Journal of the Neurological Sciences 304 (2011) 44–48

Contents lists available at ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Percutaneous endoscopic gastrostomy in amyotrophic lateral sclerosis: Effect on survival ☆

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ARTICLE INFO

Article history:
Received 4 July 2010
Received in revised form 14 February 2011
Accepted 14 February 2011
Available online 3 March 2011

Keywords:
Amyotrophic lateral sclerosis
Dysphagia
PEG
Respiratory impairment
Survival

ABSTRACT

Background: Percutaneous endoscopic gastrostomy (PEG) is offered to amyotrophic lateral sclerosis (ALS) patients with severe dysphagia. Immediate benefits of PEG are adequate food intake and weight stabilization. However, the impact of PEG on survival is still uncertain. In this work we retrospectively evaluated the effect of PEG on survival in a cohort of ALS patients followed in a tertiary referral centre.
Methods: Between 2000 and 2007, 150 dysphagic ALS patients were followed until death or tracheostomy. PEG was placed in 76 patients who accepted the procedure and survival was analysed using the Kaplan–Meier life-table method.
Results: In ALS patients submitted to PEG, no major complications were observed. Total median survival time from symptom onset was 38 months for PEG users as compared to 32 months for the remaining dysphagic patients who declined the procedure ($p = 0.05$). Among bulbar-onset patients, PEG users showed a median survival time longer than those with no PEG (28 months vs. 25 months), even though the difference was not significant. Conversely, dysphagic spinal-onset patients with PEG lived significantly longer than those who refused this palliative care (44 months vs. 36 months, $p = 0.046$). Survival in patients with PEG was not affected by the severity of the respiratory impairment, as measured by forced vital capacity.
Conclusions: This study demonstrates that PEG improves survival in dysphagic ALS patients, with few side effects. The procedure is safe and applicable even to patients with impaired respiratory function. PEG remains a milestone in palliative care in dysphagic ALS patients.

1. Introduction

Amyotrophic Lateral Sclerosis (ALS) is a fatal neurodegenerative disorder characterized by a progressive loss of motor neurons in the spinal cord, brainstem and corticospinal tracts, with a median survival from first symptom ranging from two to four years [1]. Some 25% of ALS patients show a bulbar onset, with dysphagia and dysarthria, and ultimately the majority of patients develop bulbar symptoms that result in impaired food and fluid intake [2]. Malnutrition is reported to be associated with a reduced survival in ALS patients, being itself a cause of muscle atrophy and diaphragmatic weakness [3–5]. An aggressive nutritional care is therefore warranted for severely dysphagic ALS patients [2].

The recent guidelines for the nutritional management of ALS recommend that patients receive percutaneous endoscopic gastrostomy (PEG) when nutritional status deteriorates with a weight loss of more than 10% over the baseline and before forced vital capacity (FVC) falls below 50% of those predicted [6,7]. PEG is a relatively safe procedure for dysphagic ALS patients, with few major acute and long-term complications [8–10], but its relationship to survival is still unclear and it has not received a worldwide consensus [10].

The cut-off limit for a safe PEG placement has been considered a FVC% ≥ 50 of expected values in dysphagic patients [7] and this has led to the suggestion of percutaneous radiological gastrostomy (PRG) as an alternative procedure to PEG [11,12]. While this latter approach is safe, it however requires the presence of an expert interventional radiologist [12]. A few years ago, Gregory et al. [13] reported that a PEG device could successfully be placed in a cohort of ALS patients (88% of whom were with a bulbar-onset disease), even when FVC% was scored below 30 of those predicted, with 90% survival at 60 days.

PEG should anyway be offered early to dysphagic ALS patients, before they become malnourished. However, social and cultural factors may hamper and delay the patient's decision to give his/her consent to PEG (Spataro R, *unpublished observations*).

In this study we retrospectively evaluated the safety, early mortality and survival in ALS patients who underwent or not a PEG placement. Patients were divided according to the site of onset and

☆ Disclosure: the authors have reported no conflict of interest.

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doi:10.1016/j.jns.2011.02.016

the respiratory function (i.e. using a cut-off FVC% of 50), and followed up at our tertiary ALS referral centre in Palermo, Sicily.

2. Patients and methods

This study was approved by the Ethical Committee of the Department of Experimental Biomedicine and Clinical Neurosciences, University of Palermo, Italy. Informed consent was obtained for placement of the gastrostomy tube in all patients.

Between 2000 and 2007, one-hundred and fifty non-demented dysphagic patients with probable or defined ALS were followed at our Tertiary Clinical Research Centre in Palermo, Sicily (Italy) until death or tracheostomy. Mean age (years ± SD) at onset was 60.5 ± 12.1 (M/F = 1.38). The diagnostic delay in the whole cohort was 12.54 ± 12.28 months (range: 1–82). ALS was diagnosed according to El-Escorial-WFN revised criteria [14]. Sixty-two patients (32 men and 30 women, M/F = 1.06) were bulbar-onset, while for the remaining eighty-eight (55 men and 33 women, M/F = 1.66) the onset was in one of the three spinal regions (i.e. cervical, thoraco-abdominal, lumbar-sacral).

All patients were followed-up at three-five months interval. Seated erect Forced Vital Capacity (FVC) was used as an index of respiratory function; clinical progression was evaluated with the clinimetric Appel ALS Rating Scale (AARS) [15]. Furthermore, body weight and BMI were checked at each follow-up visit. The ability to swallow solid food and liquids (water) was evaluated using anamnestic and clinical criteria. To evaluate dysphagia, we adopted the one-hundred ml water swallow test (WST) [16–18]. This technique has been validated and has substantial normative data [16,17]. Each patient was asked to drink one hundred ml water and the timing (s) to complete the task was taken. An ALS patient was considered dysphagic when the swallowing speed was less than 10 ml/s [17].

The evidence of an early dysphagia for liquids or solid food led to a nutritional education (chin-tuck manoeuvre, modifications of food and fluid consistency, use of supplements). When these measures were no longer effective, and in the presence of a significant weight loss (see below), a proposal of enteral feeding with PEG was made. An accelerated weight loss (≥10% of body weight in the previous two months) or a score ≥9 on the dysphagia subscore of the AARS were therefore considered a sufficient indication for a PEG placement.

The discussion about the placement of a PEG device was not strictly driven by the FVC values. Dysphagic ALS patients, in particular those with a primary bulbar involvement, may perform poorly on spirometry because weakness of the oro-facial muscles [19]. On the other hands, patients with FVC% lower than 50, even when placed in non-invasive ventilation (NIV), can successfully undergo the surgical procedure [13].

Patients with an indication to PEG placement were dichotomised into two groups, *i.e.* those who accepted the procedure and those who did not.

The Beck Depression Inventory (BDI) was used to evaluate the patients for depressive symptoms. Cognitive decline and behavioral impairment were assessed through the verbal fluency tests, the Mini Mental State Examination (MMSE) test and the NeuroPsychiatric Inventory (NPI).

PEG was sometimes required by patients with respiratory failure and a short life expectancy. In this case, the procedure was broadly discussed with the patient and caregivers.

In all patients submitted to PEG, a 22 Fr siliconized device was used. Each patient received a light sedation, oxygen through a nasal mask while continuous pulse oxymetry was recorded. All PEG devices were placed by one of us (LF) and the duration of the surgical procedure ranged 10–15 min. Most patients were discharged the next day. Survival after PEG was measured in months after the surgery. Short- and medium-term survival (one and six months, respectively) and early side effects after PEG were also evaluated.

2.1. Statistical analysis

Survival curves were calculated with the Kaplan–Meier method. Survival data were expressed as median and interquartile ranges and comparisons between patients submitted or not to PEG were performed using a logrank test. Parametric variables were calculated as mean ± SD, and the differences between groups analysed with ANOVA. For numerically continuous variables, the cut-off that best divided patients into distinct survival group was identified. Survival curves were calculated with day zero as the date of symptom onset. The threshold of significance was set at $p<0.05$ for all statistical analyses.

3. Results

The demographic and clinical characteristics of the dysphagic ALS patients who underwent (n = 76) or not (n = 74) to PEG are reported in Table 1. The PEG device was applied to thirty-seven (48.7%) bulbar-onset and thirty-nine (51.3%) spinal-onset patients. Patients submitted to PEG had a slightly lower BMI (21 ± 5.2 vs. 22 ± 6.1, p = ns) and a shorter diagnostic delay (10.6 ± 8.3 vs. 14.8 ± 14, $p = 0.026$) than those who did not. The median rate of disease progression, as measured by AARS, did not differ between the two groups (PEG yes: 2.72 [IQ range: 1.78–5] vs. PEG no: 2.88 [IQ range: 1.77 – 4.1], p = 0.95, rank sum test).

The shorter diagnostic delay and the slightly lower BMI in the group submitted to PEG might in part be related to both the site of onset (i.e. primarily bulbar) and to an early development of bulbar signs in the spinal-onset patients.

The FVC% when PEG was required was significantly lower in patients submitted to PEG (PEG yes, 44.2 ± 21.7 vs. PEG no, 59 ± 41, p<0.006). This difference might in part be explained by the higher proportion bulbar-onset patients in the group undergoing PEG. Most patients with primarily bulbar signs have in fact great difficulty in performing a correct spirometry due to a weakness of oro-facial muscles [19]. With regard to NIV, the proportion of patients already using the ventilator for more than four consecutive hours/day was slightly lower in patients submitted to PEG (PEG yes, 24% vs. PEG no, 35%, p = 0.17). Among the 65 NIV users, 42 (65%) were on NIV overnight, indicating a full tolerance to the procedure.

There was no significant difference between the two groups in the occurrence of depressive symptoms, as rated by the BDI (PEG yes, median score: 11 (IQ range: 8 –14] vs. PEG no, median score: 10 (IQ range: 8–13], p = ns). Patients with a frontal variant of the frontotemporal lobar degeneration, diagnosed as demented through clinical evaluation and neuropsychological tests (i.e., verbal fluency tests, MMSE, and NPI), were excluded from the study (*data not shown*).

Table. 1
Demographic and clinical characteristics of the dysphagic ALS patients who were submitted or not to PEG.

	PEG		
	Yes (n = 76)	No (n = 74)	*p*
Age at onset (years)	59.5 ± 11.6	61.5 ± 12.5	ns
M/F	1.23	1.24	
Bulbar-onset (n, %)	37 (48.7%)	25 (33.8%)	
Spinal-onset (n, %)	39 (51.3%)	49 (66.2%)	
BMI (Kg/m^2)	21 ± 5.2	22 ± 6.1	ns
Diagnostic delay (months)	10.6 ± 8.3	14.8 ± 14	0.026
FVC at baseline (percent-predicted)	70 ± 28	73.7 ± 27.4	ns
FVC when PEG is required (percent-predicted)	44.2 ± 21.7	59 ± 41	0.006
Non-invasive ventilation (NIV, %)[a]	24	35	ns

Quantitative data are expressed as mean + SD.
[a] Percent of patient under NIV at the time of the PEG placement.