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Predicting survival of endoscopic gastrostomy candidates using the underlying disease, serum cholesterol, albumin and transferrin levels

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Abstract

Background: Endoscopic gastrostomy (PEG) is the gold standard for long-term enteral feeding. An adequate PEG candidate must have life expectancy longer than a few weeks. Patients surviving less than three weeks should have a nasogastric tube, and gastrostomy should be avoided. There are few studies looking to prognostic factors and fewer attempts of creating a predictor model for PEG patient’s survival.

Aim: The aim of this study was creating a predictive survival model for PEG candidates, using underlying disease, cholesterol, albumin and transferrin.

Methods: Data was obtained from records of adult patients that underwent PEG between 1999 and 2011. Patients surviving < 3 weeks were considered short survivors; surviving ≥ 3 weeks were considered adequate survivors. A full logistic regression model was used to classify future cases into one of the two groups of survival.

Results: An equation for the probability of future cases was generated, in order to obtain a P value. In the future, patients with a P ≥ 0.88 will have a 64.7% probability of adequate surviving; patients with a P < 0.88 will have a 70.3% probability of short surviving.

Conclusions: When clinical evaluation alone does not display a clear prognosis, this equation should be included in the evaluation of gastrostomy candidates, avoiding useless gastrostomy.

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Introduction

Percutaneous endoscopic gastrostomy (PEG) is the gold standard for long-term enteral feeding. Candidates for PEG placement are mainly dysphagic patients. For most enteral nutrition teams, according to our experience, most cases of dysphagia are caused by neurological disease or by head and neck cancer. These patients frequently have speech and motor impairments, asymmetric muscle atrophy and malnutrition, all induced by dysphagia and/or systemic underlying diseases. The standard nutritional evaluation tools may not be adequate to evaluate most of these patients and enteral feeding teams must frequently rely on anthropometric and laboratory data in order to monitor the nutritional status evolution of these patients.

On the search for easily available laboratory markers that may reflect the nutritional status and also help estimate prognosis of PEG patients with a wide spectrum of underlying diseases, we focused on serum albumin, serum transferrin and total serum cholesterol levels. Serum albumin was one of the first and most used laboratory measurements for assessing nutritional status and prognosis in a large number of clinical settings as diverse as hemodialysis, pancreatic cancer and cancer. There is a large consensus about the effectiveness of albumin in the evaluation of nutritional status in elderly patients, and it shows a good correlation with the Mini Nutritional Assessment, a nutritional assessment tool especially designed for the elderly. Interestingly, albumin has also proved to be useful for nutritional evaluation and prognosis in an internal medicine setting in patients with a broad spectrum of underlying disorders of dysphagic PEG candidates. Transferrin has been found to be a useful nutritional tool especially designed for the elderly. Interest-ingly, albumin has also proved to be useful for nutritional evaluation and prognosis in an internal medicine setting in patients with a broad spectrum of underlying disorders of dysphagic PEG candidates. Transferrin has been found to be a useful nutritional tool especially designed for the elderly.

Nutritional status and prognosis in a large number of clinical settings as diverse as hemodialysis, pancreatic cancer and cancer. There is a large consensus about the effectiveness of albumin in the evaluation of nutritional status in elderly patients, and it shows a good correlation with the Mini Nutritional Assessment, a nutritional assessment tool especially designed for the elderly. Interestingly, albumin has also proved to be useful for nutritional evaluation and prognosis in an internal medicine setting. In its turn, serum transferrin has long been used in nutritional and prognostic assessment, and in a wide variety of clinical settings as well, including hemodialysis, cancer, pancreatitis and intensive care patients. Low serum transferrin is associated with poor nutrition and poor outcome in elderly patients. Finally, low serum cholesterol is a well known marker of under nutrition and poor prognosis and has been associated with shorter survival in several epidemiological studies since the 90’s (Harris et al., 1992). It has been associated with poor outcome in a broad range of clinical conditions, namely hemodialysis and heart failure in critical ill and elderly patients. Serum total cholesterol, albumin and transferrin are useful markers for all these patients and in many other clinical settings. These laboratory markers are under the bias of nutritional, inflammatory and other disease-related factors, which makes it often difficult to separate all those influences. But it is precisely this aptitude of accurately marking a poor outcome, regardless of the involved mechanisms, that makes total cholesterol, albumin and transferrin so attractive to use in gastrostomy patients, a group with a broad spectrum of underlying disorders.

An adequate PEG candidate should fulfill the three following conditions: except for proximal lesion, the digestive tube should be undamaged, endoscopy and endoscopic transillumination must be feasible and life expectancy should be longer than a few weeks. The traditional requirement was a life expectancy of 4-6 weeks and this standard is still used by some groups. Nevertheless, a shorter life expectancy, of three or even two weeks, is the criterion accepted by most teams taking care of enteral feeding patients.

As PEG placing procedure is associated with mild morbidity and a very small number (< 1%) of procedure-associated deaths, patients with very poor prognosis are better managed with a nasogastric tube. In our enteral feeding team, we seldom advocate PEG placement in patients in whom we anticipate a life expectancy shorter than three weeks. Although it is critical for gastrostomy procedure decision, estimation of patient prognosis relies mainly on clinical judgment. Some objective data that may support this decision would be most useful. Nevertheless, there are only a small number of studies regarding prognostic factors for PEG patient’s survival. We found only few attempts of creating a predictor model for PEG patient’s survival. A study of 502 hospitalized patients from nursing homes who underwent PEG identified low serum albumin (< 3 g/dl), chronic obstructive pulmonary disease and diabetes mellitus as risk factors. In a study of 198 patients, most of them (75.3%) with cerebrovascular disorders, low serum albumin and history of pneumonia before the procedure were associated with poor prognosis. In an observational prospective study with 160 patients, Moreno Pérez et al., indentified some independent prognostic factors for patients in hospital setting. Chicharro et al. (2009) identified some patient’s factors that may help the selection for gastrostomy, but only in elderly patients. In a recent study, higher age, lower BMI, and diabetes mellitus were related to worst outcomes. The Sheffield Gastrostomy Score (SGS) devised to try to improve outcomes following this procedure, using age and serum albumin to try predicting 30-day mortality risk in a cohort of patients that included stroke, oropharyngeal malignancy and neurodegenerative diseases. It was created in Sheffield and validated in four hospitals of the same region, but never reached a widespread acceptance. Certainly, the wide range of underlying diseases of dysphagic PEG patients is an obstacle for designing a global prognosis model.

The aim of the present study was to evaluate the possibility of predicting survival of PEG candidates, and therefore avoiding erroneous gastrostomy, using simple data as the underlying disease and three widespread serum markers, total serum cholesterol, serum albumin and serum transferrin.

Patients and methods

The study population included adult patients (≥ 18 years) that underwent endoscopic gastrostomy in our
hospital between November 1st, 1999 and April 30th, 2011. Patients were referred by their clinicians and evaluated together by the enteral nutrition team in order to establish the clinical indication for gastrostomy. Informed consent for endoscopic gastrostomy and for clinical and laboratory initial evaluation was obtained from every patient or from their relative/legal responsible. Serum total cholesterol (mg/dl), albumin (g/dl) and serum transferrin (mg/dl) were part of standard initial evaluation. In the day of the endoscopic procedure, before the PEG tube placement, a blood sample was taken for laboratory evaluation.

Clinical, laboratory and demographic data were obtained from medical records. Patients with incomplete records were excluded. Collected data included age, gender, underlying disease, survival after gastrostomy, and albumin, transferrin and total cholesterol levels on the day of the gastrostomy. Underlying diseases were divided into three groups: Group 1, neurological diseases; Group 2, head and neck cancers and Group 3, other diseases.

Survival was evaluated in days, from the day of the endoscopic gastrostomy until the day the patient died or until May 31st, 2011, if the patient was alive. Patients surviving less than 3 weeks (< 21 days) were considered short survivors (SS). Gastrostomy should have not been performed in most of them had this short survival time been anticipated and they could have been fed through a nasogastric tube. Patients surviving 3 weeks or more (≥ 21 days) were considered adequate survivors (AS) and, retrospectively, PEG feeding was considered the correct option.

Statistical analysis of the data was performed using the software SPSS® 19.0. A full logistic regression model was used in order to classify future cases into one of the two survival groups, SS or AS. All statistical tests were performed with a 5% level of significance.

### Results

#### Descriptive statistics

From our clinical files we selected 298 patients with complete medical records, which included 203 men and 95 women. Neurological disease was the cause of dysphagia in 165 patients, 126 had head and neck cancer and 7 suffered from other diseases.

Age ranged from 18 to 86 years. Median age was 63 (men: 61, women: 89). Initial total cholesterol ranged from 68 to 335 mg/dl (mean: 163.4). Initial transferrin ranged from 4 to 331 mg/dl (mean: 176.1). Initial albumin ranged from 1.5 to 4.8 g/dl (mean: 3.3). Survival range from 2 to 3600 days (median: 82).

Table I displays clinical and laboratorial features of both SS and AS groups.

#### Logistic regression analysis of the survival data

A full logistic regression model was used to classify future cases into one of the two survival groups defined above as a function of serum cholesterol, transferrin and albumin, and type of underlying disease.

Prior analysis of the data has shown that, in the variable set considered for this study, only albumin, cholesterol and transferrin have the potential to discriminate between groups, if strict adherence to the 5% level of statistical significance is considered, with
higher serum levels being observed amongst adequate survivors. Instead, that potential was strongly suggested for the type of pathology but not for gender or age. Since pathology is an important variable in predicting survival, it was decided to include this variable in the model. Since this is a discrete, nominal scaled variable, it is inappropriate to include it the model as if it were interval scaled.

Consequently, two design variables were generated to represent the type of pathology, namely pathology (1) and pathology (2), using the indicator contrast method with the reference category defined by the head or neck cancer pathology. Table 2 shows the codes used to define these two design variables. In the first run of the model to the full data set, the type of underlying disease was the only suggested predictor of survival \( (p = 0.070) \), with an overall poor fit, as revealed by the Hosmer-Lemeshow test \( (p = 0.023) \) and the Nagelkerke \( R^2 \) \( (0.107) \). Moreover, 3 individual patterns were identified by model residuals in excess of 0.95, which turned out to be of considerable influence. In effect, when those 3 observations were removed from calculations, the fitness improved somehow, as shown by the clearly non-significant result of the Hosmer-Lemeshow test \( (p = 0.292) \) and the Nagelkerke \( R^2 \) \( (0.157) \). More importantly, the type of underlying disease emerges now as a clearer and significant predictor of survival \( (p = 0.044) \), while the benefits of higher serum albumin towards longer survival are also suggested \( (p < 0.1) \). Moreover, of the two design variables used to represent the type of pathology, only pathology(1) reaches statistical significance, and thus predicting increased survival in cases of neurological disease when compared to head or neck cancers. Table 3 presents the structure of the model obtained in these conditions.

With the data in the table above, the following equation for the posterior probability of future cases of adequate survival, \( P \), can be used:

\[
P = \frac{1}{1 + e^{2.669 - 1.021 \times \text{pathology (1)} - 0.406 \times \text{pathology (2)} - 0.006 \times \text{transferrin} - 0.638 \times \text{albumin} - 0.007 \times \text{cholesterol}}
\]

In order to evaluate the performance of the classification scheme defined by the above equation, a ROC curve analysis was implemented (fig. 1). The asymptotic significance is below 0.05, which means that using the logistic regression model to predict future cases is better than just guessing. Moreover, the estimated area under the curve is 0.742, which represents the probability of a model’s result for a randomly chosen positive case exceeding the result for a randomly chosen negative case.

In order to select a cutoff point for the classification of future cases using the logistic model which warrants acceptable sensitivity and specificity, the coordinates of the ROC curve were analyzed. The best choice would be to use as a cutoff point the percentage of adequate survivors suggested by the sample, which is estimated as 87.5%. Thus, if a person is classified as an adequate survivor given the probability predicted by the model, \( P \), is greater than or equal to 0.880, then the overall percentage of correctly classified future cases would be 65.4%, with 70.3% of short survivors and 64.7% of adequate survivors being correctly classified. That means that, in the future, any patient with a \( P \geq 0.88 \) will have a 64.7% probability of surviving 3 weeks or more and any patient with a \( P < 0.88 \) will have a 70.3% probability of surviving less than 3 weeks.

**Discussion**

Most Parenteral and Enteral Nutrition (PEN) societies advocate gastrostomy if enteral feeding is expected to be needed for more than a few weeks. The USA PEN society, ASPEN, suggests 4 weeks \(^{30}\) while ESPEN advocates 2-3 weeks. \(^{31}\) Recent guidelines from the French health high authority for nutritional support in the elderly advice gastrostomy if swallowing disorders persist beyond 2 weeks. \(^{23}\) Nevertheless, these and other guidelines and recommendations never propose any method of prognostic evaluation, relying on clinical judgment alone. Every enteral feeding team keeps a record of a number of patients dying a few days after the gastrostomy. In most of these patients, the procedure was useless and should have not been performed.
Actually, prognosis estimation is a critical issue of gastrostomy candidate’s evaluation. Mortality analysis is an important issue because the gastrostomy would be denied in most patients surviving less than a few weeks, if this outcome could be anticipated.

The present study used three routine laboratory tests, serum cholesterol, albumin and transferrin. When considered separately, each of these serum markers showed a significant difference between the two survival groups, with higher serum levels being observed in longer survival, while such contrast was only suggested for the type of pathology. This different behavior shown by the four variables may as well reflect the different statistical power of the data analysis techniques used, t tests for the biochemical markers, and exact Fisher’s test, for type of pathology. However, when the four variables were simultaneously considered in the logistic regression model, type of pathology was the only significant predictor of adequate survival, presenting itself as a surrogate measure of those serum parameters. Nevertheless, laboratory data are still important for survival estimation in our model. Other variables were evaluated, including total lymphocyte count or clinical parameters but there was no improvement of the model. In the future, other centers and other enteral feeding teams may use this model, increasing the number of patients enrolled and confirming the validity of the model in various clinical settings.

Knowing the underlying disease (pathology group) with these laboratory data and a simple equation,

\[ P = \frac{1}{1 + e^{2.669 - 1.021 \times \text{Pathology}(1) - 0.406 \times \text{Pathology}(2) - 0.006 \times \text{Transferrin} - 0.638 \times \text{Albumin} - 0.007 \times \text{Cholesterol}}} \]

we can predict if a patient will survive more than three weeks and has a satisfactory life expectancy to be considered for gastrostomy. Conversely, if the patient has a life expectancy shorter than three weeks, gastrostomy should seldom be considered, only on the basis of very special, individual features. PEG patients and patients dying shortly after gastrostomy are a heterogeneous group, in respect to age, underlying diseases, co-morbidities and nutritional status. Nevertheless, our model is robust and there seems to be no differences between the three groups of different underlying diseases. As a matter of fact, the present model is useful independently of the heterogeneity of the gastrostomy patients. Globally, this model is effective in preventing most of the gastrostomy procedures in short survivors, but it proves itself to be wrong in a minority of patients and should not be used as a golden rule. Some patients with \( P \geq 0.88 \), with expectable adequate survival may pass away within 3 weeks. In these patients PEG would be useless. Conversely, some patients with \( P < 0.88 \), with expectable short survival, may be alive for more than 3 weeks. These ones can be fed through a nasogastric tube for a few weeks more and PEG will just be delayed. Furthermore, even in situations that clearly have a very poor outcome, an endoscopic gastrostomy may be considered in order to provide the most comfortable palliation. Obviously, this equation is no substitute for clinical evaluation. The decision process must be based on clinical features and ethical considerations and must be shared between the enteral feeding team, the patient and the family. But, despite being an imperfect model, when patient prognosis is uncertain, the present model may become part of the evaluation of PEG candidates, as a useful tool to support clinical decisions.

### Conclusions

The authors present a useful tool for predicting the outcome of gastrostomy candidates. Knowing the underlying disease of gastrostomy candidates, and evaluating total serum cholesterol, serum albumin and serum transferrin and using an equation, enteral feeding teams should be able to identify most of the gastrostomy candidates that would survive less than three weeks after the procedure, and avoid useless gastrostomy procedures. When clinical evaluation alone does not display a clear prognosis, this equation should be included in the evaluation of gastrostomy candidates.

### References


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Table III

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