 to 0.28) to significant 0.19 (0.05-0.32) in favor of PEG. In the overall study population, RD increased from −0.03 [−0.05 to 0.11] to 0.04 [−0.04 to 0.12], both nonsignificant.

TABLE 1. Study Characteristics

References	Country	Indication	Design	Period	PRG (n)	PEG (n)	Inclusion Criteria	Single (S)/Multi Center (M)
Silas et al[4]	USA	All	Retrospective	1.1.1997-1.1.2001	193	177	All initial PEG/PRG	S
Laasch et al[35]	UK	All	Prospective, nonrandomized	1.7.2000-1.2.2002	50	25	All initial PEG/PRG	M (3)
Grant et al[12]	UK	HN	Prospective, nonrandomized	1.1.2004-1.1.2005	50	121	All initial PEG/PRG	M (4)
Möller et al[13]	Sweden	All	Retrospective	1.1.1990-1.12.1994	94	12	All initial PEG/PRG	S
La Nauze et al[15]	Australia	All	Retrospective	1.1.2007-1.4.2009	97	80	All initial PEG/PRG	S
Allen et al[36]	USA	MND	Retrospective	1.1.2009-1.3.2012	51	57	All initial PEG/PRG	S
Laskaratos et al[5]	UK	All	Retrospective	1.1.2009-1.7.2011	40	53	All initial PEG/PRG	S
Rustom et al[37]	UK	HN	Retrospective	1.2.2002-1.2.2005	28	40	All initial PEG/PRG	S
Galaski et al[38]	Canada	All	Retrospective	1.12.2004-31.12.2005	30	44	All initial PEG/PRG	S
Blondet et al[39]	France	MND	Retrospective	1.1.1999-1.1.2005	22	21	All initial PEG/PRG	S
Chio[40]	Italy	MND	Retrospective	PEG: < 2000, PRG > 2000	25	25	FVC <50%, dysphagia, weight loss > 10%	S
McAllister et al[41]	UK	HN	Retrospective	1.1.2010-1.3.2013	89	21	All initial PEG/PRG	S
Desport et al[42]	France	MND	Retrospective	1.3.1996-1.11.2002	20	30	All initial PEG/PRG	S
McDermott[3]	UK	MND	Prospective	2.11.2010-31.1.2014	124	163	All initial PEG/PRG	M (24)
Rio et al[43]	UK	MND	Retrospective	1.1.1999-1.1.2006	121	21	All initial PEG/PRG	S
Elliot et al[44]	UK	All	Prospective, nonrandomized	1.1.1991-1.6.1994	45	33	All initial PEG/PRG	S

FVC indicates forced vital capacity; HN, head and neck; MND, motor neuron disease; PEG, percutaneous endoscopic gastrostomy; PRG, percutaneous radiologic gastrostomy.

Three studies applied antibiotic prophylaxis in both PEG and PRG. No antibiotics were administered neither before PEG or PRG placement in 9 studies, and in 1 study antibiotics were administered randomly. A difference in prophylactic antibiotic use between PEG and PRG was found in 3 studies.[4,38,39] Antibiotics were only administered in PEG placement in these studies. One did not properly report infectious complications.[39] The other 2 were excluded in sensitivity analysis because of the expected influence on the infectious complication rate. The RD in the overall study population remained nonsignificant in the overall pooled study population as well as in the subgroup.

Tumor Seeding

No tumor seeding has been reported in the included studies, neither for PEG nor for PRG patients.

Heterogeneity

There was no evidence for heterogeneity among studies for most outcomes, with I^2 values of respectively 0% for procedure-related mortality, 12% for 30-day mortality, and 39.12% for infectious complications. In tube-related complications, heterogeneity was considerable ($I^2 = 59.83\%$). For all outcomes, Funnel plots were symmetric as confirmed by nonsignificant Egger's tests.

DISCUSSION

We have performed a comprehensive meta-analysis that compared PEG with PRG on multiple outcomes and indications including 2027 patients. Overall, no differences were found between PEG and PRG with regard to mortality or infectious complications. Patients with PEG had a lower risk of tube-related complications compared with patients with PRG.

Mortality

Pooled procedure-related mortality rates were 1% both in patients receiving PEG and PRG [RD, 0.01 (−0.04 to 0.06)]. In a previous meta-analysis of 5680 patients, Wollman et al[16] reported a procedure-related mortality of 0.53% for PEG and 3% for PRG, whereas Yeung and Ho[46] reported 0.3% to 1% for PEG and 0% to 1.9% for PRG. Our results are in the same range and confirm those of previously published meta-analyses.

An absolute 30-day mortality rate of 7% in PEG versus 11% in PRG was found [RD, 0.06 (−0.01 to 0.13)]. The mortality rates found here are in line with a recent meta-analysis on 30-day mortality by Lim et al[17] including 2183 patients. However, Lim and colleagues found a statistically significant difference with regard to 30-day mortality [5.5% in PEG vs. 10.5% in PRG (OR, 0.60; 95% CI, 0.44-0.82; $P = 0.001$)]. Wollman et al[16] reported higher 30-day mortality rates for both groups: 14.7% in PEG versus 15.4% in PRG, with no significant differences between PEG and PRG. There are several methodological items that should be taken into account when comparing data from previous studies to our current analysis. First, we excluded studies that analyzed a single modality (PEG or PRG alone) instead of a direct comparison between both techniques. This selection criterion has not been applied in the previously

TABLE 2. Risk of Bias

	ROBINS-I	ROBINS-I Subscales							NOS Scale
Authors	Overall	Bias Due to Confounding	Bias Due to Selection into Study	Classification of Interventions	Bias Due to Deviations from Intended Interventions	Bias Due to Missing Data	Bias in Measurement of Outcomes	Bias in Selection of Reported Result	Overall
Silas et al[4]	Moderate	Moderate	Low	Low	Moderate	Low	Moderate	Moderate	9/9
Laasch et al[35]	Serious	Serious	Low	Low	Low	Low	Low	Moderate	7/9
Grant et al[12]	Serious	Serious	Low	Low	Low	Serious	Low	Moderate	6/9
Möller et al[13]	Serious	Serious	Low	Low	Low	Low	Moderate	Moderate	7/9
La Nauze et al[15]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate	7/9
Allen et al[36]	Moderate	Serious	Low	Low	Low	Low	Low	Moderate	6/9
Laskaratos et al[5]	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate	9/9
Rustom et al[37]	Serious	Serious	Low	Low	Low	Serious	Low	Moderate	6/9
Galaski et al[38]	Moderate	Moderate	Low	Low	Low	Moderate	Low	Moderate	7/9
Blondet et al[39]	Moderate	Low	Low	Low	Moderate	Low	Low	Moderate	9/9
Chio[40]	Moderate	Moderate	Low	Low	Moderate	Low	Low	Moderate	8/9
McAllister et al[41]	Serious	Serious	Low	Low	Low	Low	Low	Moderate	7/9
Desport et al[42]	Serious	Serious	Low	Low	Low	Low	Low	Moderate	7/9
McDermott[3]	Low	Low	Low	Low	Low	Low	Low	Low	8/9
Rio et al[43]	Moderate	Moderate	Low	Low	Low	Low	Low	Moderate	6/9
Elliot et al[44]	Serious	Serious	Low	Low	Moderate	Low	Low	Moderate	7/9

NOS indicates Newcastle Ottawa Scale; ROBINS, The Risk of Bias in Nonrandomized Studies.

published meta-analysis. Second, an important confounder is the general condition of the patient before gastrostomy, as this is a major factor influencing survival. Third, in order to minimize the influences from such effects, we have only included studies correcting for baseline differences in patients receiving PEG versus PRG. Fourth, we performed strict selection after quality and risk of bias assessment. For instance, Lim et al[17] included studies of low quality that were characterized by critical risk of bias. The earlier meta-analyses by Grant et al[12] and Wollman et al[16] entailed the same quality and selection bias issues.

Tube-related Complications

Tube-related complications occurred at rates of 6% in PEG versus 16% in PRG [RD, 0.16 (0.06-0.26)]. This difference may be caused by several factors. First, the inflatable balloon retention mechanism and locking pigtail as used in PRG is less solid than the flange used in PEG, and thereby more prone to dislocation. Secondly, the smaller tube size in PRG (10 to 14 Fr, mostly 12 Fr) compared with PEG (15 to 24 Fr, mostly 20 Fr) in all of the included studies, increases the risk of obstruction. Tube-related problems result in additional hospital visits with discomfort for patients. This aspect was not specifically addressed in the current analysis. In our opinion, these complications should be taken into consideration when deciding which type of gastrostomy is most suitable for a specific patient.

In the meta-analysis by Wollman et al,[16] tube-related complication rate was significantly higher in PEG (16%) than in PRG (12.1%), contrary to our results. It should be acknowledged that these studies were at high risk of bias without a head-to-head comparison, as previously has been discussed.

Infectious Complications

Our overall results indicate that infectious complications are not different among PEG and PRG, with absolute rates of 6% and 7%, respectively. Previous reviews or meta-analyses reported infectious rates of 8.4% in PEG[11] and 0.3% to 7.8% in PRG. The question arises whether the use of prophylactic antibiotics around gastrostomy placement may have influenced the infection rate. Sensitivity analysis by correcting for antibiotic use in the different modalities did not reveal any additional significant difference for infections between PEG and PRG.

Previously, a higher risk of peritonitis was reported in PRG than PEG, with rates of 4% versus 0% [RR for PEG 0.24 (95% CI, 0.05-1.16)].[12,47] Similarly, in our results, peritonitis was higher in PRG in almost all of the individual studies. Of note is that peritonitis need not to be the result of an intra-abdominal infection, but can be the result of leakage of gastric content and therefore cannot always be prevented by use of antibiotics.

Subgroup Analysis

HNC

Subgroup analysis revealed PEG to be favorable over PRG in HNC patients based on lower rates of procedure-related mortality and tube-related complications. A limitation of this subgroup analysis is the fact that only 3 studies

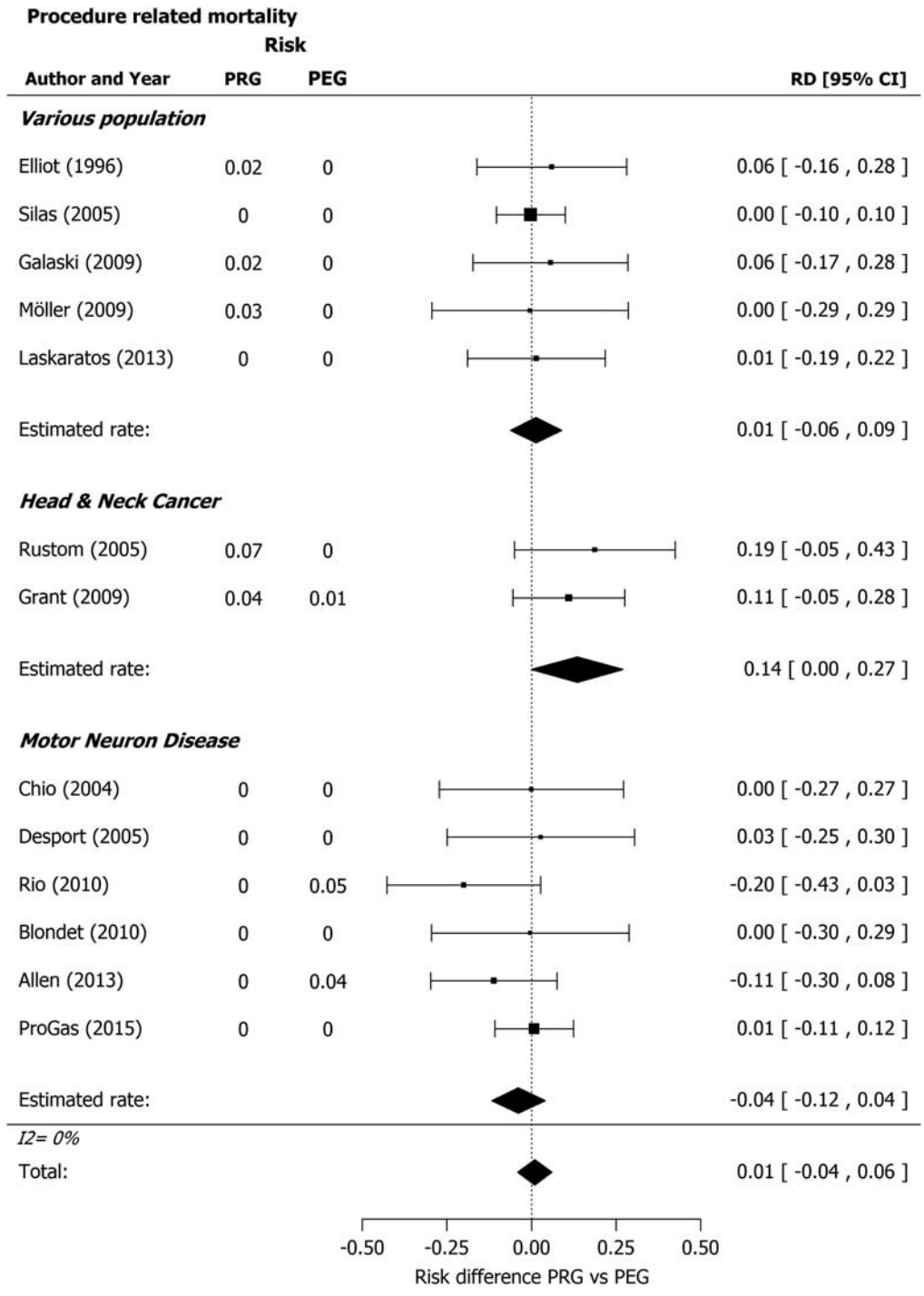

FIGURE 2. Forest plot of procedure-related mortality. CI indicates confidence interval; PEG, percutaneous endoscopic gastrostomy; PRG, percutaneous radiologic gastrostomy; RD, risk differences.

could be included, with a total of 349 patients. Sensitivity analysis revealed a significant difference in infectious complications in favor of PEG.

When analyzing the data in more depth, the difference in infectious complications, with absolute rates of 2% in PEG versus 5% in PRG, mostly entails the severe infections (eg, peritonitis). This explains the significantly higher rate in the HNC subgroup with PRG. The high rate of peritonitis contributed to the significant difference in procedure-related mortality (1% vs. 5%) in this subgroup analysis as well. Previous studies reported a lower risk of procedure-related mortality after PEG as well.[12,47]

The question arises why peritonitis is more common after PRG compared with PEG. In our analysis, only in the subgroup of patients with HNC this difference was significant. This cannot be explained by use of antibiotic prophylaxis; no

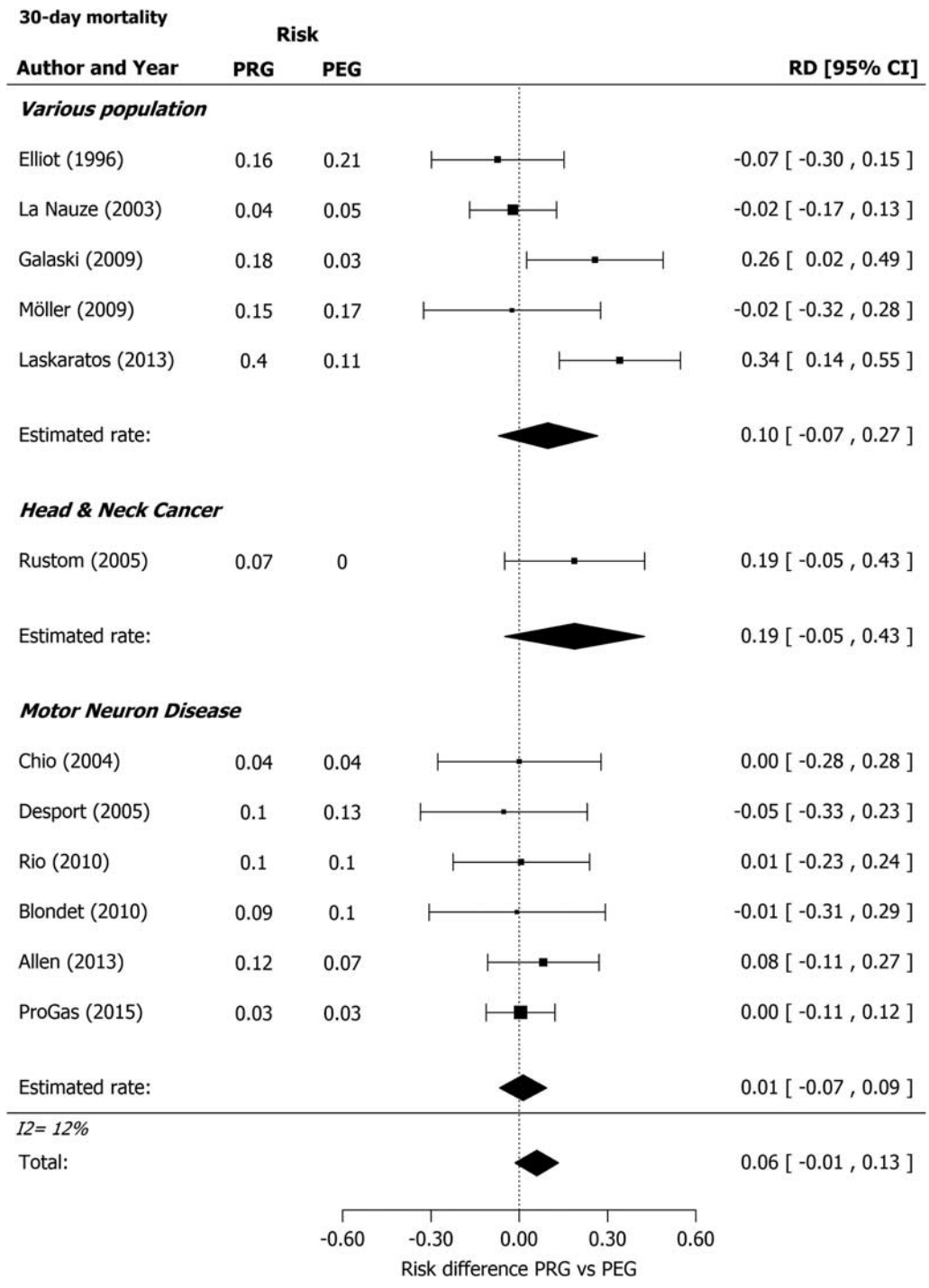

FIGURE 3. Forest plot of 30-day mortality. CI indicates confidence interval; PEG, percutaneous endoscopic gastrostomy; PRG, percutaneous radiologic gastrostomy; RD, risk differences.

differences between PEG and PRG were present with regard to antibiotic use in HNC. Rustom et al[37] described 3 patients with peritonitis (10.7%) in their PRG group, despite antibiotic prophylaxis, due to leakage. Several theories with regard to higher rate of peritonitis have been proposed. First, the higher number of dislodgements has been pointed out as a possible cause.[15,41,44] Second, also leakage, the fact that the tract is sometimes larger than the tube,[44] as well as malposition of the tube during placement, may contribute.[15] Specifically, the use of chemotherapy might also contribute, leading to a suppressed immune response with less effective wound healing and more sensitivity for bacterial wound infections.[42] This might therefore explain the fact that only in HNC patients a significant difference is seen.

In our analysis, tube-related complications were 4% in PEG and 13% in PRG in HNC patients, and thereby lower

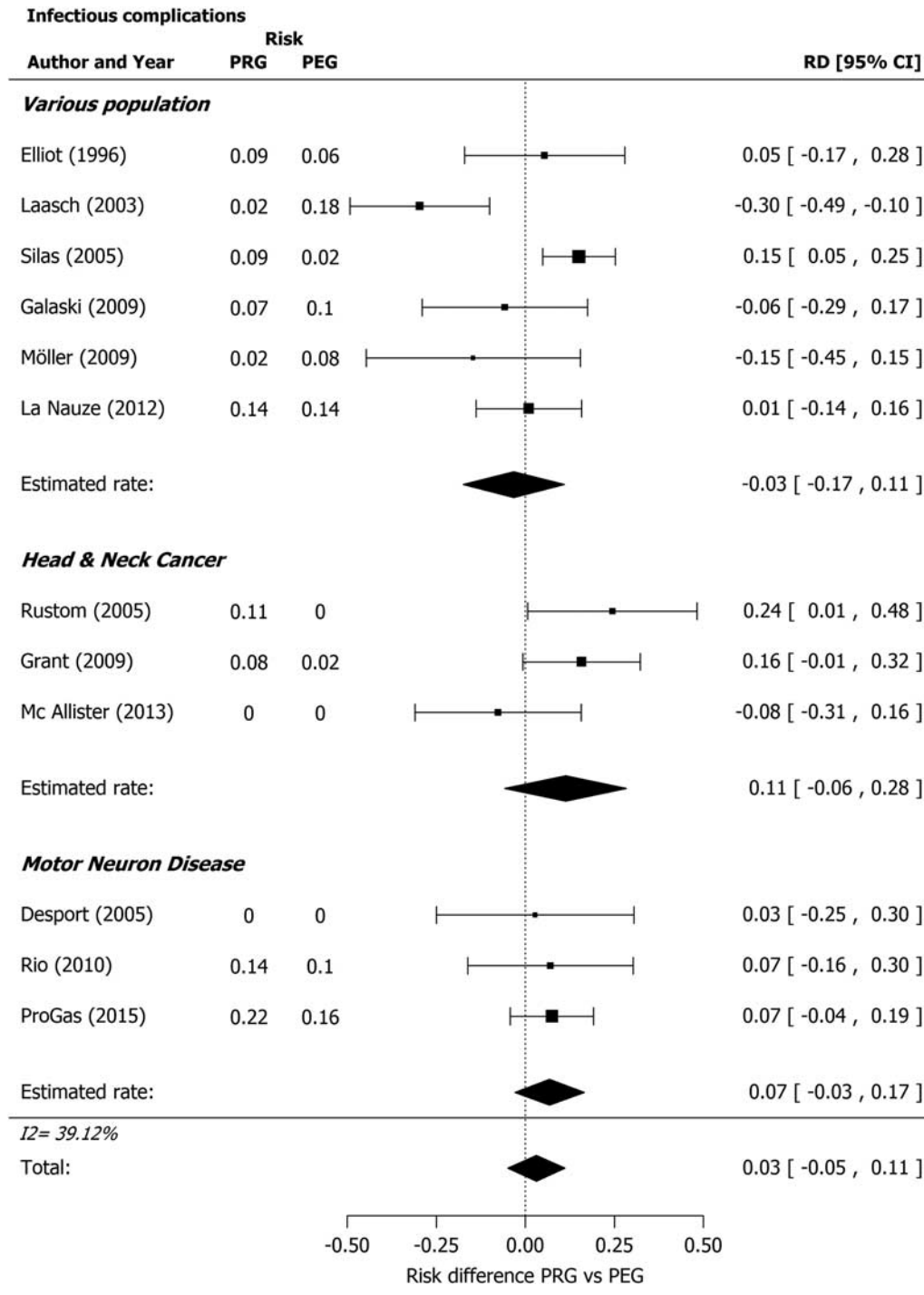

FIGURE 4. Forest plot of infectious complications. CI indicates confidence interval; PEG, percutaneous endoscopic gastrostomy; PRG, percutaneous radiologic gastrostomy; RD, risk differences.

than in the overall study population. This might be attributable to the often shorter period of use in HNC patients, where gastrostomies are often used to feed patients during chemoradiotherapy only.

In HNC patients, 30-day mortality was lower than in the overall study population (1% in PEG vs. 7% in PRG). The high number of prophylactic placements in HNC might explain this difference. The general condition before placement is better in those patients than in patients with for example MND or postcerebrovascular accident. Unfortunately, we could not perform analyses to assess certain patient characteristics in relation to outcomes on mortality or infections rates. Patient characteristics such as baseline condition could not uniformly be extracted from the included studies. Therefore, no analyses to ascertain predictors or risk factors were executed.

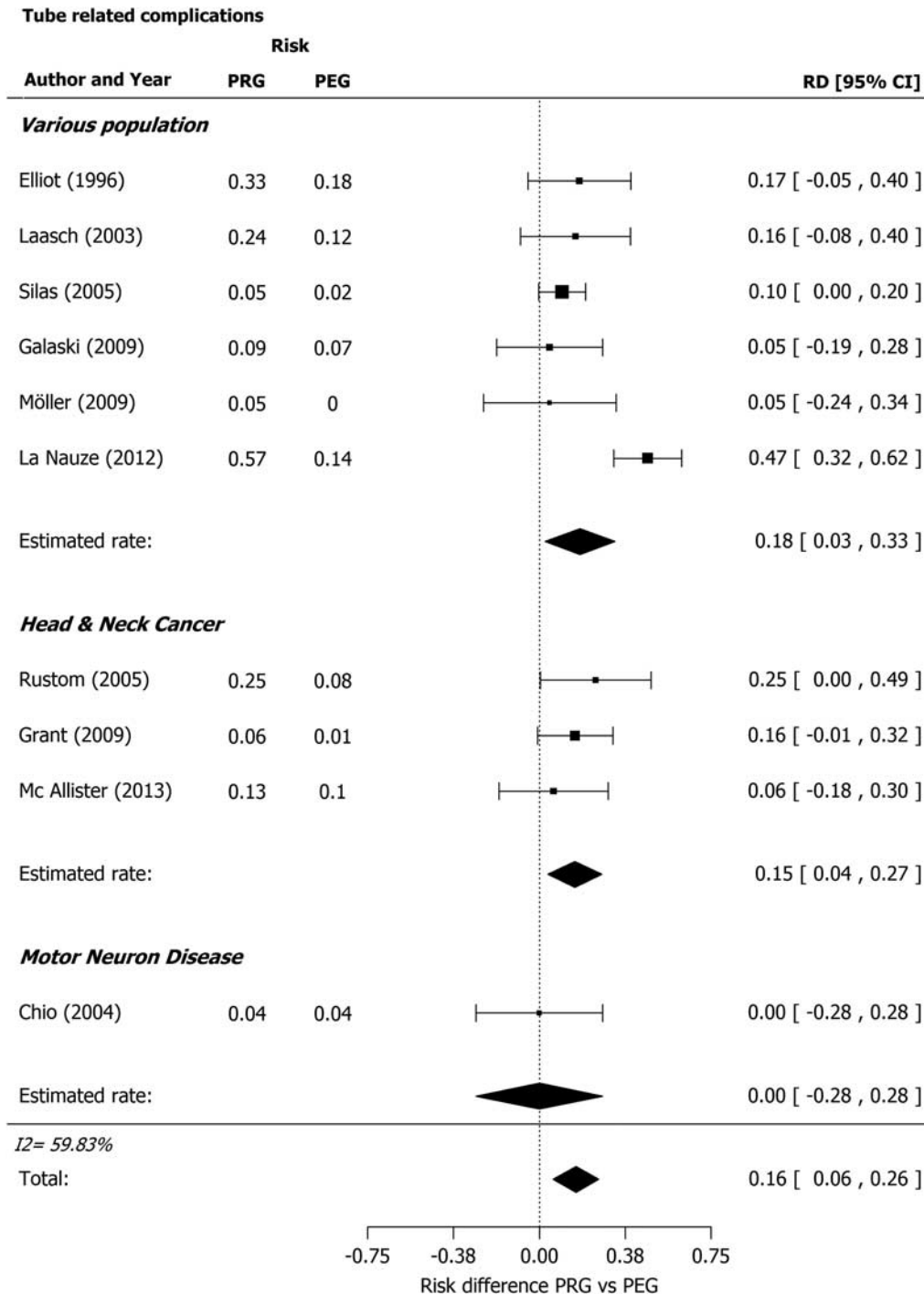

FIGURE 5. Forest plot of tube-related complications. CI indicates confidence interval; PEG, percutaneous endoscopic gastrostomy; PRG, percutaneous radiologic gastrostomy; RD, risk differences.

A much feared complication in placement of PEG in HNC is tumor seeding. Currently 49 cases after PEG have been described, whereas only one case has been described in PRG.[48–51] This has led to preferential placements of PRGs in patients with HNC. As far as the current analysis is concerned, none of the included studies reported on tumor seeding. One could argue that this apparent lack of tumor seeding could be related to an insufficient length of the follow-up period. When occurring, tumor seeding generally manifests after a mean interval of 7.8 ± 5.2 months.[44] Cases have been reported on tumor seeding occurring at a maximum of 13 months after gastrostomy placement.[50] No cases are known describing tumor seeding within 3 months after placement. With respect to the studies included in the current analyses, 5 of the studies in HNC patients had a follow-up that appeared too short for tumor seeding to

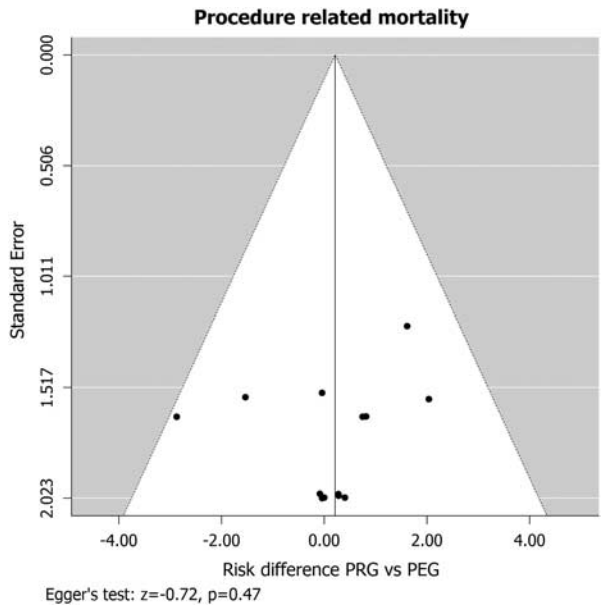

FIGURE 6. Funnel plot of procedure-related mortality. PEG indicates percutaneous endoscopic gastrostomy; PRG, percutaneous radiologic gastrostomy.

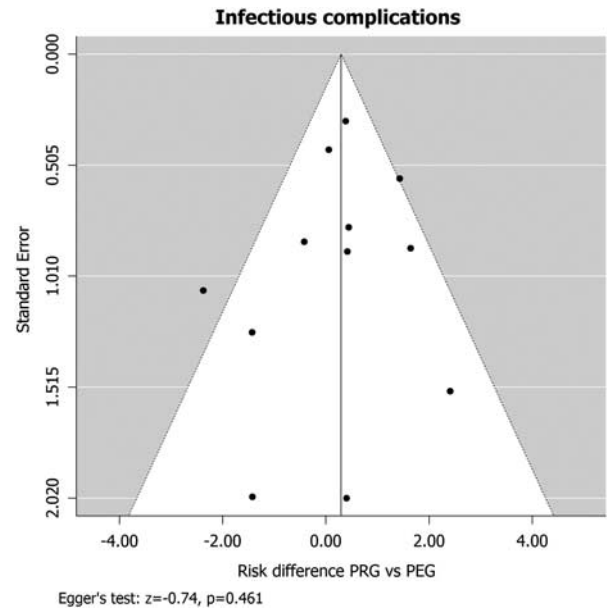

FIGURE 8. Funnel plot of infectious complications. PEG indicates percutaneous endoscopic gastrostomy; PRG, percutaneous radiologic gastrostomy.

occur (30 d),[5,13,38,41,44] however, the other 5 had sufficient duration of follow-up (6 to 18 mo), including 502 patients.[4,12,15,35,37] With this in mind, an extra subgroup analysis might seem valuable, analyzing long-term complications and in particular tumor seeding. However, in our opinion, such subgroup analysis of long-term complications is not possible due to heterogeneity in durations of follow-up resulting in reporting bias. In addition, as no tumor seeding occurred in the studies assessed, it is not possible to perform a separate analysis on this aspect and therefore no firm conclusion can be drawn with respect to the risk of tumor seeding following PEG.

Stricter patient selection may be more appropriate to prevent tumor seeding. In the included articles, indications were comparable. Clinician's or institutional preference is, in contrast, a factor of influence. For instance, Grant et al[12] reported a few clinicians in their institution that choose PRG over PEG for "risk of tumor seeding," whereas patients with similar tumors were referred for PEG as well by other clinicians. McAllister et al[41] have described a switch to PRG

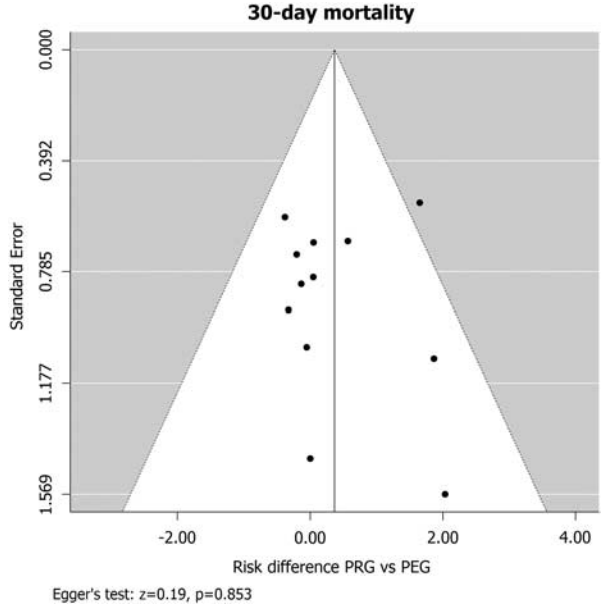

FIGURE 7. Funnel plot of 30-day mortality. PEG indicates percutaneous endoscopic gastrostomy; PRG, percutaneous radiologic gastrostomy.

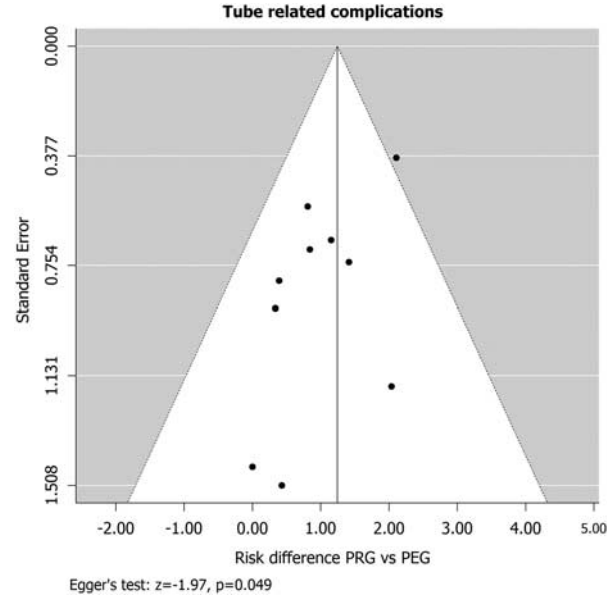

FIGURE 9. Funnel plot of tube-related complications. PEG indicates percutaneous endoscopic gastrostomy; PRG, percutaneous radiologic gastrostomy.

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TABLE 3. Absolute Rates of Complications

Complications	PEG (%)	PRG (%)
Procedure-related mortality (overall)	1	1
Various population	1	1
HNC	1	5
MND	1	1
30 d mortality (overall)	7	11
Various population	10	17
HNC	1	7
MND	6	7
Infectious complications (overall)	6	7
Various population	9	7
HNC	2	5
MND	8	13
Tube-related complications (overall)	6	16
Various population	8	19
HNC	4	13
MND	4	4

HNC indicates head and neck cancer; MND, motor neuron disease; PEG, percutaneous endoscopic gastrostomy; PRG, percutaneous radiologic gastrostomy.

during the course of their study based on local resources, despite finding a higher major complication rate. Rustom et al[37] considered all tumors eligible for PEG with the exception of obstructing oropharyngeal tumors. Apart from the risk of tumor seeding, prior surgery and/or chemoradiotherapy may contribute to narrowing the oropharyngeal tract, making PEG positioning more difficult or even impossible. The decision with regard to which mode of gastrostomy to use in patients with HNC should therefore be based on literature data, local availability and expertise with both techniques and should be personalized for each patient. Such advice is beyond the scope of the present meta-analysis.

MND

In MND, PEG, and PRG compare favorable for all outcomes, as shown in Figures 2–6. However, only a small number of studies was taken into account, so results from this subgroup analysis ought to be interpreted with caution.

Assignment of patients to either PEG or PRG was often based on clinical and practical considerations,[3,36,39] or lung function (PRG in case of an forced vital capacity <50%[42] or <60%.[43] However, baseline differences were all corrected for. In one study, baseline characteristics were similar.[40] In most studies, sedation is administered in PEG and not in PRG.[39–41,44] The largest study, however, does not mention the use of sedatives.[3]

Stavroulakis and colleagues stated in a meta-analysis among MND patients that the difference in 30-day mortality rates were 2.1% higher in PEG (rates of 4% to 13.3% vs. 4% to 10% were reported). However, these authors stated that this difference was characterized by a broad 95% CI of −6% to 11%. The meta-analysis by Lim et al[17] included only 3 studies; 2 of low quality and one not comparing PRG and PEG. However, they reported no significant differences in 30-day mortality. The discrepancies between findings across meta-analyses can to a large extent be explained by methodological differences.

TABLE 4. Absolute Peritonitis Rates

Peritonitis (overall) (%)	2.4	0.7
Various population (%)	2.1	1.4
HNC (%)	5.6	0
MND (%)	0.01	0

HNC indicates head and neck cancer; MND, motor neuron disease.

Limitations

The main limitation of our meta-analysis is that the evidence is based mostly on observational studies. Reporting bias can therefore not fully be excluded. Nevertheless, we have included the currently best available evidence, thereby providing the most accurate estimation of effects. To perform a thorough quality assessment of included studies, 2 different assessments were used (NOS and ROBINS-I). The level of evidence appears to be solid considering the low degree of heterogeneity even though only nonrandomized data are available.

CONCLUSIONS

Overall, no significant differences were found between PEG and PRG with regard to mortality or infectious complications. Patients with PEG had lower risk of tube-related complications compared with PRG. This results from higher rate of tube dislocation in the PRG group. Subgroup analysis revealed PEG to be favorable over PRG in HNC patients based on lower rates of procedure-related mortality, infectious, and tube-related complications. In MND, no differences were observed.

Considering the small differences in mortality and complications between both techniques, the local experience and availability of the technique should be taken into account in the shared decision process. In order to improve the level of evidence, future studies should be performed in a randomized controlled manner, with uniform definitions for complications and standardized follow-up. The issue of tumor seeding remains to be answered.

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