Use of Noninvasive Ventilation During Feeding Tube Placement

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Summary

Parenteral nutrition is indicated in amyotrophic lateral sclerosis (ALS) when dysphagia, loss of appetite, and difficulty protecting the airways cause malnutrition, severe weight loss, dehydration, and increased risk of aspiration pneumonia. The aim of this review is to compare percutaneous endoscopic gastrostomy (PEG), radiologically inserted G-tube (RIG), and percutaneous radiologic gastrostomy (PRG) in patients with ALS, performed with or without noninvasive ventilation (NIV). We searched PubMed, MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), the EBSCO Online Research Database, and Scopus up to December 2015. A priori selection included all randomized controlled trials (RCTs), quasi-randomized trials, and prospective and retrospective studies. The primary outcome was 30-d survival. We found no RCTs or quasi-RCTs. Seven studies about the implementation of the PEG/RIG procedure during the use of NIV and 5 studies without NIV were included. In another study of 59 subjects undergoing open gastrostomy, all with vital capacity < 30% of normal, 18 of whom were dependent on continuous NIV at full ventilatory support settings, there were no respiratory complications. Thus, the use of NIV during the implementation of these procedures, especially when used at full ventilatory support settings of pressure preset 18–25 cm H_2O, can support alveolar ventilation before, during, and after the procedures and prevent respiratory complications. The procedures investigated appear equivalent, but the methodological quality of the studies could be improved. Possible benefits with regard to nutrition parameters, quality of life, and psychological features need to be further investigated. *Key words: amyotrophic lateral sclerosis (ALS); noninvasive ventilation (NIV); gastrostomy; clinical effectiveness; quality of life (QOL); systematic review.*
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Introduction

Amyotrophic lateral sclerosis (ALS) is a neurological disorder characterized by a progressive degeneration of the motor neurons. Bulbar onset affects 25–30% of all patients, but all patients surviving long enough eventually develop severe bulbar-innervated muscle impairment that causes dysphagia, aspiration of food and saliva, and severe dysarthria.[1,2] Dysphagia causes malnutrition, dehydration, weight loss, and an increased risk of aspiration pneumonia[3] and is an important negative prognostic factor in ALS.[4] Moreover, poor appetite due to depression, reduced ability to feed oneself, and hypermetabolism can also lead to decreased oral feeding and subsequent malnutrition/dehydration.[5] Malnutrition increases muscle weakness, increases fatigue,[6] and decreases respiratory capacity.[7] This situation creates a vicious cycle, leading to the development of depression and decreasing quality of life (QOL).[8] Dietary changes are thus necessary to maintain proper caloric intake and prevent aspiration.[9,10] When oral feeding becomes insufficient, enteral nutrition in patients with ALS can be guaranteed through gastrostomy placement. The procedures include percutaneous endoscopic gastrostomy (PEG), radiologically inserted G-tube (RIG), percutaneous radiologic gastrostomy (PRG), and open gastrostomy.[11,12] Although percutaneous gastrostomy procedures are more frequently employed than those requiring general anesthesia,[13] the frequency of PEG/RIG/PRG insertion varies widely across different countries and studies.[9] To prevent and manage respiratory symptoms, the use of noninvasive ventilation (NIV), which has become synonymous with CPAP and low span (< 10 cm H_2O) bi-level PAP, is being used during the insertion of feeding tubes for many patients with FVC $< 50\%$ of predicted normal.[14] It should be noted, however, that in many centers, patients become dependent on continuous NIV at full ventilatory support settings. They require either high span (15–25 cm H_2O) bi-level PAP or intermittent positive-pressure ventilation at full ventilatory support settings, delivered via noninvasive oral, nasal, or oronasal interfaces. Generally, portable ventilators are used with active circuits on volume control mode with exhaled tidal volume > 800 mL or pressure preset at 17–25 cm H_2O.[15] Many of these patients do not undergo gastrostomy until their vital capacities (VCs) are $< 10\%$ of predicted normal.[15]

There is no consistent evidence about which of the procedures is the safest and most effective in ALS. Although literature concerning RIG/PRG and open gastrotomies is scarce, frequency of PEG in patients with ALS, which was only around 2.7% in the early 1970s,[16] has more recently increased.[12] Indeed, it has been performed on 13–40% of patients with ALS in the United States,[17,18] 14–38% in the United Kingdom,[19,20] 11–24% in Italy,[21–23] 21–60% in Japan,[9,24] and 20% in Canada.[25] Meanwhile, the apparent increasing demand for RIG/PRGs and their possible advantages and disadvantages compared with PEGs in maintaining adequate nutrition and weight stabilization have not been assessed systematically and remain unclear.[14,26] To the best of our knowledge, there has been only a single attempt to provide the best evidence to support procedures for parenteral nutrition, and it only compared PEG tube feeding with oral feeding for patients with ALS.[9] The main aim of this review is to compare PEG, RIG, and PRG, with and without NIV use, for efficacy and safety.

Methods

Literature Search Strategy

The primary literature search method employed PubMed, MEDLINE, EMBASE, the Cochrane Central Register of Controlled Trials (CENTRAL), the EBSCO Online Research Database, and Scopus. The search strategy used a combination of subject heading terms appropriate for each database and key words such as "amyotrophic lateral sclerosis," "ALS," "noninvasive ventilation," "NIV," "gastrostomy," "feeding tube," "procedure," "placement," "percutaneous endoscopic gastrostomy," "PEG," "percutaneous radiologic gastrostomy," "PRG," "radiologically inserted G-tube," and "RIG" with Boolean terms such as AND and OR. These words were searched for in the title, abstract, key words, and MeSH (medical subject headings) terms. The reference lists of all eligible trials were checked, and the Cited By research tool was used. Findings were limited to English language and to human studies between 1980 and 2015. No unpublished studies or gray literature were considered (Fig. 1).

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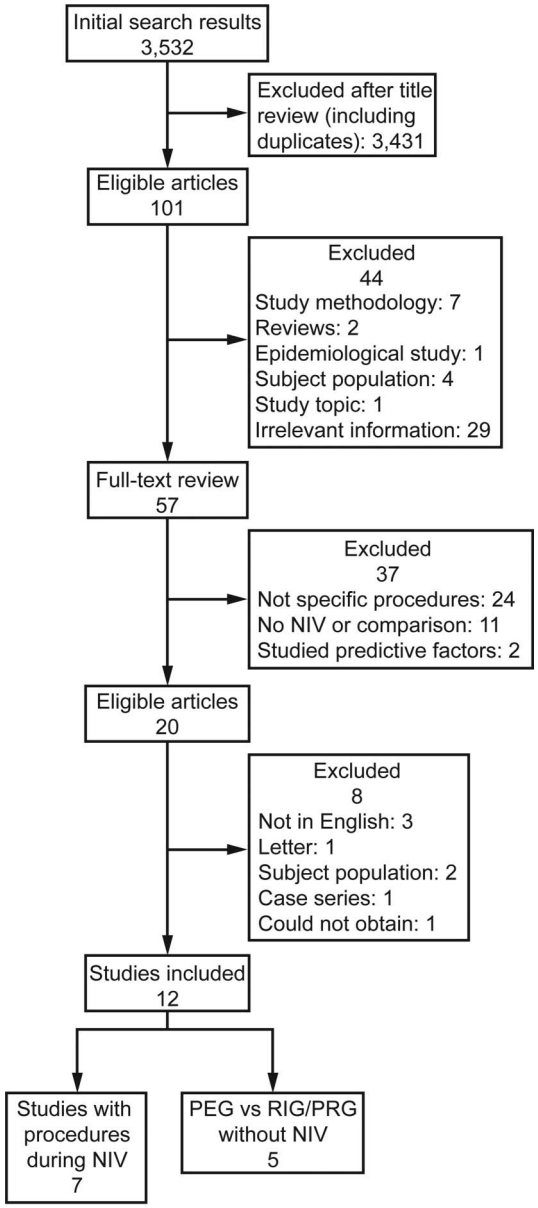

Fig. 1. Flow chart. NIV = noninvasive ventilation; PEG = percutaneous endoscopy gastrostomy; RIG = radiologically inserted G-tube; PRG = percutaneous radiologic gastrostomy.

Inclusion and Exclusion Criteria

Types of Studies. Before proceeding with the literature search, we defined the inclusion and exclusion criteria. We considered randomized controlled trials (RCTs), quasi-RCTs, prospective, and retrospective studies. Single cases, case series, and editorial letters were excluded from the data analysis.

Types of Participants. In-patients or day-hospital patients, diagnosed with definite, probable or possible ALS, according to El Escorial[27] and revised El Escorial criteria,[28] were included.

Types of Intervention. The primary intervention explored was placement of PEG or RIG/PRG during the course of ALS. There were no publications found comparing other methods. Subjects who underwent gastrostomy while using NIV or not were also compared.

Types of Outcome Measures. Primary outcome was survival time at 30 d from time of placement of the feeding tube. Secondary outcomes were complications (ie, hemorrhage, aspiration pneumonia, infections), their frequency, and the rate of death during the feeding tube placement.

Study Selection

In the primary literature search, 3,532 potential articles were identified. Two authors independently evaluated the title and abstract of each study to determine whether it met the inclusion criteria and excluded 3,431 papers because they were duplicates. Whenever titles or abstracts appeared to be relevant, they examined the full text. Any disagreement on selection was discussed with a third author. In total, 44 articles were excluded because they cited PEG or RIG/PRG but did not explain the procedure placement or excluded due to irrelevance of information and an absence of methodology. Additionally, 3 studies were excluded because they were not in English, one was not obtainable, and 4 did not meet the inclusion criteria (Fig. 1). In conclusion, this review included 5 studies comparing 2 or more feeding tube placements without NIV and 7 studies where the same procedures were used with NIV.

All of the included studies met the 3 key criteria, as required by the Cochrane Effective Practice and Organisation of Care Group (EPOC Review Group) for Control Before and After Studies. They include at least 2 intervention sites and 2 control sites (Table 1). Similarly, the pre- and the post-timing of the intervention groups are the same, and the 2 groups are comparable on key characteristics.[29]

The Interventions

The main features of the procedures as described in the studies are briefly illustrated below.

Percutaneous Endoscopic Gastrostomy. An endoscope is inserted down the esophagus into the stomach, under topical anesthesia with lidocaine or a derivative product. Sedation is not offered routinely, and, when present, midazolam (2.5–5 mg) or fentanyl (0.1 mg) is used. The light at the tip of the tube shines through the stomach and skin, directing the surgeon to the spot where the PEG tube should be inserted. The surgeon makes a small incision through the skin and the wall of the stomach and inserts the PEG

Table 1. List of Principle Inclusion Criteria

Study Characteristics	Inclusion Criteria
Study design	RCT, quasi-RCT, prospective, and retrospective
Period	1980–2015
Language	English
Participants	Definite, possible, or probable ALS, according to El Escorial and revised El Escorial criteria
Condition	In-patients or day-hospital patients
Interventions	PEG/RIG/PRG during the use of NIV vs PEG/RIG/PRG without NIV
Primary outcomes	Survival time at 30 d
Secondary outcomes	Complications and their frequency rate; death

RCT = randomized controlled trial
ALS = amyotrophic lateral sclerosis
PEG = percutaneous endoscopic gastrostomy
RIG = radiologically inserted G-tube
PRG = percutaneous radiologic gastrostomy
NIV = noninvasive ventilation

tube through it. Once the PEG tube has been inserted, the endoscope is removed.

Radiologically Inserted G-Tube. A nasogastric tube is inserted into the nose and directed into the stomach to insufflate it. It is removed immediately after the procedure is terminated. A RIG tube is inserted with the aid of fluoroscopy for the interventional radiologist to view real-time images of the patient's internal organs to find the right spot to insert the tube through the skin into the stomach (this is the main difference from the PRG procedure). To help to identify and avoid the intestines, barium is given the night before. A gastroplexy is held in place with sutures called T-tacs that are removed about 14 d after the RIG.

Percutaneous Radiologic Gastrostomy. A nasogastric tube is placed shortly before the procedure to insufflate the stomach. Local analgesia and sedation may or may not be used. Joshine N-butyl-bromide (5 mg intravenously) is administered to reduce gastric motility and for adequate distention, thus decreasing the risk of puncture of colon, liver, and other organs. With the patient supine, fluoroscopy of the abdomen is undertaken, and the position of the nasogastric tube is identified. A site for gastric puncture is chosen equidistant from the greater and lesser curves of the stomach. The needle is inserted into the air-filled stomach under fluoroscopic guidance. Aspiration of air bubbles into the syringe confirms intragastric positioning of the needle. Normally, a 12 French polyurethane tube is used and fixed by means of a loop. During the first day after the procedure, the patients receive only parenteral nutrition. During the entire procedure, NIV users are administered NIV generally via a nasal interface.

Percutaneous Endoscopic Gastrostomy During NIV in Our Experience. A respiratory therapist trains NIV-naïve patients in NIV via nasal and nasal prong interfaces before the procedures. There are at least 5 training sessions in the patients' homes, at the clinic, or at the hospital as they prefer. Its effectiveness is assessed by ambient air O_2 saturation monitoring and patient acceptance. The respiratory therapist guides the patient to the endoscopy unit, where sedation with local anesthesia with 2.5 mg of midazolam is initiated, and biological variables, such as S_{pO_2}, heart rate, breathing frequency, and blood pressure, are constantly monitored. During the entire procedure, the respiratory therapist sustains the patients on NIV via nasal interface or nasal prongs. No study comparisons were found for per-oral image-guided gastrostomy or for open gastrostomy.

Data Extraction and Coding

Two authors independently extracted data according to the inclusion criteria. Data included year, country, study design, site of onset of ALS, NIV, CoughAssist (Respironics, Murrysville, Pennsylvania) use, type of NIV interface, procedure of feeding tube placement, use of sedation, sex, number of subjects, mean age, measuring tools, dropout rate, exclusion criteria, and main findings. The principal statistical analyses were annotated. Nutritional markers, such as body mass index, hemoglobin, and serum albumin level, were also evaluated. QOL as measured by validated instruments was recorded as well. Finally, the rate of complications and types of adverse events, both during and after the procedures, were reviewed.

Risk of Bias Assessment

No RCTs were identified. Therefore, there was insufficient detail to make a judgment, using the assessment tool of the Cochrane Collaboration.[30] However, 2 authors independently attempted to obtain an overall description of the body of evidence to integrate it into a narrative synthesis as the EPOC Review Group suggests.[29] None of the trials reported methods of both random sequence generation and allocation concealment of the patients recruited.

The death and complication rates were uniformly reported except in 2 studies.[31,32] The dropout rate was not specified. Additionally, none of the studies was blinded due to the intervention itself. The follow-up time-points were only specified in one study.[33] In the other studies, the evaluations at 20–30 d before and after the procedure were noted but there was no further follow up. Finally, the integrity of the study designs was limited due to the lack

of randomization, a task that would have been extremely difficult to accomplish for both ethical and clinical reasons.

Methodological Quality

The Newcastle–Ottawa Quality Assessment Scale was used to evaluate the methodological quality of the cohort, case-control, and prospective or retrospective studies included.[34] According to this checklist, the required independent validation was guaranteed in every study. The representativeness of the cases and the selection and definition of controls were present in each study that considered the use of NIV. However, these items did not fully satisfy requirements, nor were there statements or descriptions about them. The comparability of controls was well or partly stated in the majority of the included studies, except for one. Determination of exposure was adequate; on the contrary, follow-ups and non-response rate were either not reported or were poorly described.

Description of Studies

After eligibility assessment, 20 articles were evaluated. Among these, 12 studies were included in the qualitative synthesis. In particular, 7 studies were about PEG or PRG procedures during NIV, whereas the other 5 focused on the comparison of PEG and RIG/PRG without NIV during the procedure (see supplementary Tables 1 and 2 at http://www.rcjournal.com). Controlled studies that considered the outcomes of interest are reported in the following sections.

Included Studies

Not all of the required data were available in the studies, but they had to be extrapolated from the text if relevant to the primary outcomes (ie, mortality, adverse events). In addition, although we found no open gastrostomy studies that compared efficacy with other methods, the fact that 18 were performed on continuous NIV-dependent subjects before, during, and after gastrostomy is important to point out.

Study Design and Participants

We identified 3 prospective studies, 7 retrospective studies, and 2 cohort studies. Among these, 4 studies considered the PEG placement during NIV, and 5 evaluated the same procedure without NIV. Moreover, 7 studies were based on RIG/PRG, of which 2 discussed the use of NIV and 5 were performed without it.

The overall number of participants was 804 (mean ± SD age = 62.53 ± 0.22 y). Among them, 258 subjects used NIV during the tube placement procedure, whereas 546 subjects did not. Among those who used NIV during the tube placement, 25 subjects were ongoing NIV users for 11 ± 5.6 h/d,[35] 19 subjects for > 4 h/d,[32] and 5 subjects for a mean of 5 ± 3.3 h/d.[3] In 2 other studies, 17 and 81 subjects used NIV without indication of daily hours of use.[31,33] In 3 other studies, there was no information concerning NIV utilization,[36] nor was it clear whether it was used routinely and/or during the PEG/RIG/PRG procedure.[37,38] The most common inclusion criteria for each study were diagnoses of amyotrophic lateral sclerosis according to El Escorial criteria, dysphagia, nutritional intake, weight loss of > 5–10%, FVC < 50%, the ability to cooperate and give consent, and aspiration.

Primary Outcomes

In only one study was survival at 30 d explicitly described as the primary outcome,[33] whereas in the other cases, it was a secondary outcome. The overall mean survival at 30 d is shown in Table 2 (see supplementary Tables 3 and 4).

Secondary Outcomes

All complications were clearly detailed except in 2 studies.[31,32] The major complications were (Table 3) respiratory decompensation, local wound infections, peritonitis, pneumoperitoneum, perigastrostomy tube leakage, and post-procedure pain.

The minor complications were disturbances of intestinal transit (diarrhea, vomiting, constipation), laryngospasm, upper-respiratory tract infection, G-tube site cellulitis and minor bleeding at the G-tube site, mechanical obstruction caused by tube migration, difficulty penetrating the gastric mucosa, transient hypoxia, agitation, and dislodged tooth crown. Death rates during the procedure were not indicated.

In one of our centers, 79 ALS subjects underwent gastrostomy from September 1, 2012, to December, 31, 2015, and the 30-d survival was recorded. PEG during NIV was complicated by desaturation (2 cases), which resolved by increasing the NIV settings, and by gastric hemorrhage, which resolved with embolization (one case).

Study Comparisons

In 7 studies, the interventions considered were PEG (5 studies) and PRG (2 studies) during the use of NIV. In 5 studies, the interventions were PEG versus PRG or RIG without NIV. Follow-up times varied across the different studies. Only a single study specified the major time points as follows: time of recruitment, end of gastrostomy procedure, and 3- and 12-month follow-up. However, there

Table 2. Overall Mean Survival at 30 Days From the Procedure*

Study (Year)	PEG/RIG/PRG with NIV			Study (Year)	PEG vs RIG/PRG without NIV		
	Total subjects, *N*	Survival at 30 d			Total subjects, *N*	Survival at 30 d	
		Survivors, *n*	Died (%)			Survivors, *n*	Died (%)
Sancho et al[35] (2010)	30	30	0	Thornton et al[39] (2002)	36	34	5.5
Gregory et al[32] (2002)	33	31	6.1	Miller et al[40] (2013)	108	106	1.9
Rio et al[36] (2005)	64	58	17	Desport et al[41] (2005)	50	Not present	23.4
Chiò et al[3] (2004)	50	48	4	Blondet et al[42] (2010)	43	Mortality rates 9.3%	9.3
Sarfaty et al[31] (2013)	30	28	6.7	ProGas Study Group[33] (2015)	330	318	3.6
Park and Kang[37] (2009)	25	25	0				
Czell et al[38] (2013)	26	25	3.8				
Mean	36.9	35	5.4	Mean	113.4	152.67**	8.7

* Mean death rates weighted per number of subjects in each study.
** Mean considering the information available.

Table 3. General Illustration of Major and Minor Complications of the Studies Included

PEG or RIG/PRG with NIV		PEG vs RIG/PRG without NIV	
Major Complications	Minor Complications	Major Complications	Minor Complications
Local wound infections[35,37]	Laryngospasm[38]	Respiratory decompensation[40,42]	Problem of intestinal transit (diarrhea, vomiting, constipation)[33,40,41]
Peritonitis[38]	Upper-respiratory tract infection[35,38]	Peritonitis[39]	Laryngospasm[33]
Post-procedure pain[32]	G-tube site cellulitis and minor bleeding at the G-tube site[37]	Post-procedure pain[33,40-42]	G-tube site cellulitis and minor bleeding at the G-tube site[33,40]
Pneumoperitoneum[37]	Rarely of mechanical obstruction caused by tube migration[37]	Local wound infections[33,42]	Rarely of mechanical obstruction caused by tube migration[41]
Perigastrostomy tube leakage[37]	Dislodged tooth crown[3]		Difficulty to penetrate the gastric mucosa[40]
			Transient hypoxia[40]
			Agitation[33,40–42]
			Dislodged tooth crown[40]

PEG = percutaneous endoscopic gastrostomy
RIG = radiologically inserted G-tube
PRG = percutaneous radiologic gastrostomy
NIV = noninvasive ventilation

were no 3- and 12-month data.[33] The other studies stressed the importance of evaluation 20–30 d before and after the intervention but did not report long-term follow-up. Only a single study reported the effects of PRG, noting that it was a minor procedure, its shorter duration, and the fact that sedation was not required.[3]

PEG and RIG or PRG were all noted to have high long-term success rates and low mortality, morbidity, and stress for patients.[39,43] However, it is important to note that survival is more linked to the ALS progression than to the method of gastrostomy[42] (see supplementary Tables 5 and 6). Complications and survival were not shown to be significantly different for PEG or RIG.[8] However, the videofluoroscopy study by Desport et al[41] showed that aspiration was higher in subjects who underwent a RIG compared with those who had a PEG, as suggested by a 2015 case study.[44]

Safety and Timing

None of the studies provided specific recommendations for timing PEG or RIG/PRG in subjects with ALS. According to the American Academy of Neurology, choking, weight loss, dehydration, dysphagia, and aspiration must be considered.[45] PEG or RIG/PRG can stabilize weight and facilitate medication administration.[46] Conventional criteria for gastrostomy have included FVC $< 50\%$[47,48]; weight loss $> 10\%$ from premorbid weigh; severe dysphagia, even in the absence of formal scales to evaluate its severity; and severe aspiration. Although the use of NIV

and FVC < 50% were considered important inclusion criteria in 2 studies,[35,37] the fact that 59 open gastrostomies were performed on subjects with VCs < 30% of normal, including 18 who had no ventilator-free breathing ability before, during, or after gastrostomy and had no respiratory complications at all from the procedure, indicates that when full ventilator setting noninvasive ventilatory support is used along with mechanical in-exsufflation to clear airway secretions as needed, gastrostomy can be performed safely irrespective of residual respiratory function.[11] Indeed, in a multi-center study of 355 continuous noninvasive ventilatory support-dependent ALS subjects, all 74 who underwent tracheostomy after a mean of 1.2 y of continuous noninvasive ventilatory support had to undergo gastrotomies despite having VCs < 10% and no autonomous breathing ability.[16] Thus, whereas the implementation of NIV as low-level bi-level PAP during PEG or RIG/PRG can prevent respiratory failure during the procedure for relatively mild non-continuous noninvasive ventilatory support-dependent patients, full settings of noninvasive ventilatory support are required for ventilator-unweanable continuous noninvasive ventilatory support users as well as for others who have VCs < 30% of normal, for safety.[37] None of the studies reviewed reported using full setting noninvasive ventilatory support during the PEG or RIG/PRG procedures. Their use of NIV during the procedures, however, is compared with baseline pre-intervention use of NIV in Table 4.[49]

Clinical Implications

The nutritional advantages of all of the studied procedures in ALS are clear, as is the positive effect on QOL of patients by avoiding starvation. However, PEG placement may be initiated too early by clinicians unfamiliar with noninvasive ventilatory support and the use of mechanical in-exsufflation to clear airway debris perioperatively[11,51] and, therefore, is possibly associated with higher complication rates.[14,50,52]

The studies reviewed did not shed light on the relative desirability of one intervention over another either perioperatively or long-term. Also, the studies provide no evidence for precise timing of the PEG or RIG/PRG in patients with ALS. Controversy concerning the initiation of parenteral nutrition is complicated by the fact that the underlying pathology causes protein catabolism hypermetabolism.[46]

The importance of noninvasive ventilatory support and mechanical in-exsufflation during the PEG/RIG/PRG procedures was made clear by Allen et al., who explained that respiratory failure occurred in 4 of their subjects in which gastrostomy placement was delayed without NIV,[54] whereas open gastrostomies on continuous noninvasive ventilatory support-dependent patients, including many with ALS, have been performed on patients with VC <10% with no respiratory complications.[11,12] However, there are no controlled studies regarding NIV use for these procedures. To achieve this aim, an RCT might be carried out, but this would likely be unethical. RCTs comparing gastrostomy with starvation would be unethical. Although the use of NIV/noninvasive ventilatory support during feeding tube placement is becoming the standard for best practice, it was not done in these studies. Switching from nasal to oronasal interface is essentially switching from an open to a closed system of ventilatory assistance/support. Possible hypoventilation during the procedures could have been conveniently monitored by end-tidal or transcutaneous CO_2 and O_2 saturation monitoring. If supplemental O_2 is avoided, then O_2 saturation >95% can signal significant hypercapnia as well. Hypoventilation can be resolved by increasing nasal ventilation settings and keeping the lips closed or by passing endoscopy tubes via a hole in an oronasal interface used to provide full noninvasive ventilatory support.

Few centers are experienced using continuous noninvasive ventilatory support and mechanical in-exsufflation to prevent respiratory complications.[48] Without perioperative continuous NIV and mechanical inexsufflation support for patients with very low VCs, the fact that far less than 50% of conventionally managed ALS subjects cited in the studies reviewed underwent gastrostomy, suggests that many patients who do not as yet have sufficiently severe bulbar-innervated muscle dysfunction to require the procedure may be dying from ventilatory failure because they are not placed on continuous NIV. ALS patients require tracheostomy only when bulbar innervated muscle dysfunction is due to upper motor neuron or CNS pathology and not lower motor neuron or myopathic.[55,56] The patients, are, therefore, dying prematurely. Thus, the use of FVC <50% as an indication for gastrostomy remains controversial. Some authors suggest a figure of 65–70% or, alternatively, that gastrostomy can be done safely for ALS patients with FVC < 10% and severe dysphagia of primarily lower motor neuron pathology.[55,56]

Limitations

The effects of PEG or RIG/PRG procedures on both patients and their caregivers and their health-related QOL were not well investigated. It would have been useful to have explored the patients' perspective on the procedures, from the decision making process to the changes in their daily lives, to understand better how to support them and their caregivers.

None of the studies included is an RCT or a quasi-RCT. This reduced the possibility of comparing the efficacy of the procedures studied especially in quantitative terms. All of the studies had potential selection and confounding biases and selective reporting of outcomes.

Table 4. Features of Noninvasive Ventilation Use in Studies That Consider It

Features of the Study		NIV Use		Mask	
Study (Year)	Design	NIV	Cough Assist	Type of Mask	Model of Mask
Sancho et al[35] (2010)	Prospective study	Volume- cycled control mode (PV 501 and PV 403, Breas Medical, Molndal, Sweden; Legendair, Airox, Pau, France)	Yes	(1) Nasal mask during the procedure; (2) when the procedure was finished, NIV was adjusted via an oronasal mask	(1) Healthdyne, Marietta, Georgia; (2) Mirage, Resmed, Madrid, Spain
Gregory et al[32] (2002)	Uncontrolled retrospective study	During PEG placement, each patient received NIV and oxygen; 58% of patients were previously using NIV at home > 4 h/d and continued to do so during the hospital stay	NR	(1) Nasal mask during the procedure; (2) after all were observed in the recovery room while NIV and pulse oximetry monitoring continued and were transferred to the floor when conscious with stable respiration	NR
Rio et al[36] (2005)	Retrospective review	NIV usage peri-procedure in both groups in 9% of patients	NR	NR	NR
Chio et al[3] (2004)	Prospective study	At the time of the procedure, 20% in the PRG group and 8% in the PEG group	NR	NR	NR
Sarfaty et al[31] (2013)	Retrospective review	NIV use in the FVC > 30% group: 50% of patients; in the FVC < 30% group: 70%	NR	NR	NR
Park et al[37] (2009)	5-y follow-up cohort study	At the time of the procedure, all patients used NIV	NR	NIV was provided by a nasal mask	NR
Czell et al[38] (2013)	Retrospective chart review	During the procedure, all patients used NIV	Yes	Special mask with an opening that allows insertion of the endoscope during NIV	Endoscopy mask (VBM, Medizintechnik, Sulz, Germany)

NIV = noninvasive ventilation
PEG = percutaneous endoscopic gastrostomy
NR = not reported
PRG = percutaneous radiologic gastrostomy

All of the studies claimed the importance of an evaluation 20–30 d before and after the intervention, but only one of them specified the importance a longer follow-up time without indicating the data.[34] Long term follow-up might have revealed complications specific to one intervention over another, such as possibly greater risk of reflux following RIG. Moreover, in the studies included, the dropout rate was not considered, or it was explained unsatisfactorily, and the weight change from baseline was not indicated.

Studies have shown that facing decisions during emergency hospital admissions or having the opportunity to carefully evaluate information over time can elicit different feelings and beliefs both in patients and caregivers.[53] According to the guidelines of the European Federation of Neurological Societies, patients and caregivers should be informed about both benefits and risks of the proposed procedure as well as the possibility of relying on oral intake for as long as is feasible and informed that postponing the PEG/PRG or RIG procedure could increase the respiratory risk by permitting increased aspiration of food and saliva and insidiously progressive malnutrition common in patients with ALS.[50] In addition, the occurrence of cognitive and behavioral symptoms belonging to the frontotemporal dementia spectrum and their repercussions on the decision-making processes toward the PEG or RIG/PRG procedure in patients with ALS have not been considered, with the exception of the study by Allen et al.[54] However, in this study, formal cognitive testing was not performed, and the physicians considered it present if documented in the clinical records.[54]

Although the American Academy of Neurology disseminated one of the few practice guidelines concerning PEG, affirming that it is needed when there is evidence of accelerated weight loss and severe dysphagia,[41,46] none of the studies included in this work have the same point of view on this, nor have they adopted the same approaches for placing gastrostomies. Finally, none of the studies evaluated cost-effectiveness. Knowing the insertion costs could be helpful to evaluate the advantages of a PEG or RIG/PRG.

Summary

There are various methods of feeding tube insertion, but PEG continues to be considered the accepted standard for gastrostomy and is the most commonly used method in patients with ALS. However, the indication for and timing of gastrostomy are controversial. Some suggest that it be considered at the onset of NIV usage, others that only dysphagia severity and its upper vs. lower motor neuron nature be considered. Indeed, whereas many non-bulbar ALS patients have severe respiratory orthopnea and require noninvasive ventilatory support to sleep reclining, they often have no bulbar-innervated muscle involvement at all at this point and eat and protect their airways without any difficulty. Thus, the initiation of NIV in non-bulbar patients should not be an indication for gastrostomy. With optimal noninvasive respiratory management, basing gastrostomy on dysphagia alone may be the most appropriate recommendation.

Future studies need to be more rigorous regarding internal validity and planned follow-up to compare both short- and long-term consequences of these various procedures not only for ALS, but for other diagnoses not so temporarily limited by the severe rapidly progressive pathology of ALS. Cost-effectiveness needs to be assessed as well as the use of noninvasive ventilation for not only symptom management but for ventilatory support as well.

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