Factors Associated with Mortality after Percutaneous Endoscopic Gastrostomy

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ABSTRACT

Introduction: Percutaneous endoscopic gastrostomy (PEG) is a common procedure performed world-wide on patients with different comorbidities, with many indications and overall low morbidity. However, studies showed an elevated early mortality in patients undergoing PEG placement. In this systematic review, we review the factors associated with early mortality after PEG.

Methods: The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed. The methodological index for nonrandomized studies (MINORS) score system was used to perform qualitative assessment of all included studies. Recommendations were summarized for predefined key items.

Results: The search found 283 articles. A refined total of 21 studies were included; 20 studies cohort studies and 1 case-control study. For the cohort studies, MINORS score ranged from 7 to 12 out of 16. The single case-control study scored 17 out of 24. The number of study patients ranged from 272 to 181,196. Thirty-day mortality rate varied from 2.4% to 23.5%. Albumin, age, body mass index, C-reactive protein, diabetes mellitus, and dementia were the most frequently associated factors to early mortality in patients undergoing PEG placement. Five studies reported procedure related deaths. Infection was the most commonly reported complication of PEG placement.

Conclusions: PEG tube insertion is a fast, safe and effective procedure, but is not free of complications and can have a high early mortality rate as demonstrated in this review. Patient selection should be a key factor and the identification of factors associated with early mortality is important in the elaboration of a protocol to benefit patients.

Key Words: Critical illness, Deglutition disorders, Enteral nutrition, Malnutrition, PEG tube.

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INTRODUCTION

Gastrostomy is a well-established procedure to provide enteral nutrition in patients with dysphagia.[1] Open gastrostomy placement has been associated with several complications, including surgical site infection, dehiscence, discomfort, and others.[2,3] Gauderer et al. (1980) described a new endoscopic technique performed in 12 children and 19 adults that reduced procedure related complications.[4]

Advantages of utilizing percutaneous endoscopic gastrostomy (PEG) include performing the procedure without general anesthesia, use in patients with musculoskeletal deformities, reduced postoperative pain, and reduced risk of ileus. The patients are observed for 24 hours before starting feeding through the tube.[5]

PEG is now a very common procedure performed around the globe, performed on patients with different comorbidities, with many indications, and has overall low morbidity.[6] However, many studies showed an elevated early mortality in patients undergoing PEG placement.[2,3,7–26] We sought to perform a systematic review in order to review the factors associated with early mortality after PEG.

METHODS

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines were followed during all stages of this systematic review. These guidelines use a checklist for reviewers and readers for reporting outcomes of systematic reviews based on observational case control and cohort studies. Furthermore, it specifies how to report background, methods, search strategy, results, discussion, and conclusion. This systematic review was approved by the PROSPERO registry under the number CRD42020184209.

Eligibility Criteria

The Population, Intervention, Comparison, Outcome, Study (PICOS) design strategy was used when considering studies for this analysis. We sought observational studies in which the outcome was to assess risk factors associated to mortality in patients undergoing PEG. Observational studies included cross-sectional, case control, and cohort study designs. Exclusion criteria: studies addressing other aspects of PEG, studies focused on prognostic or surgical technique, case series, editorials, or case reports. We considered studies published from 2000 and excluded conference abstracts studies with fewer than 200 patients or that did not have an appropriate statistical analysis. Manuscripts that were not in English, Portuguese, or Spanish were also excluded.

Information Sources

The following databases were used September 1, 2021 to September 30, 2021: ScieLO (Scientific Electronic Library Online), LILACS (Literatura Latino Americana em Ciências da Saúde), MEDLINE/PUBMED, Google Scholar, manual manuscripts search from references of other articles, and manuscripts from the grey literature.

Search Criteria

We conducted the search using Medical Subjects Heading (MeSH) terms: mortality AND percutaneous endoscopic gastrostomy AND factors.

Study Selection

The following steps were performed:

(1) Identification of titles of records from databases, (2) removal of duplicates, (3) screening and selection of abstracts, (4) assessment for inclusion through full-text articles, and (5) final inclusion in the study. Two reviewers (DL and RL) performed steps 1 to 5. Inclusion or exclusion of studies was decided unanimously. In cases of disagreement, a different reviewer had the final decision (LM).

Quality Assessment

The quality of all included studies was evaluated using the PRISMA guidelines[27] and methodological Index for Nonrandomized Studies (MINORS) guidelines scoring system.[28] MINORS is a validated instrument used to assess the quality of surgical studies. This score is based on an 8-item index (global ideal score of 16) for noncomparative studies and a 12-item index (global ideal score of 24) for comparative studies. Each manuscript had a MINORS score assessed by two authors (DL and RL).

Data Extraction

Two authors (DL and RL) extracted the data from the included studies and a third author (LM) checked the extracted data. Disagreements were resolved by discussion between the three authors. The following information was extracted from each included paper: authors, country, and year of publications; study design; risk factors for mortality after PEG placement; characteristics of study participants such as mean age, sex, number, and mortality rates.

RESULTS

The systematic literature search found 283 articles, of which 9 articles were duplicates and were removed. The titles and abstracts from the remaining 274 articles were then assessed. After a careful evaluation, 140 articles did not meet study criteria and were excluded; the remaining 134 studies were thoroughly assessed within their full text. Case reports, editorials, letters to the editor, and general reviews were also removed. A refined total of 21 studies were included in the final review (**Figure 1**).

Twenty studies were cohort studies and one was a case-control study. For the cohort studies, MINORS scores ranged from 7 to 12 out of 16. The single case-control study had a 17 out of 24 score (**Table 1**). The number of patients in the above studies ranged from 272 to 181,196. Thirty-day mortality rate varied from 2.4% to 23.5%. Albumin, age, body mass index (BMI), C-reactive protein (CRP), diabetes mellitus, and dementia were the most
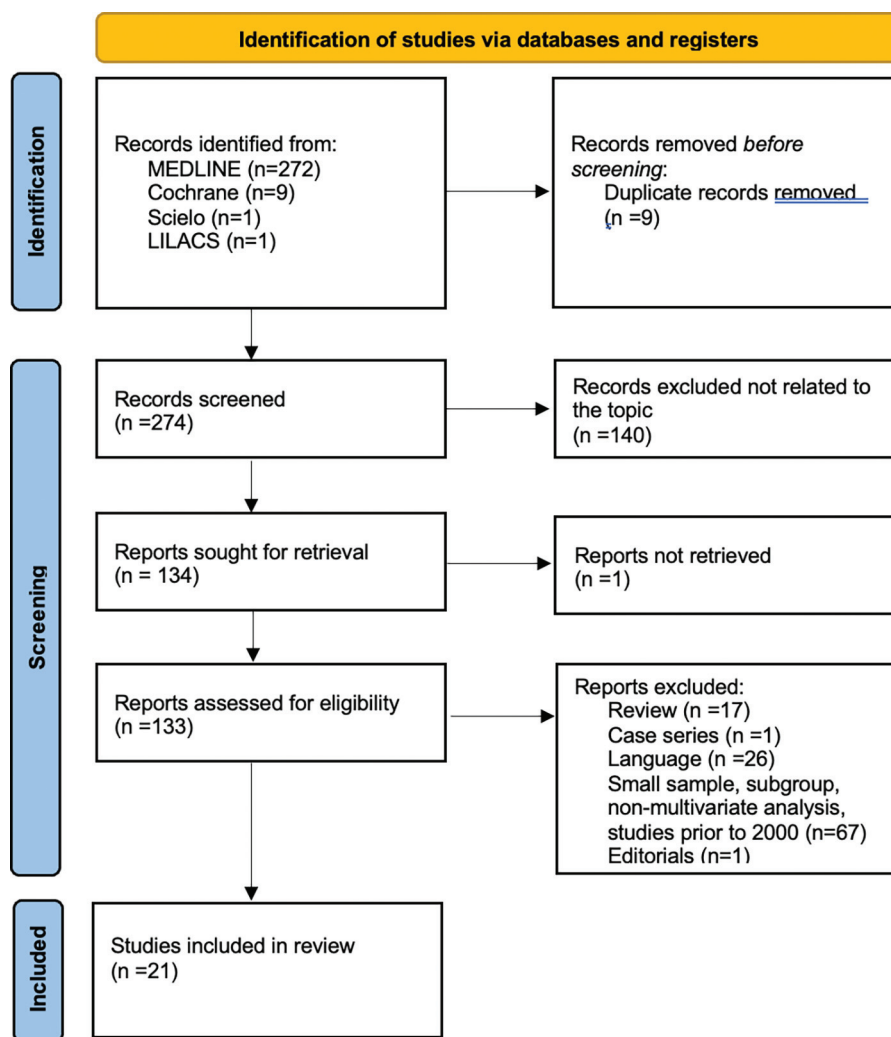
Figure 1. Preferred reporting items for systematic reviews and meta-analyses flowchart.

frequently associated factors to early mortality in patients undergoing PEG placement (**Table 2**).

Five studies reported procedure related deaths. Infection was the most commonly reported complication of PEG placement (**Table 3**).

DISCUSSION

Pioneers of the Endoscopic Feeding Tube

PEG tube placement was first described by Gauderer and Ponsky in the 1980s. Three key elements were needed to provide a safe long-term approach to the stomach without a laparotomy: reliable approximation of the stomach to the abdominal wall, protection of surrounding organs from

injury, and control of placement site.[29] Initially, the procedure was performed in 12 children (4 months to 18 years-old) and 19 adult patients.[4,30] All patients had a neurologic syndrome which prevented them from swallowing. Three years later, they reported the results of PEG in 150 patients (50 children and 100 adults) with low morbidity (10%) and no deaths related to the procedure. The most common complication was wound infection, seen in seven patients.[31] The procedure has been accepted worldwide and it was the second most common indication for upper-tract endoscopy in hospitalized patients in the United States at the end of the 20th century.[6] The impact of PEG, in combination with the development of new tube feeding formulas, the production of PEG kits by the medical device industry has significantly increased. Additionally, the increase in the number publications related to PEG was remarkable.[29]

Table 1.
Literature on Percutaneous Endoscopic Gastrostomy Tube and Factors Associated with Mortality and Quality Scoring

Authors	Year	Country	Study Design	Main Indications for PEG	Minors
Anderloni et al.	2019	Italy	Cohort	Dysphagia due to stroke	11
Arora et al.	2013	USA	Case-control	Stroke, other neurologic condition and malnutrition	17
Ayman et al.	2017	USA / Israel	Cohort	Dementia	11
Blomberg et al.	2011	Sweden	Cohort	Cancer, stroke and neurologic disease	12
Duzenli et al.	2021	Turkey	Cohort	Dementia	10
Gumaste et al.	2014	USA	Cohort	Stroke	10
Lang et al.	2004	Israel	Cohort	Dementia	9
Lee et al.	2013	Korea	Cohort	Stroke	8
Lima et al.	2021	Brazil	Cohort	Chronic neurologic dysphagia	10
Limpias et al.	2021	Japan	Cohort	Nononcological indication	10
Muratori et al.	2017	Italy	Cohort	Stroke	12
Pih et al.	2018	Korea	Cohort	Neurologic disease	7
Richter et al.	2011	Germany	Cohort	Neurogenic dysphagia	11
Sbeit et al.	2019	Israel	Cohort	Dementia	9
Smith et al.	2008	USA	Cohort	N/A	9
Suzuki et al.	2010	Japan	Cohort	Cerebrovascular diseases	12
Tabuenca et al.	2019	Spain	Cohort	Degenerative neurological diseases	10
Udd et al.	2015	Finland	Cohort	Neurologic disorders	12
Zopf et al.	2011	Germany	Cohort	Malignant disease	10
Leeds et al.	2011	UK	Cohort	Oropharyngeal malignancy	12
Macleod et al.	2021	UK	Cohort	Stroke	10

Abbreviations: PEG, percutaneous endoscopic gastrostomy.

Indications

The classic indication for PEG tube placement is dysphagia secondary to neurologic disorders, head and neck or esophageal cancer, and dementia. In our review, 12 studies had neurologic disease as the main indication for PEG.[2,7,9,10,12–14,16,18,19,21,23] Four studies had dementia as its main indication for PEG.[8,11,20,24] Two recent reviews with meta-analysis showed no benefit in survival for patient with dementia and enteral tube feeding.[32,33] The European Society for Clinical Nutrition and Metabolism guidelines on home enteral nutrition states that indication for PEG should not be used in advanced dementia or in patients with life expectancy shorter than 30 days.[34]

Factors Associated with Early Mortality After PEG

Despite being regarded as a safe, rapid, and effective in providing an enteral feeding in patients, PEG tube placement is not free of complications and is associated with high early mortality rates in some studies.[7,11,12,18,24] Moreover, many studies have investigated factors associated with 30-day mortality after PEG in different populations.[2,3,7–24] They identified heterogeneous factors that can be grouped in two large categories: factors associated with advanced signs of malnutrition and factors associated with chronic diseases.

Seven studies in our review identified low albumin as a factor associated with mortality.[10,14,20–24] High levels of CRP was also independently associated with mortality in four studies.[9,14,21,22] A prospective cohort by Blomberg et al. (2011) showed that the combination of low albumin and high CRP levels increases 30-day mortality by more than sevenfold after PEG insertion.[14] Chronic inflammatory states negatively affect metabolism and the inflammatory system, causing appetite loss and cachexia. The combination of low albumin and high CRP levels may be an indication of a severely ill patient.[14] Findings from Udd et al. (2015) corroborate this idea of frailty as an important

Table 2.
Clinical Outcomes and Factors Associated with Mortality

Authors	N	Age	30-Day Mortality	PEG Related Mortality	Factors Associated with Mortality
Neurologic disease					
Anderloni et al.	557	72.9 (15.5)	5.20%	0	Age, BMI, INR
Arora et al.	181,196	71 years (18–116 y)	10.8%*	N/A	Metastatic cancer, CHF, Renal failure, liver disease, pulmonary circulation disease, chronic pulmonary disease
Lima et al.	277	73.3 (15.7)	13%	N/A	Preoperative ICU hospitalization and low hemoglobin
Suzuki et al.	931	81.4 ± 7.8	9.80%	8 (0.8%)	Older age, higher CRP, higher BUN, lower albumin, male gender, and a previous history of ischemic heart disease*****
Macleod et al.	808	69 (14–98 years)	14%	N/A	Age > 60 years , low albumin, high CRP, low lymphocyte count
Muratori et al.	438	77.3 (12.7)	4%	0	Serum sodium ≥ 150
Pih et al.	401	68 (57 – 77)	5%	2 (0.4%)	Platelet count $< 100,000/\mu$L and CRP ≥ 5 mg/dL
Richter et al.	1041	64 ± 14.65 (18 – 97)	5.80%	0	Cancer
Gumaste et al.	284	70.5 ± 16.4	6%	0	Female sex, positive urine cultures, and low serum albumin levels
Udd et al.	401	64 ($\pm$ 15) median	11%	2 (0.4%)	≥ 75 years of age, ASA IV, CCI ≥ 4, BMI < 18.5 kg/m2, ongoing antibiotic therapy
Tabuenca et al.	289	70.1 (13.6)	13.20%	N/A	Older age, higher comorbidity and aspiration pneumonia*****
Lee et al.	1,625	64.99 ± 14.51	2.40%	2 (0.1%)	Low albumin and high CRP levels
Cancer					
Zopf et al.	787	60.7 ± 14.2	6.50%	N/A	Higher age, lower BMI, diabetes mellitus
Leeds et al.	403	200 (< 64) / 203 (> 64)	12.70%	N/A	Age/ albumin
Dementia					
Ayman et al.	392	82.9 ($\pm$ 8.48)**	9.40%	N/A	Dementia
Duzenli et al.	309	78.1 ± 12.2	12.60%	0	Higher urea levels and higher CRP to albumin ratios
Lang et al.	502	74 (15)***	8%	0	Albumin < 3, COPD, diabetes mellitus
Sbeit et al.	272	77.3 ± 14****	23.50%	N/A	Older age, higher creatinine level, elevated CRP-to-albumin ratio
Others					
Blomberg et al.	484	66 (±14)	12%	0	Low albumin and high CRP levels
Limpias et al.	388	72.04 (13.7)	3.90%	3 (0.7%)	Advanced cancer, low albumin, and high CRP levels

Authors	N	Age	30-Day Mortality	PEG Related Mortality	Factors Associated with Mortality
Smith et al.	714	68 (16)	22%	0	Older age, cancer, heart disease, nonwhite race, dialysis*****

*in hospital mortality.
**dementia group.
***hospitalized patients.
**** patients who died 30 days after PEG.
*****predictors of post-PEG death, not specifically 30-days.
Abbreviations: PEG, percutaneous endoscopic gastrostomy; INR, international normalized ratio blood test; CCI, craniocervical instability; ICU, intensive care unit; CRP, C-reactive protein; ASA, American Society of Anesthesiologists; CHF, chronic hearth failure; COPD, chronic obstructive pulmonary disease.

factor associated with early mortality as characteristics associated characteristics included: age ≥ 75 years, ASA IV, craniocervical instability ≥ 4, BMI < 18.5 kg/m^2, and ongoing antibiotic therapy.[18]

Most studies had patients with mean age varying from 60.7 to 82.9 years. Advanced age was one of the factors associated with mortality in several studies.[3,7,10,11,13,18,33] Low BMI was also associated with mortality in different studies.[3,13,18] Regarding gender, there is no consensus in the literature. Gumaste et al. showed female gender associated with early mortality.[23] However, Suzuki et al. reported male sex as a factor associated with mortality.[10]

Our previous study with 277 patients showed intensive care unit hospitalization of two weeks before the procedure as a factor associated with 30-day mortality.[2] Our first study had identified this factor associated with eight-week mortality. At the time, we did not have enough power to calculate factors associated with 30-day mortality and it was not included in this review.[5] This was the first study with a large cohort to identify this factor which also can be explained by the frailty of the patient. Diabetes mellitus was also a risk factor in two studies.[3,20] A multicenter retrospective cohort study by Muratori et al. (2017) with 438 patients identified hypernatremia (Na ≥ 150 mmol/L) independently related to one-month mortality (odds ratio 25.4; 95% confidence interval 7.4 – 86.8; $P < 0.0001$). They also found cancer, elevated CRP levels, and low albumin independently related to three-month mortality.[19]

In our review, 30-day mortality rate varied from 2.4% to an alarming 23.5%. Sbeit et al. (2019) reported a high mortality rate (23.5%) and its associated factors were older age, high creatinine level and elevated CRP-to-albumin level.[11] Duzenli et al. (2021), found a 30-day mortality rate of 12.6%, and also found that an elevated CRP to albumin level as a predictor of mortality.[24] Arora et al. (2013) performed a case-control study with more than 180,000 patients from the US Nationwide Inpatient Sample and found an in-hospital mortality of 10.8% showed metastatic cancer, chronic heart failure, renal failure, liver disease, pulmonary circulation disease, and chronic pulmonary disease as predictors of mortality.[12]

Complications

PEG tube placement is not free of complications, including death related to the procedure. In our review, complications related to PEG placement varied from 1.3% to 27.4%, wound infection being the most reported, followed by tube leakage and avulsion. Five studies reported death related to the procedure.[9,10,18,21,22] Lee et al.[21] reported two deaths due to peritonitis and septic shock within 48 hours after the procedure and no apparent perforation of the gastrointestinal tract or PEG dislodgment. Udd et al.[18] and Pih et al.[9] also reported two deaths. They considered an aspiration pneumonia as death-related to PEG and uncontrolled infection in a patient with cirrhosis that developed peritonitis after PEG placement.[9] Udd et al. reported peritonitis as the reason for the PEG-related deaths. Limpias et al. reported three deaths: one due to sepsis and two due to aspiration pneumonia.[22] Suzuki et al. did not report the reasons for PEG-related deaths.[10]

To PEG or Not to PEG

Several authors have addressed patient selection, indications, and timing for PEG tube insertion.[35–37] The European Society of Gastrointestinal Endoscopy 2021 guidelines recommends early PEG tubes in patients with chronic degenerative diseases or select types of malignancy who have

Table 3.
Complications Associated with PEG Placement

Authors	Complications Related to PEG n (%)	Most Common Complications Related to PEG
Neurologic disease		
Anderloni et al.	28 (4.8)	Infection
Arora et al.	N/A	N/A
Lima et al.	59 (21.3)	Tube avulsion
Suzuki et al.	N/A	N/A
Macleod et al.	N/A	N/A
Muratori et al.	25 (5.7)	Peristomal cutaneous inflammation
Pih et al.	38 (9.5)	Pneumoperitoneum
Richter et al.	141 (13.5)	Local infection
Gumaste et al.	8 (2.8)	Bleeding in PEG site and peristomal infection
Udd et al.	110 (27.4)	Skin problems
Tabuenca et al.	79 (27.3)	Digestive complications
Lee et al.	215 (13.2)	Fever without evident infection
Cancer		
Zopf et al.	N/A	N/A
Leeds et al.	N/A	N/A
Dementia		
Ayman et al.	N/A	N/A
Duzenli et al.	33 (13)	Tube leakage
Lang et al.	25 (6)**	Wound infection
Sbeit et al.	N/A	N/A
Others		
Blomberg et al.	50 (11)*	Peristomal infection
Limpias et al.	86 (22.2)	PEG site infection
Smith et al.	9 (1.3)	Tube displacement

*Only reports peristomal infection.
**Hospitalized patients.

weight loss despite continued oral nutrition.[38] These studies also suggest PEG tube insertion is contraindicated in patients with a life expectancy shorter than 30 days.

Dietrich et al. (2020) addresses the timing of PEG, suggesting that an early indication prior to catabolism and weight loss may benefit patients.[39] It may be reasonable to initiate tube feeding when patients are still showing early signs of eating problems or malnutrition rather than starting after late signs of malnutrition have started, or holding enteral feeding all together.[5] This is a challenging situation where a multidisciplinary team should give support to the family in the decision-making process. The use of a multidisciplinary team meeting decreased 30-day mortality from 10% to 6.6% in a study by Bond et al.[40]

A Mortality Predicting Score

Two studies tried to identify the best patients to benefit from PEG placement using the Sheffield Gastrostomy Score.[25,26] Leeds et al. (2009) created this score in a study with 403 patients. This score utilized two variables, age and albumin. The authors used this score to estimate a 30-day mortality for patients. However, the score was not designed to decide if the patient should undergo PEG placement, but rather to help clinicians, patients, and their families with the informed consent.[25] Macleod et al. (2021) applied the same score in a cohort of 808 patients and found that the score has a reasonable capacity to predict 30-day mortality after PEG. Furthermore, they suggested a revision and remodeling in the Sheffield score as

they identified elevated CRP, low lymphocyte count and outpatient status as factors associated with increased risk of mortality.[26]

MINORS Qualitative Assessment

All studies lost points in the MINORS score system due to a lack of unbiased assessment.

Furthermore, none of the studies were blinded and only one study was a case-control study. None showed information about the prospective calculation of sample size and some studies were not clear about the inclusion of consecutive patients. Many were retrospective cohorts and data was not prospectively collected.

Strengths and Limitations

The limitations of our study are possible language and publication bias. We included only manuscripts published in English, Spanish, and Portuguese. Despite the broad literature search, we may not have identified all studies regarding this topic, or a viable study may be removed due to not meeting the inclusion criteria.

The main strength of this study lies in the rigor of our systematic review process. A comprehensive literature search was performed across a variety of databases. The review was registered on PROSPERO, an international database of prospectively registered systematic reviews covering many health-related outcomes. PROSPERO aims to provide a list of systematic reviews to help avoid duplication and reduce reporting bias by enabling comparison of the review with what was initially planned in the protocol.

We included studies with large samples (n >200) and where a proper statistical analysis was employed. Finally, PRISMA reporting guidelines were followed, and the well-validated MINORS was used to perform the qualitative analysis of all studies. PRISMA was developed to help systematic reviewers transparently report what was done, how it was done, and what the authors found.[41] MINORS is a valid instrument designed to evaluate methodological quality of nonrandomized studies, comparative or noncomparative. It has been used extensively in the literature.[28]

CONCLUSIONS

PEG tube insertion although is a fast, safe, and effective procedure, is not free of complications and can have a high early mortality rate as demonstrated in this review.

Patient selection should be a key factor when discussing this procedure with patients and their families, and the identification of factors associated with early mortality is important in the elaboration of a protocol to benefit patients.

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