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Predictors of Mortality Following PEG Insertion in Stroke Patients

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Abstract

Background: Dysphagia following Stroke is very common and percutaneous endoscopic gastrostomy (PEG) tube insertion is considered as an option to help stroke patients start feeding. The aim of our study was to investigate if Specific factors could predict mortality risk in post stroke patients who had PEG tube insertion for persistent dysphagia. The FOOD trial has shown that early PEG insertion following a stroke is associated with an increase in absolute risk of death 1.0% (95% CI -10 to 11.9; p = 0.9) and increase risk of death and poor outcome 7.8% (95% CI 0.0 to 15.5; p = 0.05).

Methods: This was a retrospective study of 124 patients who had PEG tube insertion following stroke who were admitted to the stroke unit at the Royal Liverpool Hospital between 2009 to 2013. Univariable Analysis was done from time to death from date of PEG insertion analyzed using Cox's proportional hazards method. Parsimonious multivariable model was built using backwards selection with variables dropped according to Akaike's Information Criterion.

Results: Median follow-up was 6.8 years (IQR 6.0 to 7.4 years). Median event-free survival was 1.4 years (IQR: 0.7 to 1.9 years). Co-variables included age, stroke sub-type, Charlson Co-Morbidity Index (CCI), serum albumin and BMI. Survival time was strongly correlated to: increase in age, Total anterior circulation stroke (TACS), raised CCI, low serum albumin and BMI. Age was significantly associated with time to death – risk of death was 4% higher per year increase in age. Type of stroke was significantly associated with time to death – people with TACS were 65% more likely to die than those with haemorrhagic stroke. Charlson Co-Morbidity Index was significantly associated with time to death – risk of death was 15% higher per unit increase in Charlson Co-Morbidity Index.Serum albumin was significantly associated with time to death – risk of death was 5% lower per unit increase in serum albumin. BMI was significantly associated with time to death – risk of death was 5% lower per unit increase in BMI.

Conclusion: This study demonstrates a clear prognostic value of these co-variables with patients worked up for PEG insertion after stroke. Interesting find was that a combination of TACS stroke, Age >80, Albumin <30g/L, CCI >=9 and low BMI in Men had probability of upto >80 % 6 month mortality after PEG insertion. We propose that Further Multicenter research is required to determine a predictive algorithm to be used in future guidelines and management of PEG-based decisions in stroke.

Keywords: Ischemic Stroke; Percutaneous Enterogastrostomy (PEG); Dysphagia and mortality

Introduction

Swallowing problems are very common after a stroke [1]. Nutrition is vital part to recover from the stroke. Moreover, patients' nutritional status often deteriorates thereafter because of increased metabolic demands which cannot be met due to feeding difficulties [2]. Hence, the primary aim of dysphagia management has been to reduce aspiration pneumonia rather than rehabilitate the swallow and to continue feeding [3]. The dilemma comes with who is suitable to have PEG tube and who is best to

continue with Nasogastric tube (NG). Several studies indicate that early gastrostomy tube feeding is greatly superior to nasogastric tube feeding and should be the nutritional treatment of choice for patients with acute dysphagic stroke [4]. However, given it's an invasive procedure, it carries its own risk and choosing the appropriate cohort of patients is vital.

The FOOD trial has shown that early PEG insertion following a stroke is associated with an increase in absolute risk of death 1.0% (95% CI -10 to 11.9; p = 0.9) and increase risk of death and poor outcome 7.8% (95% CI 0.0 to 15.5; p = 0.05) [5]. Among the factors reported to be associated with a higher mortality following PEG insertion include low serum albumin <30g/L, Chronic Obstructive Pulmonary Disease (COPD), diabetes mellitus, high Charlson co-morbidity index, high CRP level, higher age, lower BMI [6-8].

The Royal free Hospital designed a study [9], to derive a gastrostomy risk score which was validated in 2019 called Royal Free Hospital-Gastrostomy Risk Score (RFH-GRS). Eight variables were identified, through literature review and clinical experience, as essential components of the scoring system were identified as age, prognosis, dysphagia, anatomy, comorbidities (Charlson Comorbidity Index), Nutritional status, anti-coagulation and recent infection; a subjective Override was also included. The resultant RFH-GRS was piloted and modified accordingly; intra- and inter-observer variability was assessed, and predictive validity was evaluated by retrospectively allocating scores to the 234 patients referred for gastrostomy placement between 1 January 2016 and 31 December 2017. These were followed until death or 31 December 2017, the study end-point. Outcome was found to be that patients with a RFH-GRS of 0-6 have a low risk of an adverse outcome following gastrostomy placement; 6–10 a moderate risk, so they are likely to benefit; 11–14 a medium to high risk so benefits may still outweigh the risk, and ≥15 a high risk, making it unlikely that they would benefit from the procedure.

However, these studies were not specific to PEGs inserted following a stroke. In order to identify risk factors that may predict mortality in PEG insertion following a stroke, a study was designed at Royal Liverpool Hospital. This study concentrates on the subtypes of strokes and stratify the mortality risk among patients who had PEG tube inserted.

Methods

This is a retrospective study involving 120 patients who were admitted to the acute stroke unit and had a PEG inserted following an acute stroke between 2009 - 2013 at the Royal Liverpool University Hospital. Patients whose PEG were inserted for reasons other than dysphagia following a recent stroke.

Patient data obtained from medical records included the following: Age, Serum albumin at PEG insertion, sex, stroke types (e.g. Total Anterior Circulation Infarct [TACS], Partial Anterior Circulation Infarct [PACS], Posterior Circulation infarct [POCS], Lacunar infarct [LACS], and Intracerebral Hemorrhage [ICH]); Charlson co-morbidity index, Serum CRP at PEG insertion, BMI at PEG insertion, Barthel index and mortality in 3 and 6-month after PEG procedure. The mortality data was ascertained from the patients' medical notes.

Statistical analysis

Patient Characteristics

- Categorical variables summarised with counts and percentages,
- Normally distributed continuous variables summarised with means and standard deviations,
- Skewed continuous variables summarised with medians and interquartile ranges.

Univariable Analysis

- Time to death from date of PEG insertion analysed using Cox's proportional hazards method,
- People assumed alive at 15/3/19 if date of death not recorded,
- The association of each variable with the outcome considered, variable by variable: gender, age, type of stroke, Charlson Co-Morbidity Index, CRP, serum albumin, BMI, and Barthel Index.

Multivariable Analysis

- The parsimonious (best-fitting) multivariable model was built using backwards selection with variables dropped according to Akaike's Information Criterion; Charlson co-morbidity index was forced into the final model on clinical grounds.
- Missing data were replaced with multiple imputation via chained equations.
- Model fit assessed via discrimination (Harrell's c-statistic) and calibration (calibration plot).
- Calibration refers to how closely the probability of the event predicted by the model agrees with the observed probability. It will be assessed by consideration of the calibration slope - a value of 1 implies perfect calibration.
- Discrimination refers to the ability of the prognostic model to differentiate between those who experience the event during the study and those who do not. The discriminative ability of the model will be measured with the c-index which is equivalent to the area under the ROC curve. The c-index is measured on a scale ranging from 0.5 (no better than chance) to 1 (perfect prognostic).
- Model optimism determined using bootstrap resampling with 500 resamples

Results

Patient Characteristics

Median follow-up was 6.8 years (IQR 6.0 to 7.4 years). Median event-free survival was 1.4 years (IQR: 0.7 to 1.9 years) (Tables 1-3).

Variable, n (%) unless otherwise stated	Dead (n=111)	Alive (n=12)	Total (n=123)
Gender			
Female	64 (58)	10 (83)	74 (60)
Male	47 (42)	2 (17)	49 (40)
Age (years), median (IQR)	82.0 (75.5-86.5)	71.5 (59.8-76.3)	81.0 (74.0-86.0)
Type of Stroke			
TACS	61 (57)	4 (36)	65 (55)
PACS	28 (26)	0 (0)	28 (24)
LACS	5 (5)	1 (9)	6 (5)
Haemorrhagic	13 (12)	6 (55)	19 (16)
Missing	4	1	5
Charlson Co-Morbidity Index, mean (SD)	7.4 (1.7)	6.3 (2.0)	7.0 (1.8)
CRP, median (IQR)	30.5 (11.8-52.0)	24.5 (7.5-78.5)	30.5 (10.8-52.5)
Missing	11	0	11
Serum Albumin (gm/l), mean (SD)	32.7 (4.1)	34.3 (3.8)	32.9 (4.1)
BMI, mean (SD)	23.0 (4.5)	26.5 (6.3)	23.4 (4.8)
Missing	23	0	23
Barthel Index, median (IQR)	0 (0-2)	0 (0-8)	0 (0-2)
Missing	9	1	10

Table 1: Univariable Analysis.

Variable	Categories	Hazard Ratio (95% Confidence Interval)	p-value
Gender	Female	1.00	0.14
	Male	1.34 (0.91, 1.96)	
Age (years)		1.04 (1.02, 1.06)	<0.001
Type of Stroke	TACS	1.00	
	LACS	0.51 (0.21, 1.28)	0.15
	PACS	0.88 (0.56, 1.37)	0.56
	Haemorrhagic	0.35 (0.19, 0.64)	<0.001

Charlson Co-Morbidity Index	1.15 (1.04, 1.29)	<0.01
CRP	1.00 (1.00, 1.01)	0.78
Serum Albumin (gm/l)	0.95 (0.91, 1.00)	0.04
BMI	0.95 (0.91, 0.99)	0.02
Barthel Index	0.97 (0.94, 1.01)	0.09

Table 2: Results in red are statistically significant.

- Age was significantly associated with time to death-risk of death was 4% higher per year increase in age.
- Type of stroke was significantly associated with time to death - people with TACS were 65% more likely to die than those with haemorrhagic stroke.
- Charlson Co-Morbidity Index was significantly associated with time to death - risk of death was 15% higher per unit increase in Charlson Co-Morbidity Index.
- Serum albumin was significantly associated with time to death - risk of death was 5% lower per unit increase in serum albumin.
- BMI was significantly associated with time to death - risk of death was 5% lower per unit increase in BMI.

Other variables were not statistically significantly associated with risk of death.

Multivariable Analysis

Variable	**Categories**	**Hazard Ratio (95% Confidence Interval)**	**p-value**
Gender	Female	1.00	0.02
	Male	1.66 (1.11, 2.50)	
Age (years)		1.03 (1.01, 1.06)	0.01
Type of Stroke	TACS	1.00	
	LACS	0.59 (0.23, 1.50)	0.28
	PACS	0.90 (0.56, 1.45)	0.65
	Haemorrhagic	0.38 (0.19, 0.71)	<0.01
Charlson Co-Morbidity Index		1.04 (0.91, 1.19)	0.54
Serum Albumin (gm/l)		0.96 (0.91, 1.01)	0.09
BMI		0.97 (0.92, 1.03)	0.28

Table 3: Results in red are statistically significant.

- The final multivariable model (after multiple imputation) included sex, age, stroke, albumin, BMI and Charlson which was forced into the model.
- Sex was significantly associated with time to death (when adjusted for other variables) – risk of death was 66% more likely in men than women.
- Age was significantly associated with time to death (when adjusted for other variables) – risk of death was 3% higher per year increase in age.
- Type of stroke was significantly associated with time to death (when adjusted for other variables) – people with TACS were 62% more likely to die than those with haemorrhagic stroke.

Other variables were not statistically significantly associated with risk of death.

The pooled (following multiple imputation) Harrell's c-statistic was 0.65 (0.59, 0.71). This shows moderate ability of the model to differentiate between those who experience the event during the study and those who do not. The pooled calibration slope was 1 (as expected when we assess calibration on a model we have fitted).

The optimism adjusted c-statistic (after bootstrapping) is 0.62 and the optimism-adjusted calibration slope is 0.76. This suggests that the predictions are slightly more extreme than they should be. Forest plot below (Table 4) shows that a combination of TACS stroke, Age >80, Albumin <30g/L, CCI >=9 and low BMI in Men had probability of upto >80 % 6 month mortality after PEG insertion.

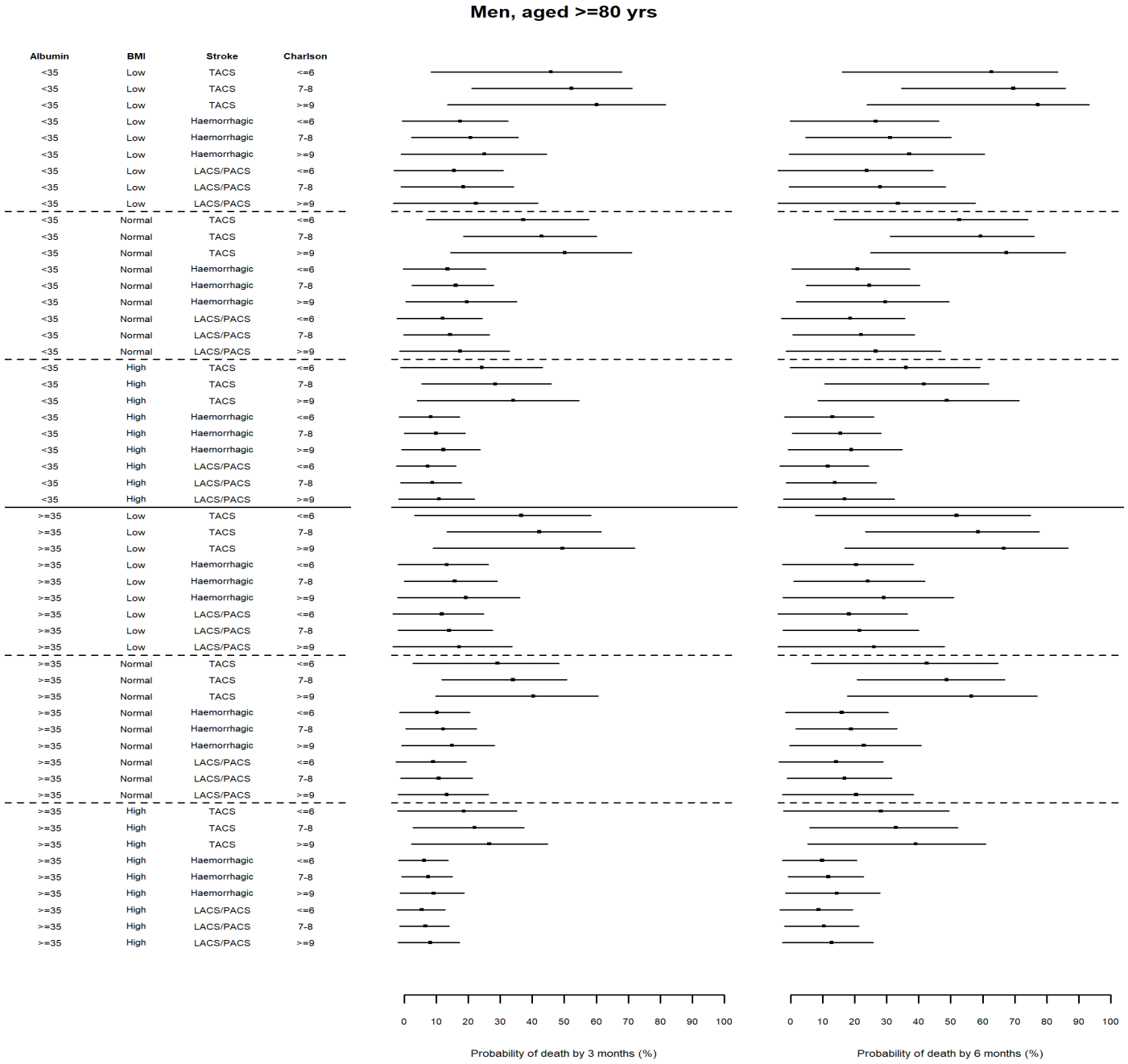

Table 4: Forest plot.

Discussion

We examined patients admitted to stroke unit at Royal Liverpool hospital who underwent PEG for enteral nutrition following a stroke. Our study has shown High rate of mortality with older age with risk of death was 4% higher per year increase in age. With advancing age comes a linear decline in food intake. Involuntary weight loss is common among older adults, especially in those who are chronically ill. Poor caloric intake and weight loss can lead to multiple problems such as muscle wasting, anaemia, and depression. There is a strong correlation between weight loss and morbidity and mortality [10]. Even with mild weight loss of 5% of their body weight in one month, institutionalized older adults are four times more likely to die within one year [11]. Similarly, community dwelling older adults who have mild weight loss are at a higher risk of death after adjusting for multiple variables [12]. Perhaps it can be considered that Age is an independent factor to mortality after a stroke due to already being disadvantaged due to the factors above let alone the complications post PEG insertion.

Some risks involved with Insertion of PEG tubes include wound infections, abdominal pain, aspiration, obstruction of the feeding tube, and agitation. After PEG tube feeding begins, some older adults become agitated and attempt to remove the tube. They may even require chemical and physical restraints for behavioral control [13]. These complications were not looked into in our study. A nursing home study found that after PEG tube placement, older adults did not experience functional improvement. PEG-related complications occurred in close to 30% of the patients and the one-year mortality rate was 50% after tube placement [14].

A novel finding in our study was that a combination of TACS stroke, Age >80, Albumin <30g/L, CCI >=9 and low BMI in Men had probability of upto >80 % 6 month mortality after PEG insertion which would need further exploration. Serum albumin was similarly found to be significantly associated with time to death – risk of death was 5% lower per unit increase in serum albumin and Low BMI was significantly associated with time to death – risk of death was 5% lower per unit increase in BMI. Poor Nutritional status beforehand could essentially mean higher mortalitilty as indicated by low albumin and BMI has previously been proven in other studies [15-20].

FOOD trial [21], compared patients with PEG and naso-gastric tube feeding found that early PEG feeding was associated with increased risk of death or poor outcome of 7.8% (CI: 0-15.5) compared to naso-gastric tube feeding after 6 months. Consequently, the authors did not support early initiation of PEG feeding in major poststroke dysphagic patients. We have identified some poor prognostic indicators such as low albumin, low BMI, TACS stroke, CCI which can perhaps guide us in making a decision whether to go for PEG after 2 weeks of persistent dysphagia or delay it with continuing to NG feed and make a decision later if it would be deemed appropriate. In terms of whether parenteral nutrition should be considered rather than enteral there is a general consensus that enteral feeding is superior [22]. Hence, we did not compare or investigate this further in our study.

Our finding that sex was significantly associated with time to death (when adjusted for other variables) - risk of death was more likely in men than women is in line with other Age-adjusted studies which indicate a lower mortality rate for women overall [23]. The current literature indicates that this disparity may result from the older age and poorer pre-stroke functional status at the time of stroke onset.

Comparisons between haemorrhagic and ischemic stroke has been difficult in the past because of disproportionate distribution of the these strokes, with Ischemic being 10-times more frequent than Hemorhagic in Western countries which can cause statistical validation difficult [24]. Haemorrhagic stroke are considered to have a higher mortality then Ischemic, previous studies have linked higher mortality to severe strokes in patients with haemorrhagic stroke [25]. In this study, type of stroke was significantly associated with time to death (when adjusted for other variables) - people with TACS were 62% more likely to die than those with haemorrhagic stroke, perhaps it can be debated that the haemorrhagic strokes were not as severe in this study which was not particularly looked at. Total anterior circulation stroke is the most severe form of stroke as per Bamford classification accounts for 17-21% of all the strokes [26].

Conclusion

The study highlights that not all patients acquire benefit from PEG. Patient who undergo PEG with severe form of stroke, underlying nutritional status, advanced age with multiple comorbidities may not improve prognosis and even hasten death as a result of the procedure being invasive involving sedation. PEG is necessary in most dysphagic post stroke patient but careful patient selection needs to be exercised. We propose that Further Multicenter research is required to determine a predictive algorithm to be used in future guidelines and management of PEG-based decisions in stroke.

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