GE – Portuguese Journal of Gastroenterology

Research Article

GE Port J Gastroenterol 2023;30:350–358 DOI: 10.1159/000525853 Received: December 3, 2021 Accepted: February 22, 2022 Published online: August 30, 2022

Impact of Percutaneous Endoscopic Gastrostomy Tube Feeding on Nutritional Status in Patients Undergoing Chemoradiotherapy for Oesophageal Cancer

Joana Lemos Garcia Rita Vale Rodrigues Susana Mão-de-Ferro Sara Ferreira Miguel Serrano Joana Castela Raquel Sacarrão Fátima Francisco Liliana Sousa António Dias Pereira Grupo Multidisciplinar de Cancro do Esófago e Estômago IPOLFG

Instituto Português de Oncologia de Lisboa Francisco Gentil, Lisbon, Portugal

Keywords

Nutritional status · Esophageal neoplasms · Gastrostomy · Neoadjuvant therapy

Abstract

Introduction: Oesophageal cancer causes dysphagia and weight loss. Malnutrition further worsens with multimodal treatment. *Aim:* The aim of the study was to evaluate the impact of percutaneous endoscopic gastrostomy (PEG) placement in the nutritional status of patients with oesophageal cancer requiring chemoradiotherapy (CRT). Methods: A comparative study with a prospective arm and a historical cohort was conducted. Oesophageal cancer patients undergoing CRT with dysphagia grade >2 and/or weight loss >10% were submitted to PEG-tube placement (pull method) before CRT. Stoma seeding was evaluated through a swab obtained after placement and, in surgical patients, the resected stoma. A matched historical cohort without PEG placementwasusedascontrol(trialACTRN12616000697482). Results: Twenty-nine patients (intervention group, IG) were compared to 30 patients (control group, CG). Main out-

Karger@karger.com www.karger.com/pjg

Karger ^{*}

∂OPEN ACCESS

© 2022 The Author(s). Published by S. Karger AG, Basel

This is an Open Access article licensed under the Creative Commons Attribution-NonCommercial-4.0 International License (CC BY-NC) (http://www.karger.com/Services/OpenAccessLicense), applicable to the online version of the article only. Usage and distribution for commercial purposes requires written permission. comes did not differ in the IG and CG: weight loss during CRT 8.1 ± 5.5 kg versus 9.1 ± 4.2 kg (p = 0.503); 6-month mortality after CRT or surgery 17.2% versus 26.7% (p = 0.383); perioperative complication rate 54.5% versus 55.6% (p = 1.000); unplanned hospital admissions 34.5% versus 40.0% (p = 0.661). In the CG, during CRT, 14 (46.7%) patients presented with dysphagia grade 3–4, of whom 12 required nasogastric tube feeding (n = 10), surgical gastrostomy (n = 1), and oesophageal dilation (n = 1). In the IG, 89.7% used the PEG tube during CRT, sometimes exclusively in 51.7%. Adverse events were mainly minor (n = 12, 41.4%), mostly late peristomal infections, 1 major complication (exploratory laparotomy due to suspected colonic interposition, not confirmed). There was no cytological or histological evidence of stomal tumour seeding. Conclusion: Weight loss, hospital admissions, surgical complications, and mortality were identical in oesophageal cancer patients referred for CRT, regardless of prophylactic PEG. However, half of the patients required exclusive enteral nutritional support, making PEG-tube placement an alternative to consider.

> © 2022 The Author(s). Published by S. Karger AG, Basel

Correspondence to: Joana Lemos Garcia, joanalemosgarcia@outlook.com Impacto da colocação de gastrostomia percutânea endoscópica (PEG) no status nutricional de doentes submetidos a quimiorradioterapia para cancro do esófago

Palavras Chave

Estado nutricional · Neoplasia do esófago · Gastrostomia · Terapêuica neoadjuvante

Resumo

Introdução: A neoplasia do esófago associa-se a disfagia e perda ponderal, sendo a desnutrição agravada pelo tratamento multimodal. Objetivo: Avaliar o impacto da colocação de gastrostomia percutânea endoscópica (PEG) no estado nutricional de doentes com neoplasia do esófago propostos para quimiorradioterapia (QRT). Métodos: Estudo comparativo com braço prospetivo e controlo retrospetivo. Incluídos doentes com neoplasia do esófago propostos para QRT definitiva ou neoadjuvante, com disfagia grau >2 e/ou perda de peso >10%. Colocada PEG (método pull) antes do início de QRT. Avaliada sementeira tumoral por zaragatoa e histologia. Como controlo, utilizada coorte histórica de doentes sem PEG. Registo ACTRN12616000697482. Resultados: 29 doentes (grupo intervenção, GI) foram comparados com 30 controlos (GC). Sem diferença significativa nos principais out*comes*: perda de peso durante a QRT 8.1 \pm 5.5 kg versus 9.1 \pm 4.2 kg (p = 0.503); mortalidade aos 6 meses após QRT ou cirurgia 17.2% versus 26.7% (p = 0.383); taxa de complicações perioperatórias 54.5% versus 55.6% (p = 1.000); admissões hospitalares não planeadas 34.5% versus 40.0% (p = 0.661). No GC, durante a QRT, 14 (46.7%) apresentaram disfagia graus 3-4, dos quais 12 necessitaram de nutrição por sonda nasogástrica (n = 10), gastrostomia cirúrgica (n = 1) ou dilatação esofágica (n = 1). No Gl, 89.7% utilizaram a PEG durante QRT, em algum momento de forma exclusiva em 51.7%. Os eventos adversos foram sobretudo minor (n = 12; 41.4%), sobretudo infeções tardias peri-estoma; 1 complicação major (laparotomia exploradora por suspeita de interposição de cólon, não confirmada). Sem evidência citológica ou histológica de sementeira tumoral no estoma. Conclusão: Embora não se tenham observado diferenças na perda de peso, complicações cirúrgicas e mortalidade entre grupos, metade dos utentes necessitou de nutrição entérica exclusiva, tornando a colocação de PEG uma alternativa a considerar.

> © 2022 The Author(s). Published by S. Karger AG, Basel

Introduction

Oesophageal cancer is the seventh most incident globally and the sixth in terms of mortality, with a mortality/incidence ratio of 0.89 [1]. It belongs to the cancer types with the highest risk for weight loss and malnutrition [2] and nutritional status is expected to further worsen with multimodal treatment [3]. In fact, nutritional intervention may lead to an improved treatment tolerance for patients receiving chemoradiation [3], while those who experience severe preoperative weight loss face a higher 5-year mortality rate after oesophagectomy [4].

Nutritional risk in these patients can potentially be ameliorated by the placement of a percutaneous endoscopic gastrostomy (PEG) tube. Some studies, most of them retrospective, have evaluated the benefits of PEGtube placement in oesophageal cancer patients before multimodal treatments. Although some demonstrated better nutritional management in these cases, most had equal results in terms of perioperative complications, tolerance to chemoradiotherapy (CRT), and overall survival [3, 5-8]. Additional concerns regarding PEG-tube placement are the risk of tumour cells seeding in the stoma and affecting gastric vascularization, thereby precluding surgeons from using a gastric conduit after oesophagectomy, which is the reason why international guidelines so far advise against percutaneous gastrostomy in surgical patients [9]. Nevertheless, evidence suggests that these are rare events [5, 7, 8, 10].

Comparing PEG with other nutritional methods, it is less invasive and is associated with lower complication rates than jejunostomy [11]. Nasogastric tubes usually have lower functional and aesthetical tolerability in mid to long term [12] and, regarding endoscopic stents, although effective in improving dysphagia, it has not been demonstrated that these are effective in improving nutritional status [13–16] and may even be associated with a high complication rate [17].

The primary goal of this study was to assess the impact of PEG-tube placement on the nutritional status of patients with oesophageal cancer requiring definitive or neoadjuvant CRT. Secondary outcomes were (i) to evaluate procedure safety; (ii) to assess feasibility of oesophagectomy with a gastric conduit in these patients; (iii) to assess the risk of stoma tumour seeding.

Materials and Methods

A comparative study with a prospective arm (2016–2020) and a retrospective historical control cohort (2008–2010) was conducted in a Portuguese oncological centre.

Population

Patients aged 18 or higher with oesophageal cancer (squamous cell carcinoma or adenocarcinoma) or oesophageal-gastric junction cancer Siewert I (adenocarcinoma) with dysphagia grade >2 and/or weight loss >10% of body weight requiring isolated or neoadjuvant CRT were proposed for PEG-tube placement on a weekly multidisciplinary meeting, prior to the onset of therapeutic protocol (1–3 weeks before CRT, based on the clinical discretion of the treating physicians). Exclusion criteria included contraindication to PEG-tube placement (such as incapacity of handling the PEG tube, decompensated chronic liver disease, or presence of ascites with a clinical significance).

The study protocol was approved by the hospital's Ethical Committee (*Unidade de Investigação Clínica*) with the approval number UI/1011 and registered in the Australian New Zealand Clinical Trials Registry platform with the trial number AC-TRN12616000697482. All patients provided written and oral informed consent to participate in the study and for publication of the results at least 48 h before the procedure.

The control group (CG) was a historical cohort of patients with the same characteristics (grade of dysphagia, weight loss, treatment with CRT) from existing records of oesophageal/oesophageal-gastric junction cancer patients, with first evaluation from January 2008 until December 2010. They were selected orderly starting with the most recent, in order to prevent selection bias, regardless of nutritional interventions during follow-up. No records were excluded.

Sample Size Calculation

Since this was a pilot study, there were no data available on the likelihood of finding positive results, so, according to the central limit theory which states that the sample distribution will be normal or almost normal if the sample size is large enough, generally assuming that a sample size of 30 is considered appropriate, it was assumed that it would be necessary to include 30 patients in the study.

PEG-Tube Placement Procedure

The PEG tube was placed by two gastroenterologists using the pull method, with antibiotic prophylaxis with intravenous cefazoline (2 g) administered immediately before the procedure. Standard gastroscopes were used (Olympus series 165 or 190). If the oesophageal tumour caused an unsurpassable stenosis with the endoscope with the smallest diameter available (ultra-thin endoscopes were available only in the second half of the study period), an oesophageal dilation was also performed by an experienced gastroenterologist, using a Savary-Gilliard® dilator (9 mm) or a hydrostatic balloon (10 mm). After PEG insertion, a peri-stoma swab was collected, with subsequent cytopathological evaluation. After the procedure, the patient was hospitalized for surveillance for 24 h and started enteral bolus 3 h post-procedure, if no complications occurred. Throughout the course of treatment, the patient could maintain oral diet in addition to enteral nutrition. A nutritional plan was established by a dietitian. In patients undergoing oesophagectomy, the PEG tube was removed during surgery and the peristoma tissue was sent for histopathological evaluation by a pathologist with expertise in digestive pathology. In non-surgical patients, the PEG was removed at the end of the treatment if oral nutrition was possible.

Chemoradiotherapy

According to the institution's protocol, T2–4 or N+ patients unfit for surgery, T3–T4a or N+ patients with conditions for surgery, and any patient with cervical oesophageal cancer undergo CRT with two cycles of 5-FU combined with cisplatin and radiotherapy (50.4 Gy), which may be personalized by the attending oncologist. These patients are re-staged after 4–6 weeks and the final decision to undergo surgery or proceed to definitive CRT is made.

Follow-Up

Nutritional outcomes, surgical complications, urgent hospital admissions, and any complication related to the PEG were registered. Nutritional status was evaluated using body mass index (kg/m²). According to the hospital's protocol for oesophageal cancer patients, they have a first nutritional evaluation by the dietitian at diagnosis, at least twice during CRT (more often in case of increased nutritional risk), and after treatments. These records were used for the CG and were complement by medical records whenever necessary, since weight and dysphagia were systematically documented in the Oncology appointments, which occur every 2 weeks during CRT. In the intervention group (IG), patients' weight was also registered by a Gastroenterology Nurse (see later) every 2 weeks before CRT, weekly thereafter, at weeks 2 and 4 after CRT, and 1 month after surgery.

PEG-related complications were assessed according to type of complication, approach and severity (medical – minor, endoscopic or surgical – major adverse events [AEs]), and time (immediate – until 24 h after procedure, early – less than 7 days, late – 7 days or later). All the records were made by a nurse with more than 5 years of experience in the management of patients with gastrostomies. Follow-up was completed 6 months after surgery or definitive CRT.

Statistical Analysis

For statistical analysis, SPSS Statistics 26 (IBM) was used. Demographic and clinical characteristics were presented as frequencies. Continuous variables were expressed as average and standard deviation or as median and interquartile range, according to data distribution, and were compared using *t*-Student or Wilcoxon tests, respectively. Qualitative variables were compared using χ^2 or Fisher exact tests. A *p* value lower than 0.05 was considered statistically significant.

Results

Forty-seven patients were considered for the trial, of which 29 were included (IG) (Fig. 1). The initial goal of 30 patients was not achieved because of the time allocated for the study. These were compared to 30 patients from the historic cohort (CG). Both groups were similar reDownloaded from http://karger.com/pjg/article-pdf/30/5/350/4022024/000525853.pdf by guest on 21 November 2023

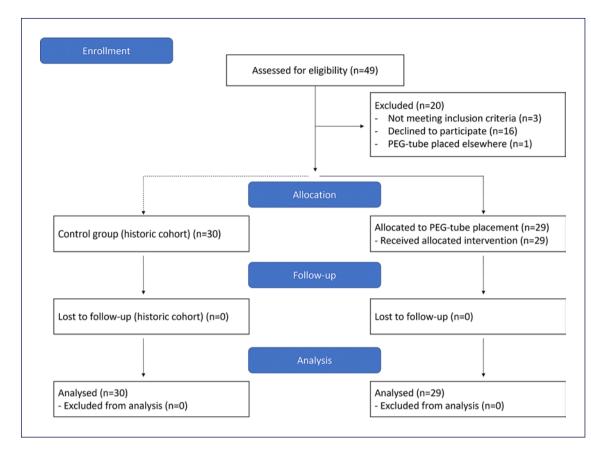


Fig. 1. Schematic representation of eligible patients.

garding demographic and clinical characteristics at baseline. In the IG and in the CG, there were mainly males, aged above 60 years old, with significant past or active alcoholic habits. The most common diagnosis was squamous cell carcinoma, frequently diagnosed in advanced stages. A weight loss higher than 10% was frequently found and dysphagia grade at diagnosis was higher than 2 in over a third of the cases. Table 1 describes patients' characteristics in detail.

In the CG, before CRT, 10 (33.3%) patients required oesophageal dilation and 2 (6.7%) enteral feeding by the nasogastric tube. During CRT, 14 (46.7%) patients presented with dysphagia grades 3 or 4, 12 of them with the need of additional nutritional therapy: nasogastric tube feeding (n = 10), surgical gastrostomy (n = 1), and oesophageal dilation (n = 1).

In the IG, PEG-tube placement success rate was 100%. Pre-procedural oesophageal dilation was necessary in 11 patients (37.9%). 89.3% patients used the PEG tube during CRT, exclusively at some point in 50%. The procedure was mainly associated with minor AEs (n = 12, 42.9%)

and 1 major (exploratory laparotomy due to suspected colonic interposition, not confirmed). Minor AEs were managed conservatively and included bleeding (n = 2, 6.9%), which occurred in the first 24 h after procedure and peristomal infection (n = 10, 34.5%) which was diagnosed early (24 h to 7 days) after procedure in 3 patients and later in 7 cases. In those who underwent surgery (n = 12), technical success was not affected by PEG and it did not influence the type of surgery nor implied the use of colon as a conduit after oesophagectomy. There was no evidence of cytological or histological evidence of tumour seeding in the stoma.

After initial staging, neoadjuvant CRT was proposed to 55.2% (n = 16) of the IG and 60.0% (n = 18) of the CG (p = 0.708), but the strategy was changed to definitive CRT in 4 patients of the IG and 8 of the CG (Table 2). This was due to other comorbidities (IG, n = 2; CG, n = 1), disease progression (IG, n = 2; CG, n = 6), and patient's choice (CG, n = 1). Body mass index variation during CRT was similar between groups (median and IQR in the IG: -2.6 [-4.4, -1.7] and in the CG: -1.9 [-3.2, -0.9], p =

GE Port J Gastroenterol 2023;30:350–358 DOI: 10.1159/000525853

Table 1. Pa	tients' chara	acteristics	at baseline
-------------	---------------	-------------	-------------

	IG (<i>n</i> = 29)	CG (<i>n</i> = 30)	<i>p</i> value
Male sex, <i>n</i> (%)	28 (96.6)	27 (90.0)	0.612
Age, mean \pm SD (min–max), years	65.38±8.60 (50–79)	61.94±9.79 (40–78)	0.158
Alcohol, n (%)	28 (96.6)	25 (83.4)	
Past habits	19 (65.5)	5 (16.7)	0.195
Current habits	9 (31.0)	20 (66.7)	
Tobacco, n (%)	22 (75.8)	25 (83.4)	
Past habits	15 (51.7)	11 (36.7)	0.476
Current habits	7 (24.1)	14 (46.7)	
Squamous cell carcinoma, n (%)	26 (89.7)	24 (80.0)	0.216
Stage III–IV (AJCC 8th edition), n (%)	22 (75.9)	23 (76.7)	0.582
Location, n (%)			
Cervical oesophagus	10 (34.5)	3 (10.0)	
Upper thoracic oesophagus	1 (3.4)	5 (16.7)	
Mid thoracic oesophagus	10 (34.5)	13 (43.3)	0.115
Lower oesophagus	6 (20.7)	8 (26.7)	
Gastroesophageal junction	2 (6.9)	1 (3.3)	
Dysphagia at diagnosis, n (%)			
No dysphagia	1 (3.4)	0	
Grade 1/2	19 (65.5)	19 (63.3)	0.064
Grade 3/4	9 (31.0)	11 (36.6)	
BMI at diagnosis, mean \pm SD (min–max), kg/m ²	22.1±3.9 (16.0-30.8)	22.2±4.2 (15.3-31.6)	0.918
Weight loss at diagnosis, mean \pm SD, kg	-8.1±5.5 (11.54±7.72%)	-9.1±4.2 (12.69±5.09%)	0.503
BMI variation at diagnosis, mean \pm SD, kg/m ²	-3.0±1.9	-3.2±0.4	0.332

Table 2. Treatment modalities

	IG (<i>n</i> = 29)	CG (<i>n</i> = 30)	<i>p</i> value
Treatment modality performed, <i>n</i> (%)			
Neoadjuvant CRT	12 (41.4)	10 (33.3)	0 5 2 2
Definitive CRT	17 (58.6)	20 (66.7)	0.523
Type of surgery, <i>n</i> (%)			
Mckeown oesophagectomy	4 (33.3)	6 (60.0)	
Ivor Lewis oesophagectomy	8 (27.6)	2 (20.0)	0.099
Transhiatal oesophagectomy	0	2 (20.0)	

0.292) (Fig. 2), as were 6-month mortality after surgery or CRT (IG 17.2% and CG 26.7%, p = 0.383), perioperative complications (IG 54.5% and CG 55.6%, p = 1.000), and unplanned hospital admissions (IG 34.5% and CG 40.0%, p = 0.661) (Table 3).

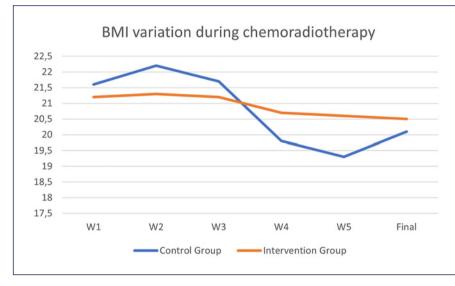
In the univariate analysis, significant weight loss during CRT, defined as a weight loss of at least 10% during this period, was not associated with age (p = 0.302), alcohol (p = 0.851) or tobacco (p = 0.627) consumption, weight loss at diagnosis (p = 0.543), histological type (p =0.803), tumour grade (p = 0.812), stage (p = 0.572), dysphagia grade at diagnosis (p = 0.255) or during CRT (p = 0.097). Similarly, unplanned hospital admission did not show a significant association with these variables (Table 4).

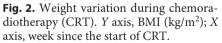
Discussion/Conclusion

In patients with oesophageal cancer treated with definitive or adjuvant CRT, prophylactic PEG-tube placement did not improve the most relevant clinical outcomes, namely, weight loss during CRT, unplanned hospital admissions, surgical complications, and mortality.

Table 3. Outcomes during and after treatment

	IG (<i>n</i> = 29)	CG (<i>n</i> = 30)	<i>p</i> value
Weight loss during CRT, median (IQR), k q	-5.0 (-6.0, -1.5) (6.85% [2.57-10.70%])	-5.2 (-8.9, -2.0) (8.30% [3.62-13.61%])	0.289
BMI loss during CRT, kg/m ²	-2.6 (-4.4, -1.7)	-1.9 (-3.2, -0.9)	0.292
Highest grade of dysphagia during CRT, n (%)			
Grade 1/2	14 (48.3)	16 (53.3)	
Grade 3/4	15 (51.7)	14 (46.7)	0.100
Highest grade of dysphagia after CRT, n (%)			
Grade 1/2	11 (37.9)	14 (46.7)	
Grade 3/4	15 (51.7)	14 (46.7)	0.953
6-Month mortality after CRT or surgery, %	17.2 (<i>n</i> = 5)	26.7 (<i>n</i> = 8)	0.383
Perioperative complications	6/12 patients	5/10 patients	
Fistula, n (%)	2	2 (6.7)	
Anastomotic dehiscence, n (%)	1 (10.3)	0	
Pneumonia/aspiration, n (%)	3 (10.3)	2 (6.7)	1.000
Arrhythmia, n (%)	0	1 (3.3)	
Days in intensive care after surgery, median (IQR)	6.0 (4.0-8.0)	4.0 (3.0–13.8)	0.654
Unplanned hospital admissions, n (%)	10 (34.5)	12 (40.0)	0.661
Infectious complications not PEG-related or febrile neutropenia	9 (31.0)	7 (58.3)	
Dysphagia	0	4 (33.3)	
Disease progression	1 (3.4)	0	0.254
Duration, median (IQR), days	10.0 (7.3–13.8)	5.5 (4.3–15.0)	





This was in line with the findings of retrospective studies such as that of Bhatti et al. [7], as well as others with smaller samples [5, 6, 10]. Nevertheless, as depicted in Figure 2, weight variation was more pronounced in the CG, with possible metabolic implications, since weight fluctuation might be associated with an increased risk of all-cause mortality, as shown in the general population [18]. Comparing both groups, it was striking that almost half of the patients who were not submitted to PEG-tube placement before CRT required enteric nutritional support during treatment, which usually consisted of nasogastric tube feeding. On the other hand, most of the patients with prophylactic PEG used it complementarily and, in half of the cases, as an exclusive way of nutrition at some point during CRT. Table 4. Risk factors for significant weight loss during CRT (≥10% of weight at diagnosis) and for unplanned hospital admissions (univariate/multivariate analysis)

Variable	Significant weight loss	Unplanned hospital admissions
Age	<i>p</i> = 0.302	<i>p</i> = 0.848
Weight loss at diagnosis	p = 0.543	<i>p</i> = 0.224
BMI at diagnosis	<i>p</i> = 0.058	<i>p</i> = 0.339
Alcohol	<i>p</i> = 0.851	<i>p</i> = 0.190
Tobacco	p = 0.627	p = 0.069
Histology	<i>p</i> = 0.803	<i>p</i> = 0.409
Tumour grade	<i>p</i> = 0.812	<i>p</i> = 0.340
Tumour stage	p = 0.572	<i>p</i> = 0.488
Dysphagia at diagnosis	p = 0.255	<i>p</i> = 0.167
Dysphagia during CRT	p = 0.097	p = 0.596
Treatment modality (isolated or neoadjuvant CRT)	p = 0.408	p = 0.098

PEG-tube placement was a feasible procedure, with minor AEs in around 40% of the cases, mostly late peristomal infections. However, 1 patient needed an exploratory laparotomy because colonic interposition was suspected but not confirmed. Infectious complications are already known to be the most common PEG-associated AEs [19, 20]. Zopf et al. [19] conducted a prospective multicentre study including 390 patients, where 33.6% had peristomal infection and the presence of malignant disease had a significant association with this risk, which may explain our findings. This complication rate is nonetheless higher than that reported in other studies such as that conducted by Margolis et al. [8], in which 103 patients with oesophageal cancer and PEG-tube placement were retrospectively evaluated. It is not clear whether this difference is due to technical differences, bias associated with the study type, or other reasons. Whether the high rate of peristomal infection is also attributable to the technique chosen (pull vs. "push"/gastropexy) is not clear since there are discordant reports comparing these groups [19, 21, 22].

Importantly, the PEG tube did not affect type of surgery or surgical technical success, as reported in other studies [5, 7, 10]. Matsumoto et al. [5] further consolidated these conclusions through intraoperative thermal imaging, which demonstrated that gastric blood flow was not affected by previous PEG.

Recently published guidelines from the European Society of Gastrointestinal Endoscopy recommend the percutaneous introducer ("push") technique for PEG placement in patients with head and neck cancer or oesophageal cancer [23, 24]. The main reason underlying this recommendation is the risk of metastasis to the PEG site. The meta-analysis from Siu et al. [25], including 121 cases, reported rates of 0.56% (95% CI: 0.40–0.79%) with the "pull" technique and 0.29% (95% CI: 0.15–0.55%) with the "push" technique. This difference is not neglectable and must be considered, despite the null rate of stoma tumour cells found in our study. It is also noteworthy that even in the "push" group, PEG site metastasis was found, supporting haematogenous or lymphatic spread of the tumour cells, an important mechanism, as already suggested in the literature [26, 27].

A notable advantage of this study was its prospective nature, which allowed a precise and unbiased data collection in the intervention arm. This was performed in a hospital with expertise in Oncology, where the best standard-of-care was applied, allowing an extrapolation of the results.

There are important limitations to mention, namely, the retrospective evaluation of the CG. However, since the patients in the historic cohort had both medical and nutritional follow-up, the records were very complete and possible errors in retrospective data collection were mitigated. It is also worth noticing that a small sample was used and it is possible that the study may have not been adequately powered. Other nutritional endpoints such as hand grip strength and albumin were not systematically assessed and were not included in our results, further limiting conclusion withdrawal. It would have been interesting to know the nutritional status of these patients 6 months post-CRT, but this variable was not foreseen, thereby not prospectively collected and not included due to the risk of collecting biased information.

In conclusion, this study strengthens current knowledge about prophylactic PEG-tube placement in oesophageal cancer patients undergoing multimodal treatment. This is a safe procedure, with predominantly minor AEs and no evidence of tumour cells seeding in the stoma in the population studied. One of the main advantages of this intervention is avoiding invasive procedures aiming for enteral feeding during CRT.

Acknowledgments

We would like to thank Doctor Sandra Faias, coordinator of the team dedicated to percutaneous gastrostomies in our Gastroenterology Department, as well as all the staff involved in the management of the patients studied.

Statement of Ethics

The study protocol was approved by the hospital's Ethical Committee (Unidade de Investigação Clínica) with the approval number UI/1011 and registered in the Australian New Zealand Clinical Trials Registry 104 platform with the trial number ACTRN12616000697482.

Conflict of Interest Statement

All authors have no conflict of interest to declare.

Funding Sources

There was no funding for this study.

Author Contributions

Rita Vale Rodrigues elaborated the study protocol and was the main investigator together with Joana Lemos Garcia. Susana Mãode-Ferro was the main person involved in reviewing scientific data. Sara Ferreira, Miguel Serrano, and Joana Castela were doctors involved in recruiting of the patients and data collection.

Raquel Sacarrão, Fátima Francisco and Liliana Sousa were the nurses involved in the regular follow-up of these patients. They were responsible for data collection during follow-up. António Dias Pereira was the Head of Department and supervised the process in all the steps.

Grupo Multidisciplinar de Cancro de Esófago e Estômago is the multidisciplinary team where these patients were recruited. It served as the link between Gastroenterologists, Surgeons, Oncologists, Radiotherapists, and Pathologists involved in these patients' process.

Data Availability Statement

Raw data are not publicly available since they were not foreseen during informed consent.

References

- Bray F, Ferlay J, Soerjomataram I, Siegel RL, Torre LA, Jemal A. Global cancer statistics 2018: GLOBOCAN estimates of incidence and mortality worldwide for 36 cancers in 185 countries. CA Cancer J Clin. 2018;68(6):394– 424.
- 2 Steenhagen E, van Vulpen JK, van Hillegersberg R, May AM, Siersema PD. Nutrition in peri-operative esophageal cancer management. Expert Rev Gastroenterol Hepatol. 2017;11(7):663–72.
- 3 Odelli C, Burgess D, Bateman L, Hughes A, Ackland S, Gillies J, et al. Nutrition support improves patient outcomes, treatment tolerance and admission characteristics in oesophageal cancer. Clin Oncol. 2005;17(8):639–45.
- 4 van der Schaaf MK, Tilanus HW, van Lanschot JJB, Johar AM, Lagergren P, Lagergren J, et al. The influence of preoperative weight loss on the postoperative course after esophageal cancer resection. J Thorac Cardiovasc Surg. 2014;147(1):490–5.
- 5 Matsumoto A, Yuda M, Tanaka Y, Tanishima Y, Yano F, Nishikawa K, et al. Efficacy of percutaneous endoscopic gastrostomy for patients with esophageal cancer during preoperative therapy. Anticancer Res. 2019;39(8): 4243–8.

- 6 Mitchell S, Williams JP, Bhatti H, Kachaamy T, Weber J, Weiss GJ. A retrospective matched cohort study evaluating the effects of percutaneous endoscopic gastrostomy feeding tubes on nutritional status and survival in patients with advanced gastroesophageal malignancies undergoing systemic anti-cancer therapy. PLoS One. 2017;12(11):e0188628.
- 7 Bhatti ABH, Rizvi FH, Waheed A, Raza SH, Syed AA, Khattak S, et al. Does prior percutaneous endoscopic gastrostomy alter post-operative outcome after esophagectomy. World J Surg. 2015;39(2):441–5.
- 8 Margolis M, Alexander P, Trachiotis GD, Gharagozloo F, Lipman T. Percutaneous endoscopic gastrostomy before multimodality therapy in patients with esophageal cancer. Ann Thorac Surg. 2003;76(5):1694–8.
- 9 NCCN Guidelines Panel. Esophageal and esophagogastric junction cancers v. 2.2018. NCCN; 2017.
- 10 Wright GP, Foster SM, Chung MH. Esophagectomy in patients with prior percutaneous endoscopic gastrostomy tube placement. Am J Surg. 2014;207(3):361–5; discussion 364–5.

- 11 Ao P, Sebastianski M, Selvarajah V, Gramlich L. Comparison of complication rates, types, and average tube patency between jejunostomy tubes and percutaneous gastrostomy tubes in a regional home enteral nutrition support program. Nutr Clin Pract. 2015; 30(3):393–7.
- 12 Löser C, Aschl G, Hebuterne X, Mathus-Vliegen EMH, Muscaritoli M, Niv Y, et al. ESPEN guidelines on artificial enteral nutrition: percutaneous endoscopic gastrostomy (PEG). Clin Nutr. 2005;24(5):848–61.
- 13 Martin RCG, Cannon RM, Brown RE, Ellis SF, Williams S, Scoggins C, et al. Evaluation of quality of life following placement of selfexpanding plastic stents as a bridge to surgery in patients receiving neoadjuvant therapy for esophageal cancer. Oncologist. 2014;19(3): 259–65.
- 14 Bower M, Jones W, Vessels B, Scoggins C, Martin R. Nutritional support with endoluminal stenting during neoadjuvant therapy for esophageal malignancy. Ann Surg Oncol. 2009;16(11):3161–8.
- 15 Pellen MGC, Sabri S, Razack A, Gilani SQ, Jain PK. Safety and efficacy of self-expanding removable metal esophageal stents during neoadjuvant chemotherapy for resectable esophageal cancer. Dis Esophagus. 2012; 25(1):48–53.

- 16 Siddiqui AA, Sarkar A, Beltz S, Lewis J, Loren D, Kowalski T, et al. Placement of fully covered self-expandable metal stents in patients with locally advanced esophageal cancer before neoadjuvant therapy. Gastrointest Endosc. 2012;76(1):44–51.
- 17 Mão-de-Ferro S, Serrano M, Ferreira S, Rosa I, Lage P, Alexandre DP, et al. Stents in patients with esophageal cancer before chemoradiotherapy: high risk of complications and no impact on the nutritional status. Eur J Clin Nutr. 2016;70(3):409–10.
- 18 Zhang Y, Hou F, Li J, Yu H, Li L, Hu S, et al. The association between weight fluctuation and all-cause mortality: a systematic review and meta-analysis. Medicine. 2019;98(42): e17513.
- 19 Zopf Y, Konturek P, Nuernberger A, Maiss J, Zenk J, Iro H, et al. Local infection after placement of percutaneous endoscopic gastrostomy tubes: a prospective study evaluating risk factors. Can J Gastroenterol. 2008;22(12): 987–91.

- 20 Rahnemai-Azar AA, Rahnemaiazar AA, Naghshizadian R, Kurtz A, Farkas DT. Percutaneous endoscopic gastrostomy: indications, technique, complications and management. World J Gastroenterol. 2014;20(24): 7739–51.
- 21 Tucker AT, Gourin CG, Ghegan MD, Porubsky ES, Martindale RG, Terris DJ. "Push" Versus "Pull" percutaneous endoscopic gastrostomy tube placement in patients with advanced head and neck cancer. Laryngoscope. 2003;113(11):1898–902.
- 22 Retes FA, Kawaguti FS, de Lima MS, da Costa Martins B, Uemura RS, de Paulo GA, et al. Comparison of the pull and introducer percutaneous endoscopic gastrostomy techniques in patients with head and neck cancer. United Eur Gastroenterol J. 2017;5(3):365–73.
- 23 Arvanitakis M, Gkolfakis P, Despott EJ, Ballarin A, Beyna T, Boeykens K, et al. Endoscopic management of enteral tubes in adult patients: part 1 – definitions and indications European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2021;53(1): 81–92.

- 24 Gkolfakis P, Arvanitakis M, Despott EJ, Ballarin A, Beyna T, Boeykens K, et al. Endoscopic management of enteral tubes in adult patients: part 2 peri- and post-procedural management. European Society of Gastrointestinal Endoscopy (ESGE) Guideline. Endoscopy. 2021;53(2):178–95.
- 25 Siu J, Fuller K, Nadler A, Pugash R, Cohen L, Deutsch K, et al. Metastasis to gastrostomy sites from upper aerodigestive tract malignancies: a systematic review and meta-analysis. Gastrointest Endosc. 2020;91(5):1005–14. e17.
- 26 Brown MC. Cancer metastasis at percutaneous endoscopic gastrostomy stomata is related to the hematogenous or lymphatic spread of circulating tumor cells. Am J Gastroenterol. 2000;95(11):3288–91.
- 27 Strodel WE, Kenady DE, Zweng TN. Avoiding stoma seeding in head and neck cancer patients. Surg Endosc. 1995 Oct;9(10):1142– 3.