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Gastrostomía endoscópica para el soporte nutricional en la disfagia posterior a un accidente cerebrovascular

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ABSTRACT

Introduction: persistent dysphagia affects 15 % of stroke patients and contributes to malnutrition, aspiration, and death. This study aimed to characterize patients with post-stroke dysphagia who

underwent percutaneous endoscopic gastrostomy (PEG), and to assess the impact of PEG feeding on nutritional status and outcome.

Methods: an observational and retrospective study using records from patients with post-stroke dysphagia who underwent PEG. Body mass index (BMI), serum albumin, transferrin, and cholesterol were recorded at the time of PEG insertion (T0) and 3 months later (T3). The evolution of these parameters was analyzed and compared to survival.

Results: we obtained data from 158 patients (53.2 % males) with a median age of 75 years. Most strokes were ischemic (n = 135, 85.4 %). Median time between stroke and PEG was 2 months. Median survival after gastrostomy was 16 months. At admission, 41.6 % of patients had low BMI, 62.3 % low albumin, 68.6 % low transferrin, and 59.6 % low cholesterol levels. The prevalence of low albumin and low transferrin was higher in the patients who underwent PEG more than 2 months after stroke. A significant increase in albumin and transferrin, and a normalization of cholesterol levels was observed after 3 months of PEG feeding. Mortality was 12.9 %, 27.7 %, and 40 % at 1, 3, and 12 months, respectively. Survival was lower in patients with low albumin, transferrin or total cholesterol at admission.

Conclusions: the prevalence of malnutrition is high among patients with post-stroke dysphagia. PEG feeding improves albumin, transferrin, and cholesterol levels. Early post-PEG mortality is high and must be considered on an individual basis.

Keywords: Stroke. Dysphagia. Nutrition. Gastrostomy.

RESUMEN

Introducción: la disfagia persistente afecta al 15 % de los pacientes con accidente cerebrovascular (AVC) y contribuye a producir desnutrición, aspiración y muerte. Este estudio tuvo como objetivo

caracterizar a los pacientes con disfagia post-AVC sometidos a gastrostomía endoscópica percutánea (PEG) y evaluar el impacto de la alimentación con PEG sobre el estado nutricional.

Métodos: estudio observacional y retrospectivo que utiliza registros de pacientes con disfagia post-AVC sometidos a PEG. El índice de masa corporal (IMC) y los niveles de albúmina, transferrina y colesterol séricos se registraron en el momento de la inserción de la PEG (T0) y 3 meses después (T3). La evolución de estos parámetros se analizó y comparó con la supervivencia.

Resultados: se obtuvieron datos de 158 pacientes (53,2 % hombres) con una edad media de 75 años. La mayoría de los AVC fueron isquémicos (n = 135, 85,4 %). El tiempo medio entre el AVC y la PEG fue de 2 meses. La supervivencia media después de la gastrostomía fue de 16 meses. Al ingreso, el 41,6 % de los pacientes presentaba un IMC bajo, el 62,3 % un nivel bajo de albúmina, el 68,6 % un nivel bajo de transferrina y el 59,6 % un nivel bajo de colesterol. La prevalencia de los niveles bajos de albúmina y de transferrina fue mayor en los pacientes que se sometieron a la PEG más de 2 meses después del AVC. Se observó un aumento significativo de la albúmina y la transferrina, y una normalización de los niveles de colesterol, después de 3 meses de alimentación con PEG. La mortalidad fue del 12,9 %, 27,7 % y 40 % a 1, 3 y 12 meses, respectivamente. La supervivencia fue menor en los pacientes con nivel bajo de albúmina, transferrina o colesterol total al ingreso.

Conclusiones: la prevalencia de la malnutrición es alta entre los pacientes con disfagia post-AVC. La alimentación con PEG mejora los niveles de albúmina, transferrina y colesterol. La mortalidad temprana post-PEG es alta y debe considerarse de forma individual.

Palabras clave: Accidente cerebrovascular. Disfagia. Nutrición. Gastrostomía.

INTRODUCTION

Stroke is a major public health problem, being one of the leading causes of death in developed countries along with cardiovascular disease (1,2). In addition, stroke is the most important cause of permanent disability in adulthood, thus impairing many activities of daily living (1). The consequences of stroke may be overwhelming and, together with the well-known impact in mobility and communication skills, dysphagia is one of the most disabling sequelae (2).

In the early stages after stroke, 30 to 50 % of patients suffer from dysphagia (3,4). Although most patients recover within the first four weeks, 15 % of patients may develop long-term swallowing difficulties (5,6). Dysphagia may contribute to poor nutritional status and, if not promptly recognized, may lead to dehydration and malnutrition (3,7,8). Furthermore, dysphagia is a major cause of aspiration pneumonia, which may be the leading cause of death in these patients (1,7). All of these consequences can be deleterious for stroke patients and may counteract clinical recovery, promote infections, prolong in-hospital stay, increase healthcare costs, and affect quality of life (9-13). Due to its prognostic relevance, early detection of stroke-related dysphagia and a suitable nutritional management are therefore of utmost clinical importance (3,8). In this context, the most recent ESPEN guidelines recommend that a formal screening for dysphagia should be performed as early as possible, and that all stroke patients should be screened for risk of malnutrition (8).

The available evidence suggests that patients with prolonged severe dysphagia after stroke, presumably lasting for more than seven days, should receive early (not later than 72 hours) enteral tube feeding (8). Since most patients with post-stroke dysphagia recover within the first few weeks, it is advisable to consider initially a minimally invasive nutritional access by nasogastric tube. However, if enteral feeding is likely necessary for a longer period of time (more than 3-4

weeks), nutritional support provided by percutaneous endoscopic gastrostomy (PEG) is preferable. Actually, PEG should be performed in a stable clinical phase (after 2-4 weeks), according to the recommendations of the ESPEN guidelines (7,8).

Despite these recommendations, it remains controversial whether these patients with post-stroke persistent dysphagia and severe disability benefit from PEG placement to improve survival and quality of life. There is some evidence suggesting that some patients will not benefit from PEG placement, even in the short term, due to the high early mortality (mostly due to respiratory and cardiac comorbidities) reported. Thus, this issue remains a difficult clinical and ethical dilemma for both physicians and families (14-16).

The overall aims of this retrospective study were:

- To assess the nutritional status of patients with post-stroke persistent dysphagia when they are referred for PEG placement.
- To evaluate the effectiveness of PEG feeding for nutritional support, reviewing the experience of our artificial feeding team.
- To assess the survival of PEG patients and the relationship between survival and the anthropometric and laboratory parameters evaluated immediately before the gastrostomy procedure.
- Document PEG procedure complications in this setting.

MATERIAL AND METHODS

Study design

A single-center, observational, longitudinal, retrospective study was performed in a hospital setting. This project was approved by the Ethics Committee of our hospital.

Patients

The authors studied consecutive patients with post-stroke dysphagia who were referred to the Artificial Feeding Team (GENE) of the

Gastroenterology Department and underwent endoscopic gastrostomy to improve nutritional support from 2005 to 2017. All patients were followed up at the Artificial Nutrition Outpatient Clinic.

The diagnosis of stroke was based on both clinical and imaging (computed tomography and/or magnetic resonance) features. Data regarding age and gender, type (ischemic and hemorrhagic) and location (unilateral [right or left-sided], bilateral, cortical/subcortical, vertebrobasilar or with basal ganglia involvement) of stroke, date of stroke and of gastrostomy procedure, post-PEG complications, and mortality were collected.

The decision for PEG insertion was individualized to each patient through an interdisciplinary evaluation, including speech therapist swallowing assessment, which determined if enteral tube feeding was necessary to avoid malnutrition and aspiration risk, to correct significant nutritional deficiencies, or to rehydrate the patient. Informed consent for PEG placement was obtained from patients or their caregivers. Patients with concomitant neurological disorders, including dementia or other neurodegenerative disease with severe motor impairment were excluded.

Clinical outcome

Patients were included into four categories according to their outcome: deceased, lost to follow-up, alive and still PEG-fed, or alive having resumed oral feeding (with tube removal and gastrostomy fistula closed). Time span from stroke diagnosis to gastrostomy procedure and to death (or until 31 May 2018) was rounded up to the nearest month. Reports of major complications were evaluated.

Anthropometric evaluation

The anthropometric evaluation was performed according to the manual of the International Society for the Advancement of Kinanthropometry (ISAK) just before the gastrostomy procedure (T0), between 8:00 and 10:00 AM. The average of three consecutive

measurements was then recorded. The anthropometric evaluation was repeated three months later (T3) for surviving patients followed up in the Artificial Nutrition Outpatient Clinic.

– Body mass index (BMI) was obtained using the equation weight / height^2. If patients were unable to easily stand up for weight and height evaluation, BMI was estimated using the mid-upper-arm circumference and regression equations described by Powell-Tuck and Hennessy (17), which are proven to provide a reliable BMI estimation in PEG-feeding patients (18). Each patient was classified according to age, having low weight if BMI < 18.5 kg/m^2 for patients under 65 years or BMI < 22 kg/m^2 for patients 65 years old or older (19).

– Mid-upper-arm circumference (MUAC) was measured in centimeters using a flexible measuring tape wrapped around the mid-upper arm, halfway between the olecranon and the acromion process.

Laboratory evaluation

A blood sample for serum albumin, transferrin, and total cholesterol was obtained minutes before the endoscopic gastrostomy (T0), between 8:00 and 10:00 AM, after at least 12 h of fasting. The whole laboratory evaluation was repeated three months later (T3) for surviving patients not lost to follow-up. Values of albumin < 3.5 g/dL, transferrin < 200 mg/dL, and total cholesterol < 160 mg/dL were considered low values, suggestive of malnutrition and/or poor prognosis.

Statistical analysis

The statistical analysis was performed using the SPSS software, version 21 (SPSS, Chicago, IL, USA). Normality was assessed using the Kolmogorov-Smirnov test. Mean and standard deviation (s.d.) or median and interquartile range 25-75 % (IQR) were used for continuous variables. Frequencies were used for categorical variables.

Continuous variables were compared using Student's t-test or the Mann-Whitney test, and the Chi-square test or Fisher's test were used for categorical variables. For correlation analysis between anthropometric or laboratory measurements and patient survival, Spearman's correlation coefficients were calculated. A p-value < 0.05 was considered statistically significant.

RESULTS

Data from a total of 158 patients with post-stroke dysphagia who underwent PEG for nutritional support were retrieved. The median age was 73.2 ± 13.4 years (range, 33-96); 122 patients (77.2 %) were 65 years old or older, and 84 patients (53.2 %) were male. Regarding the type of stroke, most patients had suffered an ischemic stroke (n = 135, 85.4 %) involving the anterior circulation (n = 111), and with a cortical-subcortical location (n = 46). More detailed demographics and stroke-related data are shown in table I. Patients were followed up from PEG placement to death or up to May 2018, for a median time of 16 months [IQR, 3-40].

The period between stroke and PEG placement ranged from two weeks to 85 months (median, 2 months [IQR, 1-5] and mean 6 ± 12.7 months). Eighty-seven (55.1 %) patients underwent PEG within the first two months after stroke. There were no major immediate complications associated with the gastrostomy procedure.

At admission, the authors obtained information about BMI in 144 patients. The median value was 22.5 kg/m^2 (IQR 19.6-25.06), and BMI was considered low in 60 cases (41.6 %). Twenty-one patients (14.6 %) were overweight or obese at T0. There was a higher prevalence of undernutrition in patients over 65 years compared to younger patients (47.3 % vs 21.9 %, p = 0.01). Regarding the laboratory results at T0, 96/154 patients (62.3 %) had low serum albumin, 105/153 (68.6 %) had low transferrin, and 90/151 (59.6 %) had low total cholesterol (Table II). There were no statistically

significant differences regarding these biochemical parameters according to patient age (elderly vs non-elderly).

When we compared the group of patients who underwent PEG within the first two months after stroke with those who had it placed later, we found no differences in the prevalence of low BMI. However, we found a higher prevalence of low albumin (47.6 % vs 72.41 %, p = 0.002) and low transferrin (59.7 % vs 75.6 %, p = 0.03) in the group of patients undergoing PEG more than two months after stroke. Although the percentage of patients with low total cholesterol was higher in the group that underwent PEG later, this difference was not significant (57.4 % vs 62.4 %, p = 0.61).

Regarding BMI changes over time, mean BMI decreased significantly from T0 to T3 (22.35 vs 21.56 kg/m^2, p = 0.009). Considering only the patients who were overweight at admission, there was a decrease in BMI at three months (T3) compared to baseline (T0), from 28.1 to 25.63 kg/m^2 (p = 0.02). Amongst patients with normal or low BMI at T0, the variation of BMI was not significant at 3 months (21.6 vs 21.1 kg/m^2, p = 0.07).

Concerning biochemical biomarkers, mean serum albumin increased significantly after 3 months of PEG feeding (3.26 g/dL vs 3.58 g/dL, p < 0.001), as well as mean transferrin (181 mg/dL vs 201 mg/dL, p < 0.001) and total cholesterol (154.04 mg/dL vs 165.77 mg/dL, p = 0.002).

At the end of the study period, from the 158 patients included, 119 had died, 36 were alive, and three were lost to follow-up. Among the 36 living patients, oral feeding was resumed in eight and the PEG tube was removed, with an average period to removal of 8.4 ± 3.89 months. Considering all patients, median survival after PEG insertion was 16 months and ranged from less than one month to the maximum of 142 months. Regarding the patients who died during the study period, the median time from PEG placement to death was 8.5 months [IQR, 1-28].

Of the 155 patients who completed follow-up, 20 patients (12.9 %) died less than one month after PEG placement and 43 patients (27.7 %) within the first three months (Fig. 1). At 12 months after gastrostomy, the mortality rate was 43.9 %. There were no differences in survival, neither between different genders, nor between types (ischemic or hemorrhagic) and location of stroke.

Although there was a positive correlation between albumin, transferrin, and total cholesterol with survival after PEG, it did not reach statistical significance.

Nevertheless, mortality at the end of the follow-up period was higher in patients who had low albumin (85.1 % vs 64.91 %; p = 0.005), low transferrin (83.7 % vs 65.2 %; p = 0.018), or low total cholesterol (84.1 % vs 65 %; p = 0.01) at admission.

DISCUSSION

Dysphagia is a common and pressing problem in the acute phase of stroke, and is associated with potentially life-threatening complications as well as with increased morbidity and mortality. In this context, current recommendations advocate for the evaluation of swallowing in stroke patients as early as possible, ideally within the first 24 hours. Following this initial screening, it is essential to implement nutritional support measures in patients with dysphagia and risk of malnutrition (8).

It is estimated that during the acute phase of stroke up to 30 % of patients require tube feeding (3). A question thus arises as to who are the patients who will mostly benefit from this nutritional support, as well as the proper timing to start it. The FOOD trial showed a trend towards reduced mortality in post-stroke dysphagic patients by 5.8 % (p = 0.09) in the group with early tube feeding (initiated within seven days after stroke) (20,21). In the light of current knowledge, it is recommended that patients with dysphagia who are not expected to ensure sufficient nutritional intake for more than one week should initiate tube feeding within the first 72 hours after stroke. In addition,

when nutritional support is anticipated to last for more than 28 days PEG is recommended (8).

However, some studies report a high early mortality (first 3 months) after PEG placement in the post-stroke dysphagia setting, largely due to cardiac and respiratory events, suggesting that certain patients may not benefit from PEG even in the short-term (4). Our study corroborates these data concerning high early mortality. In our sample, there was a 12.9 % mortality rate in the first four weeks after PEG, and 27.7 % during the first three months. Moreover, at the end of the first year of follow-up mortality was greater than 40 %. Specific causes of death were not assessed in our patients since most died after hospital discharge. The previously reported predictors of early mortality in PEG patients include advanced age, hypoalbuminemia, low BMI, cardiac risk factors, a higher Charlson comorbidity index, and malignancy (4). Jiang et al. evaluated mortality specifically in PEG patients with post-stroke dysphagia and proposed that age, ASA score, and albumin level at the time of PEG insertion should be included as factors to assist in the selection of patients who are likely to survive more than 3 months post-PEG insertion (4). A more accurate prediction of long term survival may lead to better selection of the patients who would benefit from this invasive procedure. Actually, in our study, an increased mortality rate was observed in patients with low albumin, low transferrin, and/or low total cholesterol.

Another important point is the significant prevalence of malnutrition at the time of admission, prior to PEG placement. At baseline, 41.6 % of patients had low BMI, a finding that was more striking in the group of patients over 65 years. Also, more than half of the patients had low levels of albumin, transferrin, or total cholesterol before PEG. Data from the literature showed that at the time of stroke approximately 20 % of patients are already malnourished, probably due to older age and previous disabilities (22). However, the authors believe that the delay in PEG placement after stroke can lead to increased prevalence

of malnutrition. In the present study, the mean time between stroke and PEG placement was 6 months, which may have contributed to further worsening of malnutrition. Although some patients remained with a nasogastric tube until PEG placement, long-term nasogastric tube feeding may be less effective than PEG nutrition and may perpetuate the deterioration of nutritional status (23).

After 3 months of PEG feeding, there was a decrease in BMI in patients who maintained follow-up. This decline in BMI may be due to several reasons. 1) Around 14 % of our sample was overweight at admission and, since obesity is a risk factor for cerebrovascular disease, a better balanced diet may have contributed to weight loss in this group of patients. 2) Three months may be too short a time period for nutritional support to restore metabolic reserves in previously undernourished patients and to allow significant weight gain. 3) It should also be noted that post-stroke patients often become bedridden, lose autonomy, and have a lower functional performance status, which in turn contributes to sarcopenic obesity. Maybe more importantly, BMI decreased at 3 months after PEG feeding in overweight but not in normal/low-weight patients. Hence, this may suggest that enteral nutrition through PEG may contribute to normalize weight and reduce cardiovascular risk in these patients.

Unlike BMI, which did not increase at 3 months, there was a significant increase in albumin, transferrin, and total cholesterol levels. Although these biochemical parameters are influenced by several factors, since they are negative acute phase reagents, our data show that PEG feeding had a positive biochemical impact. Also, it should be noted that cholesterol changes may still be influenced by statins, given that dyslipidemia is a cardiovascular risk factor and that most stroke patients take lipid-lowering treatment as part of secondary stroke prevention. Probably, in a longer period of follow-up this nutritional impact of PEG feeding would also have a positive impact on BMI.

Regarding survival after PEG placement, although there was a positive correlation with values of albumin, transferrin, and total cholesterol in T0, it did not reach statistical significance. This may be due to the high early mortality and the relatively small size of long-term survivals sample. However, we found that the mortality rate was higher in the group of patients who presented with low albumin, transferrin, or cholesterol, confirming that these nutritional parameters could be associated with a worse prognosis.

Our study has some limitations. This is a retrospective study, and data collection is dependent on clinical records. A convenience sample was used and in this clinical setting it would not be possible to use a control group to compare nutritional evolution and survival in patients with/without PEG. Although only three patients were lost to follow-up, considerable early mortality decreased the size of the sample available for paired comparison at three months. Nevertheless, we considered our data important, as this is one of the few studies showing the evolution of biochemical and anthropometric parameters in PEG-fed patients with post-stroke dysphagia.

CONCLUSIONS

In our experience with patients with post-stroke dysphagia, PEG is a safe procedure. Evidence of low albumin, transferrin, and total cholesterol just before the gastrostomy procedure was associated with poor post-PEG survival. PEG feeding can improve albumin, transferrin, and total cholesterol in post-stroke PEG-fed patients as early as after 3 months. Based on our results and the high early mortality seen after PEG in our sample, we recommend that, in this setting, PEG should be considered on an individual basis, taking into account its potential benefit on aspiration risk, nutritional status, and survival.

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Table I. Baseline characteristics of the included patients

	All (n = 158)
Age (years; mean ± s.d. [range])	73.2 ± 13.4 (33-96)
≥ 65 years	122 (77.2 %)
< 65 years	36 (22.8 %)
Gender	
Male	84 (53.2 %)
Female	74 (46.8 %)
Type of stroke	
Ischemic	135 (85.4 %)
Hemorrhagic	23 (14.6 %)
Location of stroke	
Anterior circulation	**111 (70.3 %)**
Cortico-subcortical involvement	46 (41.5 %)
- left-sided	22 (47.8 %)
- right-sided	21 (45.7 %)
- bilateral	3 (6.5 %)
Deep basal ganglia involvement	27 (24.3 %)
- left-sided	9 (33.3 %)
- right-sided	11 (40.8 %)
- bilateral	7 (25.9 %)
Both	38 (34.2 %)
- left-sided	20 (52.6 %)
- right-sided	14 (36.9 %)
- bilateral	4 (10.5 %)
Posterior circulation (vertebrobasilar)	**28 (17.7 %)**
Brainstem	15 (53.6 %)
Cerebellum	4 (14.3 %)
Multiple locations	9 (32.1 %)
Unknown	**19 (12.0 %)**

Table II. Evaluation of body mass index and laboratory parameters at baseline (T0) and at 3 months (T3)

BMI	T0			T3		
	Non-elderly (n = 32)	Elderly (n = 112)	Total (n = 144)	Non-elderly (n = 19)	Elderly (n = 64)	Total (n = 83)
Undernutrition	7 (4.8 %)	53 (36.8 %)	60 (41.6 %)	2 (2.4 %)	32 (38.6 %)	34 (41 %)
Normal weight	17 (11.9 %)	46 (31.9 %)	63 (43.8 %)	14 (16.9 %)	29 (34.9 %)	43 (51.8 %)
Overweight/obesity	8 (5.6 %)	13 (9 %)	21 (14.6 %)	3 (3.6 %)	3 (3.6 %)	6 (7.2 %)
Albumin				**(n = 109)**		
Low (< 3.5 g/dL)	**(n = 154)**			44 (40.4 %)		
	96 (62.3 %)			65 (59.6 %)		
Normal (≥ 3.5 g/dL)	58 (37.7 %)					
Transferrin				**(n = 92)**		
Low (< 200 mg/dL)	**(n = 153)**			48 (52.2 %)		
	105 (68.6 %)			44 (48.8 %)		
Normal (≥ 200 mg/dL)	48 (31.4 %)					
Total cholesterol				**(n = 83)**		
Low (< 160 mg/dL)	**(n = 151)**			42 (50.6 %)		
	90 (59.6 %)			41 (49.4 %)		
Normal (≥ 160 mg/dL)	61 (40.4 %)					

Table III. Body mass index (BMI) and laboratory evolution during patient follow-up (paired samples)

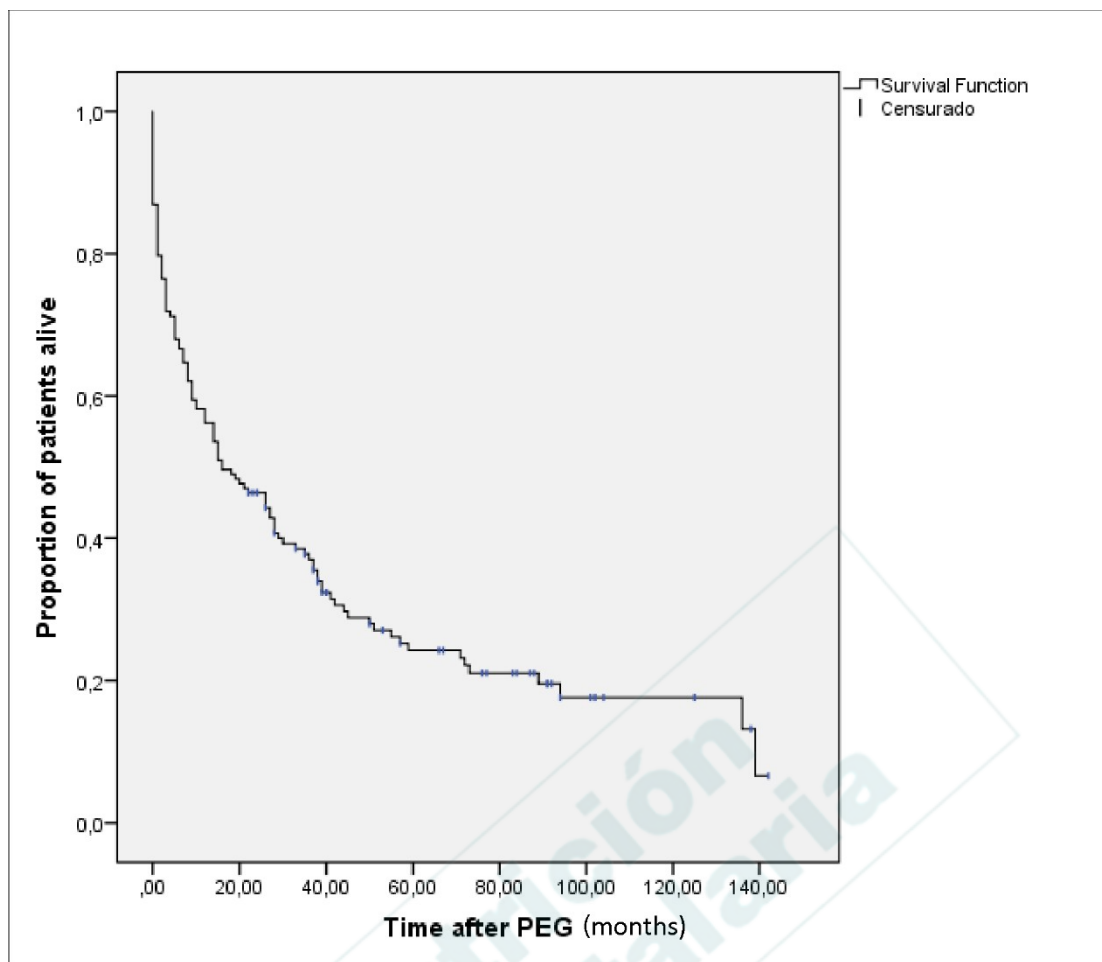|	Mean ± s.d. T0	Mean ± s.d. T3	p-value
BMI (kg/m²) (n = 80)	22.35 ± 3.86	21.56 ± 3.56	0.009
Albumin (g/dL) (n = 109)	3.26 ± 0.62	3.58 ± 0.49	< 0.001
Transferrin (mg/dL) (n = 90)	181 ± 43.48	200.4 ± 50.01	< 0.001
Total cholesterol (mg/dL) (n = 82)	154.03 ± 40.19	165.77 ± 46.33	0.002

Fig. 1. Kaplan-Meier curve of patient survival after PEG (survival analysis).