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Original article

Enteral tube feeding and mortality in hospitalized older patients: A multicenter longitudinal study

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SUMMARY

Background & aims: The literature regarding enteral nutrition and mortality in older frail people is limited and still conflicting. Moreover, the potential role of comprehensive geriatric assessment is poorly explored. We therefore aimed to investigate whether the Multidimensional Prognostic Index (MPI), an established tool that assesses measures of frailty and predicts mortality, may help physicians in identifying patients in whom ETF (enteral tube feeding) is effective in terms of reduced mortality.
Methods: Observational, longitudinal, multicenter study with one year of follow-up. Data regarding ETF were recorded through medical records. A standardized comprehensive geriatric assessment was used to calculate the MPI. Participants were divided in low (MPI-1), moderate (MPI-2) or severe (MPI-3) risk of mortality. Data regarding mortality were recorded through administrative information.
Results: 1064 patients were included, with 79 (13 in MPI 1–2 and 66 in MPI-3 class) receiving ETF. In multivariable analysis, patients receiving ETF experienced a higher risk of death (odds ratio, OR = 2.00; 95% confidence intervals, CI: 1.19–3.38). However, after stratifying for their MPI at admission, mortality was higher in MPI-3 class patients (OR = 2.03; 95%CI: 1.09–3.76), but not in MPI 1–2 class patients (OR = 1.51; 95%CI: 0.44–5.25). The use of propensity score confirmed these findings.
Conclusions: ETF is associated with a higher risk of death. However, this is limited to more frail patients, suggesting the importance of the MPI in the prognostic evaluation of ETF.

1. Introduction

Poor food intake and malnutrition are common in hospitalized frail people. Using the mini-nutritional assessment (MNA), a recent meta-analysis found that about one quarter of hospitalized older people can be considered malnourished [1]. Indeed, the loss of normal physiological drivers of appetite and satiety and/or difficulties with swallowing, both in the oral and in the pharyngeal

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phases of deglutition, are very common in this patient population [2], especially in subjects with cognitive decline or dementia [2].

Enteral nutrition could be useful in acute frail hospitalized patients to prevent aspiration pneumonia and to improve nutritional status and the consequences of malnutrition, such as pressure ulcers, infections, starvation and finally death [3]. However, the decision to start enteral tube feeding (ETF) in hospitalized older patients is often controversial and current guidelines do not provide clear recommendations [4]. A seminal Cochrane review found that enteral nutrition did not increase survival in patients receiving ETF and that there was no evidence of benefit in terms of nutritional status in older patients with dementia [3]. Similar lack of evidence applies for older people hospitalized with acute illness [5]. However, these studies did not consider the potential role of prognostic indexes [6] in the decision to initiate enteral nutrition [3].

Among the prognostic indexes used in the hospital setting, the Multidimensional Prognostic Index (MPI) [7] has been identified as a well-calibrated tool, having a good discrimination and accuracy for predicting mortality [8], with the highest scores of validity and reliability when compared to other fourteen tools assessing frail older inpatients [9]. Recently the Guideline Development Group of the National Institute for Health and Care Excellence (NICE) identified the MPI as one of the very few accurate tools predicting reduced life expectancy [10].

The MPI does not consider only health status aspects, but also functional, cognitive, and nutritional domains, as well as multimorbidity, polypharmacy and co-habitation status by using standardized and extensively validated rating scales, in the context of a comprehensive geriatric assessment (CGA) [7]. Indeed, previous literature has shown that MPI is useful in determining appropriate pharmacological interventions in older patients [11–14], suggesting its potential role also for clinical-decision making in enteral nutrition in frail subjects.

Given this background, we aimed to prospectively investigate if the CGA-based MPI assessed at hospital admission may help physicians in identifying patients in whom ETF is effective in terms of reduced mortality in a large cohort of hospitalized older patients.

2. Methods

2.1. Study population

This was an observational study conducted according to the World Medical Association's 2008 Declaration of Helsinki, the guidelines for Good Clinical Practice, and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines [15].

Inclusion criteria were: 1) age $\geq$65 years; 2) admitted to hospital for an acute medical condition or for a relapse of a chronic disease; 3) ability to provide informed consent or availability of a proxy for informed consent and willingness to participate in the study; 4) complete CGA during hospitalization.

2.2. Nine geriatric units across Europe and Australia were included

The Ethical Committees of each center approved this observational study. Informed consent was given by participants who underwent initial evaluation and/or their proxies for their clinical records to be used in this study. All patient records and information were anonymized and de-identified prior to the analysis.

2.3. Main exposure

The main exposure of this research was enteral nutrition defined as a method providing nutrition through a tube placed into the nose (nasogastric tube or nasoenteral tube), the stomach (percutaneous endoscopic gastrostomy, PEG) or the small intestine (percutaneous endoscopic jejunostomy, PEJ). Data regarding ETF were recorded through medical records.

2.4. Multidimensional prognostic index (MPI)

MPI was developed by the inclusion of information from eight different domains of the CGA [7]:

1. Functional status was evaluated by Katz's Activities of Daily Living (ADL) index [16], which defines the level of dependence/independence in six daily personal care activities (bathing, toileting, feeding, dressing, urine and bowel continence and transferring in and out of bed or chair);
2. Independence in the Lawton's Instrumental Activities of Daily Living (IADL) [17] which assesses independence in eight activities that are more cognitively and physically demanding than ADL, i.e. managing finances, using telephone, taking medications, hopping, using transportation, preparing meals, doing housework and washing;
3. Cognitive status through the Short Portable Mental Status Questionnaire (SPMSQ) [18], a ten item questionnaire investigating orientation, memory, attention, calculation, and language; validated versions were used in each local language.
4. Co-morbidity was examined using the Cumulative Illness Rating Scale (CIRS) [19]. The CIRS uses a 5-point ordinal scale (score 1–5) to estimate the severity of pathology in each of 13 systems, including cardiac, vascular, respiratory, eye-ear-nose-throat, upper and lower gastrointestinal, hepatic, renal, genitourinary, musculo-skeletal, skin disorder, nervous system, endocrino-metabolic and psychiatric behavioural disorders. Based on the ratings, the Comorbidity Index (CIRS-CI) score, which reflects the number of concomitant diseases, were derived from the total number of categories in which moderate or severe levels (grade from 3 to 5) of disease were identified (range from 0 to 13). Comorbidities, at hospital admission, were descriptively reported using the International Classification of Disease, 10th version [20].
5. Nutritional status was investigated with the Mini Nutritional Assessment Short Form (MNA-SF) [21], which includes information on: a) anthropometric measures (body mass index, BMI; weight loss); b) neuropsychological problems and recent psychological stress; c) mobility; d) decline in food intake.
6. Risk of developing pressure sores was evaluated through the Exton Smith Scale (ESS), a five items questionnaire determining physical and mental condition, activity, mobility and incontinence [22].
7. Medication use was defined according to the Anatomical Therapeutics Chemical Classification code system (ATC classification) and the number of drugs used by patients at admission was recorded. Patients were defined as drug users if they took a medication included in the ATC classification at the moment of hospital admission.
8. Cohabitation status included living alone, in an institution, or with family members.

For each domain, a tripartite hierarchy was used, i.e. 0 = no problems, 0.5 = minor problems, and 1 = major problems, based on conventional cut-off points derived from the literature for the singular items. The sum of the calculated scores from the eight domains was divided by 8 to obtain a final MPI risk score ranging from 0 = no risk to 1 = higher risk of mortality. Also, the MPI was expressed as three grades of risk: MPI-1 low risk (MPI value $\leq$ 0.33), MPI-2 moderate risk (MPI value between 0.34 and 0.66) and MPI-3 high risk (MPI value > 0.66) [7]. For the aims of this research, MPI-1 and 2 categories were merged, since only one participant in the

MPI-1 category had an ETF. MPI requires between 15 and 25 min for its complete execution and the results can be automatically obtained through the MPI calculator software downloaded by the www.mpiage.eu website. The MPI on admission was used for this specific research.

2.5. Main outcome

Subjects were followed for 12 months from hospital discharge and mortality was categorized as in-hospital (if it happened in the index hospital admission) or post discharge. Vital status was assessed by consulting the Registry Offices of the cities in which the patients were residents at the time of the evaluation. Overall mortality (as sum of in-hospital and one-year, at home) was considered as primary outcome of our research.

2.6. Statistical analysis

General characteristics were reported as frequencies (percentages) and mean ± standard deviation (SD), for categorical and continuous variables, respectively in people having enteral nutrition vs. those without.

Logistic binary regression analysis was run, taking as exposure the placement of enteral nutrition tools, stratified for their MPI at admission (in categories) and overall mortality as outcome. The strength of the association between enteral nutrition and death (stratified for MPI at admission) was reported as odds ratios (ORs) with corresponding 95% confidence intervals (CIs), adjusted for age, sex, center and MPI at baseline. A similar analysis was run using the propensity score [23] as covariate dividing this score in quintiles.

Two-sided alternatives with a significance level alpha = 0.05 were considered for all the tests. STATA 12 (StataCorp, Stata Statistical Software: Release 12, College Station, TX, USA) software was used.

3. Results

The study included 1140 hospitalized patients, from which we excluded 20 patients having parenteral nutrition and 56 lost at follow-up. Thus, 1064 patients were included.

The mean age was 84.1 ± 7.4 years (range: 65–104), with a higher prevalence of women (61.3%). A total of 79 patients (=7.4%) received ETF. Table 1 shows the baseline characteristics according to whether or not ETF was provided. The 79 patients with ETF did not differ in terms of mean age and gender percentage compared to the 985 not having ETF. On the contrary, patients with ETF had a significant lower body mass index, were more disabled and with worse cognitive status, more malnourished, bedridden and with higher presence of comorbidities, even if no significant differences emerged for number of medications used or cohabitation status (Table 1). As expected, the mean MPI was significantly higher in patients with ETF than those without (0.76 ± 0.11 vs. 0.56 ± 0.20 points, $p < 0.0001$) (Table 1).

Table 2 shows the association between ETF and mortality over one year of follow-up. In multivariable analysis, adjusted for age, sex, center and baseline MPI, patients receiving ETF experienced a higher risk of death (OR 2.00; 95% CI 1.19–3.38). Similar results were evident using the propensity score as covariate. However, after stratifying for their MPI at admission, only people in MPI-3 group reported an increased risk of mortality (OR 2.03; 95% CI 1.09–3.76), whilst people in the MPI 1–2 group had not (OR 1.51; 95 %CI 0.44–5.25). Using the propensity score did not change the results (Table 2).

4. Discussion

In this study, including more than 1000 older patients hospitalized for any-cause, we found that enteral nutrition is associated with an increased risk of death, but this was limited to patients with higher frailty.

A first comment should be given to the high prevalence of enteral nutrition (7.4%) in our cohort. It was reported that more than one third of severely cognitively impaired residents in American nursing homes have feeding tubes [24], remarking the clinical and epidemiological importance of this issue.

Previous studies have reported conflicting results regarding the relationship between enteral nutrition and survival in frail older patients. In a previous paper, Mitchell et al. found no association between the use of feeding tube and survival in a large cohort of nursing home residents [24]. On the contrary, Jaul et al. found that the median survival time in patients with nasogastric tube was significantly increased compared to those with normal oral intake, however these differences disappeared when adjusting for potential confounders [25]. No other study found a significant association between enteral feeding and decreased risk of mortality [3].

In this regard, our study adds some new concepts to this topic. Overall, we found that the placement of enteral nutrition is associated with an increased risk of death in frail hospitalized older patients, but this finding is limited to only people with higher frailty and risk of death at baseline, i.e. in the MPI-3 group. On the contrary, no significant effect of enteral nutrition on mortality was found in people in the MPI 1–2 group. Our research suggests the idea that ETF should be probably used earlier in the history of terminal diseases. In this regard, Suzuki et al., proposed that improvement in quality of life, after PEG insertion may be expected more in milder dementia than in advanced dementia [26]. Finally,

Table 1
Descriptive characteristics by presence or not of enteral nutrition.

	Enteral nutrition (n = 79)	No enteral nutrition (n = 985)	p-value
Age (years)	84.0 (7.4)	84.1 (7.4)	0.85
Men (n, %)	26 (32.9)	386 (39.2)	0.28
BMI (kg/m^2)	23.6 (3.9)	25.7 (5.1)	<0.0001
Activities of Daily Living (ADL) (points)	1.0 (1.2)	3.0 (2.3)	<0.0001
Instrumental Activities of Daily Living (IADL) (points)	1.2 (1.5)	2.8 (2.6)	<0.0001
Short Portable Mental Status Questionnaire (SPMSQ) (points)	5.2 (3.6)	4.0 (3.3)	<0.0001
Mini Nutritional Assessment Short Form (MNA-SF) (points)	5.4 (2.9)	8.9 (3.1)	<0.0001
Exton-Smith scale (ESS) (points)	10.2 (2.7)	14.6 (3.5)	<0.0001
Comorbidity Index Rating Scale (CIRS) (points)	5.9 (2.1)	4.8 (2.2)	<0.0001
Number of medications	7.4 (2.6)	7.2 (3.4)	0.36
Living alone (n, %)	22 (27.8)	332 (33.7)	0.14
MPI (points)	0.76 (0.11)	0.56 (0.20)	<0.0001

Abbreviations: MPI: Multidimensional Prognostic Index.

Table 2
Logistic regression on nutritional support and death by baseline MPI value.

	Enteral nutrition/total	Adjusted logistic regression[a] (Odds ratio) (95% confidence intervals) p-value	Propensity score[b] (Odds ratio) (95% confidence intervals) p-value
All sample	79/1064	2.00 (1.19–3.38) P = 0.009	1.89 (1.14–3.17) P = 0.01
MPI 1–2	13/632	1.59 (0.45–5.61) P = 0.47	1.51 (0.44–5.25) P = 0.52
MPI-3	66/432	2.03 (1.09–3.76) P = 0.03	1.84 (1.04–3.25) P = 0.04

Notes: All data are reported as odds ratios (ORs), taking those without nutritional support as reference.
[a] Adjusted for age, sex, center and multidimensional prognostic index (MPI) at baseline.
[b] Propensity score is calculated using as covariates age, gender, center and MPI at baseline and divided into quintiles.

the guidelines proposed by the ESPEN and by the American Geriatrics Society propose that the decision for or against nutritional interventions should be made on an individual basis, after carefully taking into account general prognosis [27,28].

Thus, our study highlights once again the importance of assessing prognosis in older patients, in taking the decision to initiate (or not) enteral nutrition. In this regard, the current literature regarding CGA as important for initiating or not the enteral nutrition is, unfortunately, extremely limited, even if the outcomes of parenteral nutrition in elderly population have been found to have a worse prognosis than younger people [29]. The importance of a multidisciplinary approach is indirectly supported by some guidelines indicating that decisions on route, content, and management of nutritional support in hospitalized adults are best made by multidisciplinary nutrition teams than individual approaches [5]. However, our study can be considered the first using a tool of the CGA for better stratifying the prognosis of patients undergoing enteral nutrition.

The findings of our study should be interpreted within its limitations. First, the follow-up of these patients was limited to one year. Even if this follow-up period was comparable to the other studies available for this specific topic (i.e. enteral nutrition and death), we cannot exclude that significant differences in predicting negative outcomes by MPI categories in older patients could emerge with longer follow-up. Second, we did not have information regarding the tool used for enteral nutrition (nasogastric tube or PEG or PEJ) and, therefore, we were not able to run any sensitivity analysis regarding this specific issue. Finally, some important nutritional indexes (e.g. serum albumin) were not considered such as the quality of life associated with enteral nutrition. Therefore, future studies are needed in this sense.

In conclusion, our study suggests that ETF is associated with a higher risk of mortality. However, these data are limited only to frail older patients, suggesting the importance of the multidimensional geriatric assessment in the prognostic evaluation of ETF.

Conflicts of interest

None.

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Appendix

MPI_AGE Investigators

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