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Percutaneous endoscopic gastrostomy and jejunostomy: Indications and techniques

Fugazza A *et al*. Percutaneous endoscopic gastrostomy

Abstract

Nutritional support is essential in patients who have a limited capability to maintain their body weight, therefore oral feeding is the main approach for such patients. When physiological nutrition is not possible, positioning of a nasogastric, nasojejunal tube or other different percutaneous devices may be feasible alternatives. Creating a percutaneous endoscopic gastrostomy (PEG) is a suitable option to be evaluated for patients that need nutritional support for more than 4 wk. Many diseases require nutritional support by PEG, with neurological, oncological, and catabolic diseases being the most common. PEG can be performed endoscopically by various techniques, radiologically or surgically, with different outcomes and related adverse events (AEs). Moreover, some patients that need a PEG placement are fragile and are unable to express their will or sign a written informed consent. These conditions highlight many ethical problems that become difficult to manage as treatment progresses. The aim of this manuscript is to review all current endoscopic techniques for percutaneous access, their indications, postprocedural follow-up and AEs.

Key Words: Percutaneous endoscopic gastrostomy; Enteral nutrition; Gastrostomy; Percutaneous endoscopic jejunostomy; Indications and techniques

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Core Tip: Percutaneous endoscopic gastrostomy (PEG) represents the first choice for long-term enteral nutrition support. The aim of this manuscript is to provide a comprehensive overview of PEG placement, including indications, contraindications, preprocedural clinical assessment, endoscopic techniques, adverse events and postprocedural follow-up. Furthermore, endoscopic procedures for jejunal nutrition are

also addressed. In consideration with the increasing frequency with which PEG placements are requested, this review may be a useful tool for clinical guidance both for endoscopists and physicians in different fields, with a particular focus on appropriateness of the indications and safety of this procedure.

INTRODUCTION

Nutritional support is essential in patients who have a limited capability to maintain their body weight with normal diet. In best practice, oral feeding is the main approach to choose for these patients[1]. Many patients cannot consume food by mouth or in some cases, oral intake can be even dangerous for patients with neurological conditions or obstructive causes, although their gastrointestinal (GI) tract are properly functional[2]. In these cases, physicians can support alimentary intake by positioning a nasogastric, nasojejunal tube or creating a direct access into the stomach, through a percutaneous endoscopic gastrostomy (PEG)[3]. This allows to maintain normal physiological activities of the GI tract, in order to avoid alterations in the intestinal barrier functions and long-term complications related to intravenous nutritional support[4,5]. The choice between whether the feeding tubes are placed *via* oral route over a PEG needs to be evaluated case-by-case by a multidisciplinary team, considering there are multiple factors related to procedural indications, such as patient's conditions, clinical scenario and risk of adverse events (AEs) for the patient. However, when the GI tract does not work properly, such as in cases of obstruction, intravenous nutritional support should be preferred. Parenteral nutrition (PN) is a nutritional support therapy that is provided through the intravenous administration of nutrients such as glucose, electrolytes, amino acids, lipids and vitamins. Moreover, PN can be associated with AEs and is poorly tolerated, especially in patients with heart failure, renal insufficiency and diabetes mellitus[6]. A recent systematic review with meta-analysis based on oncologic patients, reported no differences between EN and PN with regards to nutritional outcomes, with a higher incidence of infections in the PN group [risk ratio (RR) = 1.09, 95% confidence interval (CI): 1.01-1.18; P = 0.03][7]. For these reasons, the recent European Society for

Clinical Nutrition and Metabolism guidelines recommends administering TPN only when patients are unable to reach their nutritional outcomes with oral nutrition or EN[6]. Although the benefit of percutaneous access for EN have been reported for a while, several controversies and major concerns still exist regarding these procedures and the related AEs. The aim of this manuscript is to review all current techniques for percutaneous access for EN, their indications, postprocedural follow-up and AEs.

INDICATIONS

Nowadays, many diseases result in long-term reduction of caloric intake. For this reason, placement of a percutaneous endoscopic access is needed, in order to improve nutritional conditions. Percutaneous endoscopic nutrition can be achieved by either a transgastric approach through PEG, or a transjejunal approach, namely percutaneous endoscopic jejunostomy (PEJ).

Ever since the first endoscopic insertion of a gastrostomy[8], there has been a worldwide diffusion of these techniques and an increase in indications for this medical approach. A summary list of indications for PEG placement is reported in Table 1. However, nutritional support is often only necessary for a short period, such as less than one month, in case of stroke with fast recovery, mild head trauma, acute pancreatitis, post-head and neck surgery, post-upper GI surgery and other temporary diseases. In these patients, nasogastric tube is easier to insert and to manage directly at bedside. On the other hand, some patients need nutritional support for longer periods of time.

In the recently published European Society of Gastrointestinal Endoscopy (ESGE) guidelines regarding endoscopic management of enteral tubes in adult patients, it is recommended to consider EN by percutaneous access when nutritional support is needed for more than 4 wk on a case-by-case basis[3]. The 4-wk cut-off is arbitrary and has been chosen to avoid many AEs that are related to percutaneous access (*e.g.*, infections). When indicated, the gastric route through a PEG is more desirable than the jejunal approach, due to its better tolerance, ease of procedure and its possibility to be

performed bedside[9]. In case of altered anatomy, delayed gastric emptying, gastric outlet obstruction, duodenal obstruction, severe gastroesophageal reflux, or increased risk of aspiration pneumonia, PEJ must be considered[9].

Benign diseases

Neurological diseases often need nutritional support, especially in patients that cannot consume food orally due to neurological injury. Specifically, dementia is a common disease that needs EN. Patients with dementia often cannot or would not swallow. This condition mainly occurs later in the course of the disease, when patients are in an advanced stage[10] and when they cannot express their will[11]. Currently, studies about EN in patients with dementia are scarce. A systematic review regarding patients with final stage dementia did not show differences between EN and no nutritional support in terms of survival, quality of life, nutritional status, function, behavior or psychiatric symptoms[12]. For these reasons, recent published ESGE guidelines recommend to avoid PEG placement in patients with advanced dementia, especially if they have a life expectancy of less than 4 wk[3]. Stroke is another common neurological cause of dysphagia, with an incidence of 23%-50%[13]. Some patients recover slowly or do not retrieve the capability to consume food through the oral route, leading to a high risk of aspiration pneumonia and low nutritional intake. Motor neuron diseases often involve varying swallowing functions[14]. A recent cohort study on 957 patients (278 with PEG) affected by amyotrophic lateral sclerosis showed that PEG nutrition support improved overall survival expectancy (21 *vs* 15 mo, $P < 0.001$)[15]. Moreover, dysphagia can be present after head injury with neurological damage. A review focused on randomized controlled trials of nutrition in patients with head injury showed that survival expectancy and disability were improved by early parenteral or EN[16]. Patients with Parkinson's disease can develop motor alteration like dysphagia and EN should be considered, due to the increased risk of aspiration pneumonia and difficulties in oral intake[17]. There is poor evidence to support PEG placement in patients with other benign diseases such as cerebral palsy, anorexia, frailty, burn patients and

hypercatabolic diseases, even though each case must be evaluated individually. Furthermore, cases of PEG placement are reported in patients with benign esophageal strictures such as caustic stricture, Zenker diverticulum, post endoscopic therapy [endoscopic mucosal resection, endoscopic submucosal dissection (ESD), radiofrequency ablation] and achalasia[18,19].

Malignant diseases

Head and neck malignancies can lead to dysphagia in 35%-50 % of cases[20]. The reported high-risk factors are hypopharyngeal localization, advanced neoplasia (T4) and combined chemoradiation. In these settings, the main indications for PEG are the onset of dysphagia, low nutritional intake and loss of body weight[21]. A recent published study evaluated no PEG (n 61) *vs* prophylactic PEG placement (n 69) in patients with a head-neck tumor, who underwent chemoradiotherapy. The authors showed that prophylactic PEG improved nutritional parameters and unexpected hospitalization[22]. Esophageal cancer is another indication for enteral nutrition, if patients present symptoms of severe dysphagia, when palliation by placement of an endoscopic stent is not feasible[23]. In general, all oncological diseases that imply hyper catabolism that is not compensated by oral intake, may require EN by nasogastric tube or PEG[3].

Other indications

Other indications of PEG that are not for nutritional purposes, have also been described. An endoscopic gastrostomy may be placed in patients with gastric outlet obstruction or intestinal strictures that cannot be managed through a usual endoscopic approach, by placement of an endoscopic stent or creating an Endoscopic Ultrasound (EUS) guided gastroentero-anastomoses[24-27]. These conditions can benefit of gastric decompression by PEG[28]. This technique aims to improve the patient's symptoms and reduce GI distension. Primarily, it can be connected to an aspirator to quickly relieve symptoms. Later, it can be connected to a drop bag to improve compliance. This also allows

patients to eat small quantities of food, in order to guarantee a better quality of life, although some poor nutritional benefits may remain. In a recent systematic review with 1194 cases, 90% of technique success rate had been reported. However, it showed 19.8% of minor AEs (leak 6.7%; peristomal infections 5.1%; device malfunction 2.8% and dislodgement 2.1%) and 1.9% of major AEs (2 deaths for sepsis and bleeding)[29]. Moreover, Baron *et al*[30] described the use of a surgical gastrostomy as access for duodenoscope in order to perform an ERCP[30]. This technique can be used effectively in patients with biliary diseases and previous bariatric Roux-en-Y gastric bypass surgery[31]. A percutaneous intragastric trocar was designed to serve as a trocar for the endoscopist's introduction of rigid laparoscopic instruments, in order to better aid endoscopic therapeutic procedures. This device was placed following PEG placement and was successfully used in pigs to perform ESD, full-thickness resections and intragastric stapling[32]. The PEG could be also used as an access route to perform combined antegrade and retrograde dilations in esophageal strictures that cause complete obstruction, and are difficult to dilate with standard endoscopic techniques[18,33,34].

Pediatric indications

PEG is also indicated in the pediatric setting, when there is a low nutritional intake, malabsorption and dysphagia that leads to malnutrition[35]. This procedure is considered safe in a pediatric population weighing less than 6 kg, with complex neurologic disability, congenital heart disease, cancer or other complex medical comorbidities[36]. Down syndrome is regarded as an indication for PEG placement in the pediatric setting, when there is poor nutritional intake[37]. Likewise, cerebral palsy may represent an indication for EN, but substantial evidence to support this indication is scarce[3]. Other indications for PEG placement are congenital malformations, such as congenital heart failure which can lead to chronic malnutrition[38]. In a pediatric oncological setting, PEG placement results in improvement of body weight, malnutrition and oncological outcome[39,40].

PRE-EVALUATION AND CONTRAINDICATIONS TO PEG PLACEMENT

All patients must be evaluated carefully prior to undergoing a PEG. A complete visit with medical history, physical examinations and current therapy must be completed[41]. Observational studies showed that a multidisciplinary team can select patients that are suitable for PEG placement[42]. Indeed, a gastroenterologist, a PEG specialist nurse, a dietician and a speech and language therapist must evaluate the situation on a case-by-case basis. The time of observation of the patient by the nutritional team could require up to 7 d prior to deciding whether the procedure is appropriate or not. This period, defined as the "Cooling off period", is reported as a high-risk phase, where 43% of patients pass away. For this reason, waiting a week could avoid inappropriate procedures in patients with a short life expectancy[43]. However, there are some conditions that represent relative or absolute contraindications for PEG placement. The most common are reported in Table 2. Recent peptic ulcer bleeding with high risk of re-bleeding, hemodynamic and respiratory instability are considered relative contraindications[44]. There are also controversial studies about PEG placement in patients with ascites. In a retrospective study of 29 patients with advanced cirrhosis, Baltz *et al*[45] reported high mortality in patients with ascites who underwent PEG placement. Another case-control study evaluated 583 cirrhotic patients, 107 of which with ascites. It showed no difference in terms of mortality, infections and bleeding after PEG insertion[46]. Furthermore, particular attention must be paid in patients with ventriculoperitoneal shunts (VPS). In a systematic review, a high incidence of infections and PEG malfunctions were reported (12% and 4% respectively) in these patients[47]. VPSs infections are more frequently reported in case of PEG placement before the shunt procedure (21, 8%) or when a simultaneous PEG and VPS placement were performed (50%). For these reasons, the authors of this study suggest performing PEG placement 7-10 d after the VPS. Since many patients that require gastrostomy placement suffer from chronic constipation, which can predispose the transverse colon to move in front of the anterior gastric wall, enemas or a macrogol solution through a nasogastric tube

should be given to decompress the colon and reduce the risk of colonic interposition, during the endoscopic procedure (Figure 1).

Moreover, anatomical alterations of abdominal wall (*e.g.*, ostomy, scars and adhesions) can make PEG insertion difficult. When these conditions are present, PEG placement must be carried out at least 2 cm away from the scar[44]. PEG placement should not be performed in cases of fever, abdominal wall infection or other signs of sepsis, in order to reduce the risk of PEG site infection.

Additionally, PEG placement is considered a high bleeding risk procedure[3,48]. Pre-procedural blood tests, with platelet count and coagulation tests, should be done. Indeed, a platelet count < 50000 mm^3 and an international normalized ratio (INR) > 1.5 are considered contraindications for PEG placement[48].

Moreover, home antiplatelet and anticoagulant therapy should be evaluated, as all patients are stratified in high or low thrombotic risk. Patients with low thrombotic risk, that take antiplatelet (anti-P2Y12), should discontinue the medication 5 d prior to PEG placement. On the other hand, patients with a high thrombotic risk must continue cardioaspirin monotherapy, while other antiplatelet medications are to be assessed by a cardiologist. Traditional anticoagulants should be discontinued 5-2 d prior to the procedure, depending on patient comorbidities, renal function and should be replaced by low molecular weight heparin with an INR below 1.5. New anticoagulant should be discontinued 2-3 d prior, based on the different drug subtypes and renal function[48]. However, all antiplatelet and anticoagulant drugs should be resumed 2 d after PEG placement[48].

ENDOSCOPIC VS RADIOLOGIC VS SURGICAL GASTROSTOMY

Gastrostomy tube placement can be performed by three different techniques: endoscopic (PEG), radiologic (RG) and surgical procedures (SG)[49]. Frequently, PEG is considered the standard procedure, but others techniques are often performed, mainly in patients that are unable to undergo the endoscopic approach[50,51]. Several AEs were reported after all sub-types of gastrostomy placement[52,53]. The most common AEs were

device malfunction (52%) and infections (19%)[54]. Some comparative studies about PEG *vs* RG reported results that were univocal. One meta-analysis of 5680 patients reports fewer major AEs in patients undergoing RG than in those undergoing PEG (success rate RG: 99.2% *vs* PEG: 95.7%, $P < 0.001$; major complications RG: 5.9% *vs* PEG: 9.4% *vs* SG: 19.9%, $P < 0.001$)[55]. Moreover, another systematic review and meta-analysis evaluated 934 PEG and 1093 RG, indicating that PEG was safer than RG[56]. However, many studies report no statistical differences between these techniques[57,58]. A retrospective study including 184068 patients comparing PEG, RG and SG was recently published. The authors of this study reported that PEG was safer than RG and SG procedures. In particular, when compared to radiological and surgical procedures, PEG showed a low rate of infections (RG: 1.28; $P = 0.006$ and SG: 1.61; $P < 0.001$), bleeding [odds ratio (OR) RG: 1.84; $P = 0.002$ and SG: 1.09; $P < 0.001$), perforation (OR RG: 1.90; $P = 0.002$ and SG: 6.65; $P < 0.001$) readmission (OR RG: 1.07; $P = 0.002$ and SG: 1.13; $P = 0.01$) and mortality (OR RG: 1.09; $P = 0.01$ and SG: 1.55; $P < 0.001$)[54]. In conclusion, it is not clear which technique is better among the three mentioned above. Nevertheless, PEG seems to have the lower rate of AEs reported. Moreover, not all hospitals have tools and staff dedicated to performing these procedures. For this reason, it seems reasonable to use the safest method available in the facility.

PEG TECHNIQUES

Different endoscopic techniques for PEG placement have been proposed during the years, including the pull technique, the introducer technique, and the push technique.

Pull technique

The pull technique is the most used procedure for PEG placement[59]. This technique was first described in 1980 by Gauderer *et al*[60]. Two operators are needed: One to manage the endoscopic part of the procedure and one to manage the percutaneous site of the procedure. With the patient placed in the supine position, the abdomen is draped in a sterile fashion and the gastroscope is inserted perorally into the stomach, under

conscious sedation or deep sedation. Gastric distention with endoscopic air insufflation, brings the anterior gastric wall in contact with the abdominal wall. The lights in the room should be dimmed so that the puncture site can be localized on the abdominal wall by endoscopic transillumination and by clear endoscopic visualization of the indentation of the stomach, by external palpation on the marked point. Then, the "safe track technique"[61] is performed by inserting a 25 G needle attached to a 10-mL syringe that is partially filled with saline solution at the marked point. If bubbles appear in the syringe while aspirating immediately before the needle passes into the stomach, there may be an intervening loop of bowel present. This maneuver could be performed also while withdrawing the needle. Once the puncture site is identified, local anesthesia is given and a skin incision with a surgical blade of 3-5 mm is made, so that a 14-G trocar can be inserted under direct endoscopic visualization, while keeping constant endoscopic air insufflation of the stomach. Endoscopically a snare, passed through the gastroscope, is looped around the sheath. A dedicated gastrostomy kit wire is then passed through the sheath and into the stomach. It is grasped by the snare and is brought out through the mouth, together with the endoscope. Thereafter, the gastrostomy kit tube is attached to the wire, and they are pulled back together through the mouth, the esophagus, the stomach and out through the cutaneous puncture site until the internal bumper reaches the anterior wall of the stomach. Finally, the external bumper must be fixed against the skin (Figure 2). The described technique can also be done by passing an ultra slim endoscope and the gastrostomy probe trans-nasally. This variant of the procedure has been described to be well tolerated even in non-sedated patients.

Introducer technique

The direct percutaneous technique, namely the introducer, was first described in 1984 by Russell *et al*[65] and then revised by Brown *et al*[66] in which the stomach is fastened to the abdominal wall with T-fastener sutures. In this technique, two operators are needed, and the gastrostomy site is identified in the same manner as in the "pull" technique.

However, while maintaining full gastric endoscopic insufflation, a gastropexy is made by placing two to four T-fasteners circumferentially over the anterior abdominal wall under endoscopic guidance. Within the area between the T-fasteners, lies the site for the gastrostomy tube placement[67]. A horizontal incision is made at the identified site so that a trocar can be inserted, and a guidewire introduced into the stomach. Then, the tract is dilated using dilators that are introduced over the guidewire. Finally, a gastrostomy balloon-type probe is placed over the guidewire through the dilator peel-away sheath and into the stomach (Figure 3). Using this technique, the gastrostomy probe is introduced directly from the exterior through the abdominal wall percutaneously, avoiding contamination of the probe during the passage in the upper digestive tract. This technique should be preferred in patients with esophageal strictures or head and neck cancer to reduce the risk of tumor seeding[3]. In the literature, various cases of gastrostomy site metastasis in patients with upper aerodigestive tract malignancies, have been reported and a recent meta-analysis found that the incidence rate increases particularly in patients with advanced-stage disease[68,69].

Other percutaneous gastrostomy techniques

The "push method" or Sacks-Vine[70] technique is similar to the "pull" method except that the gastrostomy probe is passed over a guidewire from the mouth to the cutaneous side of the gastrostomy. This requires that the tube needs to be much longer and is made of two pieces connected together with a small dilator. EUS-guided PEG placement has also been described[71,72]. In the Baile-Maxía *et al*[71], case series, a EUS target was created by filling a sterile glove with saline and was placed over the abdomen of the patient. A linear echoendoscope was passed perorally into the stomach and was positioned against the anterior gastric wall, where the EUS target was identified. The abdominal wall was then punctured from inside the stomach with a 19 G needle, and a guidewire was advanced. The guidewire was tied to a string which was passed into the stomach and taken out through the mouth. The following passages are

the same of the pull technique. This variation of the pull technique could be selected in obese patients or in patients with previous abdominal surgeries, where transillumination could be absent.

AES

Aspiration

This is the most common periprocedural AEs[73,74] which has been reported to be around 1%. Risk factors for aspiration are advanced age, need for sedation, and neurologic impairment[75].

Pneumoperitoneum

Transient subclinical pneumoperitoneum is commonly found after the procedure and generally doesn't have clinical relevance[76].

Injury to adjacent viscera

Under transillumination, if the indentation site is identified and the "safe track technique" is used during the PEG placement, there is a very low risk of injury to the organs adjacent to the anterior abdominal wall, such as colon or liver. If the patient presents a severe postprocedural hypotension, liver laceration should be suspected, and urgent computed tomography (CT) scan is required. Transhepatic insertion of a gastrostomy tube is a rare and serious AE. Cases reported in literature have been managed conservatively if the patient remained asymptomatic[77], or surgically if a life-threatening complication such as severe haemorrhage has occurred[78]. Colonic injury can present a few days after the procedure, with leakage of the intestinal contents around the gastrostomy tube, abdominal pain and fever[79]. A CT scan using a hydro soluble, contrast agent should be done, and if no leak into the peritoneal cavity is detected, the complication can be managed with endoscopic closure of the fistulous tracts[80]. If the patient develops generalized peritonitis then surgical revision is mandatory. However, in most cases, a gastro-colonic-cutaneous fistula remains

clinically silent until, months after the gastrostomy placement, the first implanted probe is removed, and the replacement tube is placed into the colon (Figure 4). Once nutritional feeding is resumed, diarrhoea develops. If a new gastrostomy placement is needed, laparoscopic gastrostomy should be considered[81,82].

Bleeding

Mild intraprocedural oozing from capillaries could be encountered during the procedure, that usually are self-limiting or managed with endoscopic therapy. Major bleeding is a rare AEs and is usually caused by the puncture of the left gastric or gastroepiploic arteries or one of their branches[83].

Wound infection

The systematic use of prophylactic antibiotic therapy has drastically reduced the incidence of this complication[84]. It generally manifests in redness, edema and leakage of pus from the gastrostomy site and is usually managed with systemic antibiotic therapy and local wound care. If not treated adequately it can result in necrotizing fasciitis, a rare but potentially fatal complication (Figure 5).

Granulation tissue

Re-epithelialization of gastric mucosa could cause the development of excessive granulation tissue at the gastrostomy site. Treatment consists in avoiding occlusive dressings and, if the mucosa causes persistent minor bleeding, topical silver nitrate or argon plasma coagulation can be applied to the tissue[85].

Buried bumper syndrome

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Buried bumper syndrome (BBS) is defined by the migration of the internal bumper along the gastrostomy fistula tract. It is generally related to excessive traction from the outside of the internal bumper which perpetuates over time, leading to a local tissue pressure necrosis and subsequent progressive migration of the internal bumper. To

avoid this AEs, it is recommended to keep the outer bumper loose from the skin and to periodically check that the gastrostomy tube remains easily rotatable. When the internal bumper has reached the subcutaneous plane, a bulging on the skin is visible at the gastrostomy site, which is hard to the touch, and the gastrostomy tube is not moveable. If, on the other hand, the internal bumper is in the gastric wall, the peristomal skin may appear regular, but the gastrostomy tube will still not be moveable. Based on the depth of the buried bumper, different extraction techniques can be applied[86,87]. When part of the internal bumper is still endoscopically visible, the buried bumper, after inserting a wire through the gastrostomy tube from the outside, can be effectively pushed back into the stomach with a dilator (*e.g.*, Savary bougie size 15 Fr in 20 Fr gastrostomy tube). Totally or near-totally ingrown bumpers can be removed by cutting the overlying mucosa with an endoscopically guided application of electrosurgical current using a sphincterotome, a needle-knife or a hook knife. In case of clear extra-gastric localization, surgical treatment may be needed. In a recent study, Costa *et al*[88] reported the use of a novel endoscopic dedicated device, the Flamingo device, for BBS management. The Flamingo device is inserted over the guidewire into the stomach, through the external insertion of a partially cut gastrostomy probe. The distal part of the Flamingo device is flexed to 180° using its dedicated handle, exposing the bowstring, sphincterotome-like cutting wire. External traction is then applied to the Flamingo device from the cutaneous side of the gastrostomy, pulling the flexed cutting wire toward the granulomatous tissue through direct endoscopic visualization, until apposition is achieved, and the overgrown tissue is then incised.

Tube displacement

If probe removal occurs earlier than 4 wk after the gastrostomy placement, the fistula may not have consolidated, so a percutaneous replacement should not be attempted. After the probe removal, the patient must be placed under broad antibiotic coverage and be fasting for at least 24 h. The placement of a new endoscopic gastrostomy should be scheduled after complete wound healing. In the case of a probe removal after 4 wk,

the attempt to percutaneously place a replacement probe is indicated and should be done quickly because in the absence of a tube in the gastrostomy tract, the gastrocutaneous fistula tends to close spontaneously within 12-24 h[89]. Our advice is that if a replacement probe is not available at the time of displacement, another tube (*e.g.*, 18-20 Fr Foley catheter) should be placed temporarily as soon as possible in order to avoid the risk of closure of the fistulous tract.

Peristomal leakage of gastric content

This is generally linked to a patient's clinical condition that led to a delayed gastric emptying which may be due to either pre-existing conditions such as gastroparesis or to the presence of fecal impacts, that alter intestinal transit leading to sub-occlusive symptoms. It can be managed by trying to improve gastric emptying with the use of prokinetics, in order to reduce gastric secretions with the use of protein-protein interactions, and to improve intestinal canalization with the periodic administration of macrogol through the gastrostomy tube. Local skin irritation can be prevented by stoma adhesive powder or zinc oxide application. When the condition does not resolve with the optimization of medical therapy, the positioning of a jejunal extension is indicated to prevent the feeding solution from remaining in the stomach, and so that the gastric tube can be used as a drainage of gastric secretions to progressively reduce the peristomal leakage.

Gastrocutaneous fistula

Once the probe has been removed, the gastrostomy usually closes within 12-24 h. The non-closure of the fistula is often caused by severe malnutrition and a reduced thickness of the fistulous tract. If the external bumper is positioned too close to the skin, the continuous compression of the skin leads to tissue ischemia with reduction of the thickness of the fistulous tract. When the thickness of the fistulous tract is 1-2 mm, the closure of the fistula by a secondary intervention becomes very difficult and it is often

necessary to perform an endoscopic closure, using techniques similarly to GI perforation[90-94] (Figure 6).

POST-PROCEDURAL CONSIDERATIONS

At the gastrostomy site, the PEG tube can be used for infusion after 12-24 h of placement. To start, begin with water followed by regular enteral feeding with progressive increase in the infusion rate. In the first 72 h, the external bumper must be fixed against the skin to allow an adequate attachment of the abdominal wall to the gastric wall which is fundamental for a correct maturation of the fistula. After 72 h the external bumper should be detached from the skin by at least 0.5-1.5 cm to avoid compression of the skin as the patient's position changes. This compression would increase the risk of developing subcutaneous infections and, in the long term, would lead to ischemia of the wall itself, with a progressive reduction in the thickness of the fistula wall. At least 4 wk after the PEG creation, the gastrocutaneous fistula is considered to be fully consolidated. In very undernourished patients, the maturation of the fistula may take longer. The peristomal skin should be kept clean daily by using only mild soap and water, and the gastrostomy site should be left open without occlusive dressings, which may lead to peristomal skin maceration.

Enteral tube replacement

There are no exact evidence-based guidelines regarding the replacement of PEG tubes. Therefore, each center adopts its own protocol based on the management of these patients, which is very complex because they are generally very fragile, undernourished and may have neurological diseases that compromise their autonomy. We can certainly distinguish the timing of replacement of the first implanted probe based on the material of which the probe is made[95]. There are probes, generally those that can only be removed perorally, that are manufactured using resistant materials and remain functional even after 1 or 2 years. On the other hand, there are probes which can be removed percutaneously using traction, which are made of more flexible materials.

However, these tend to wear out more quickly over time. The deterioration of the probe becomes evident externally, which then corresponds to the deterioration of the internal bumper, which in turn becomes more rigid, compromising the flexibility necessary for removal by percutaneous traction. Therefore, the removable traction probes should be removed usually about 6 mo after placement at bedside without endoscopic control. However, when the attempt of removal of this type of tube is made after many months, the percutaneous traction removal becomes more and more difficult, requiring a different approach. In this situation, the probe is removed by cutting the tube from the external skin margin and the internal bumper is left in the stomach. Endoscopic retrieval of the bumper in the stomach is recommended in patients at risk of intestinal occlusion[3]. Regarding the balloon-type gastrostomy probes[96], which are applied during the procedure of direct percutaneous gastrostomy and are used as replacement after removal of the first implanted probes, they have a balloon as an internal bumper. This balloon, after the percutaneous insertion of the tube and when the gastric cavity is reached, is filled with sterile water. The advantage of a balloon-type probe is that it can be easily removed by just deflating the internal balloon. The disadvantages are that they tend to wear out quite quickly over time and that they can be easily removed accidentally. The substitution of this type of probe should be made every 3-6 mo.

Follow up of patients with a gastrostomy tube

The management of patients after a gastrostomy placement varies according to local protocols. It is generally a multidisciplinary management that involves home care nursing, nutritional planning and specialized medical support. Training courses are held for the relatives of the patients, who will play a fundamental role in caring for these patients. The balloon type tubes can be easily replaced at home by dedicated staff with a low risk of AEs[97]. The home management of these patients is essential because they are very fragile and, in most cases, not mobile or independent and therefore, staying in the hospital is risky and difficult to manage[98].

PEG WITH JEJUNAL EXTENSION

Percutaneous endoscopic transgastric jejunostomy (PEG-J) is a gastrostomy with a jejunal extension tube. The jejunal extension tube can be positioned "beneath the scope", grasped endoscopically with forceps in the stomach lumen and dragged into the jejunum, or "over the wire", that is advanced over an endoscopically or radiologically placed guidewire. The placement of the jejunal extension tube should be attempted in patients with gastrostomy feeding-related AEs, such as aspiration pneumonia due to gastroesophageal reflux of the gastric feed and uncontrolled peristomal leakage[9]. The feeding solution can be administered from the jejunal extension tube, and the gastric tube can perform the gastric decompression function. PEG-J is also used in Parkinson's disease patients for delivering the levodopa-carbidopa intestinal gel[99]. In this case, the jejunal extension tube allows a continuous delivery of the drug into the small bowel[99] (Figure 7). The disadvantages of these probes are that the jejunal extension tubes are usually long (median length of 55 cm) and small in diameter (median diameter of 10 Fr) and thus, are more prone to occlusion, kinking or dislocation[100]. These tubes also have limited longevity and tend to wear out after 3-6 mo, especially if they are used as enteral feeding devices.

DIRECT PEJ

Direct PEJ (DPEJ), described in 1997 by Shike *et al*[101], is an alternative method of enteral feeding in patients that cannot undergo gastrostomy placement because of previous resection of the esophagus or stomach, or in patients with frequent clogging or migration of PEG-J l extension. In these circumstances, DPEJ placement is performed using the same passages of the gastrostomy technique. Likewise, this technique is needed to achieve the proximal or medium jejunum under endoscopic visualization, by a push enteroscopy, single-balloon or double-balloon enteroscopy or underwater enteroscopy[102]. The use of ultrasonography, fluoroscopy, or anchoring a needle to the jejunum can be used to facilitate correct placement. Jejunal probes placed through DPEJ

are shorter and greater in diameter compared to jejunal tubes placed through PEG, making them less prone to tube dysfunctions.

However, DPEJ is a challenging technique with a successful placement between 68% and 83%, which is highly variable based on local expertise. Endoscopic access up to the jejunum is not straightforward, and once obtained, the major difficulty is to identify the target jejunal puncture site. Serious periprocedural AEs have been reported, such as bowel perforation (up to 2.5%) and volvulus. A frequently reported post-procedure AEs is peristomal leakage with fistula enlargement, which is aggravated by leakage of pancreatic juice and bile, causing peristomal irritation and severe dermatitis[103,104]. DPEJ is a useful technique in order to avoid the need for surgery, when long-term nutritional jejunal access is needed. However, it is associated with a moderate or severe complication risk in up to about 10% of the cases, which physicians should be aware of.

FUTURE PERSPECTIVES

The data within this paper confirms that PEG placement is a safe procedure. The selection of patients requiring PEG will be of paramount importance to understand which individuals may benefit more from this nutritional support than others, maximizing the outcomes and reducing the AEs. Considering the complexity of these patients, a dedicated multidisciplinary team for pre- and post- procedural management are required for patient care. Moreover, the development of a home health care service for nutrition support and device management, consisting of a gastroenterologist, nurse, and nutritionist is fundamental to avoid patient transportation. In particular, the coronavirus disease 2019 outbreak has significantly impacted our clinical practice and we have established infection prevention measures in order to protect both patients and personnel[105-108]. Moreover, the pandemic definitively underlined the importance to reduce hospital visits, especially for such fragile patients[27]. Currently, the main purpose of PEG placement is for nutritional support. However, other ingenious gastrostomy related procedures have been described in literature that are not for nutritional purposes, including gastric decompression in GI malignancies, access for

ERCP in patient with surgically altered anatomy and access of trocar for therapeutic procedures. The introduction of dedicated devices into clinical practice for therapeutic procedures through a PEG, will expand the possible indication for PEG placement.

CONCLUSION

PEG is a safe and effective procedure even if performed in fragile patients. The selection of patients and the creation of a dedicated team for pre- and post- procedural care is fundamental to obtain good outcomes and reduce AEs. Moreover, careful selection of the best approach used over the different endoscopic approaches, is required. Finally, the stoma can be used not only for nutritional purposes but also as an access route for advanced endoscopic procedures.

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