Predictive Factors for Percutaneous Endoscopic Gastrostomy in Patients with Spontaneous Intracranial Hemorrhage

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Key Words

Neurocritical care • Intracranial hemorrhage •
Percutaneous endoscopic gastrostomy

Abstract

Background: Dysphagia is frequent after hemorrhagic stroke, and some of the affected patients require prolonged enteral nutrition, most often via percutaneous endoscopic gastrostomy (PEG) tubes. The identification of patients at risk of prolonged dysphagia permits earlier tube placement and helps guide clinicians in the decision-making process. **Methods:** This retrospective study included all patients with spontaneous ICH admitted to a tertiary university hospital from 2007 until 2009 (n = 208). Fifty-one patients received PEG tubes. PEG tube placement was conducted in ventilated patients within 30 days and in spontaneously breathing patients if swallowing did not improve within 14 days. **Results:** Twenty-five percent of patients received PEG tubes. Those patients had larger lobar hemorrhages, intraventricular hemorrhage and occlusive hydrocephalus and higher ICH scores. Furthermore, patients with PEG scored worse on Glasgow Coma Scale (GCS), National Institute of Health Stroke Scale (NIHSS) and Acute Physiology And Chronic Health Evaluation (APACHE II), more frequently needed mechanical ventilation, and had more inflammatory and renal complications. A multivariate regression analysis identified

GCS, occlusive hydrocephalus, mechanical ventilation, and systemic sepsis as independent risk factors for PEG tube placement. **Conclusion:** Disease severity and neurocritical care complications represent the major influencing parameters for PEG tube placement in spontaneous ICH patients.

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Introduction

Oropharyngeal dysphagia is a disorder of deglutition which frequently occurs after stroke. In light of varying methods of detection and time of assessment the incidence of dysphagia ranges between 29 and 81% [1–3]. Apart from aspiration, malnutrition is the most severe complication of oropharyngeal dysphagia [4, 5]. Malnutrition is a common and sometimes unrecognized problem in elderly patients admitted to the hospital [6] and the nutritional status of stroke patients may worsen during hospital stay [4, 7–10]. As poor nutritional status is associated with reduced muscle strength and elevated risk of infection [11, 12], which account for increased morbidity and mortality [4, 5, 7, 8, 10, 13–15], feeding of dysphagic stroke patients is considered essential. Most patients re-

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cover from dysphagia within a week [16, 17]. However, dysphagia persists in some patients [1, 18, 19]. In order to maintain sufficient hydration and nutrition in those patients, (par-)enteral feeding is essential, and percutaneous endoscopic gastrostomy (PEG) placement in stroke patients is typically performed if patients are unable to take food orally for an extended period of time while their gastrointestinal tract works [20].

In this retrospective study, we analyzed how routine PEG placement in a large tertiary University hospital is performed and identified early predictors for the placement of PEG tubes in patients with intracranial hemorrhage (ICH) in order to guide clinicians in the decision-making process.

Methods

Patient Selection

All consecutive patients with spontaneous ICH who were admitted either to the neurocritical care or stroke unit of the Department of Neurology, University of Erlangen, from January 2007 until February 2009 were included into this retrospective analysis. The study was based on a prospectively organized database into which clinical and neuroradiological data of all patients with ICH were included.

Two-hundred and thirty-six patients with the diagnosis of spontaneous ICH were admitted. We did not include patients with secondary ICH, i.e. ICH related to oral anticoagulant therapy, trauma, tumor, arteriovenous malformations, central venous thrombosis, subarachnoid hemorrhage, or ICH associated with acute thrombolysis or coagulopathy with platelet counts below 50,000/ μ l, nor did we include patients with pre-existing swallowing disorders. Moreover, we excluded those patients who received 'do not treat' or 'do not resuscitate' orders within 72 h of admission ($n = 14$). Patients who were discharged for rehabilitation without receiving a PEG beforehand were followed until day 60 after the initial event to obtain information on whether PEG tubes had been placed after discharge from our hospital. No patients were lost to follow-up until day 61. Hence, 208 patients remained eligible for this analysis.

Acquisition of Clinical Parameters and Neuroradiological Data

Clinical Presentation. All clinical parameter that were collected during hospital stay (GCS, NIHSS, ICH score, APACHE II score, body temperature, and mean arterial blood pressure) were obtained by reviewing the patient's medical charts, emergency protocols, and institutional databases.

Laboratory Parameters. Laboratory data (such as white blood cells, C-reactive protein etc.) were obtained by reviewing institutional databases. Categorization of data was performed – if necessary – according to institutional laboratory threshold values.

Pre-Admission Status and Past Medical History. Clinical status as well as medical history prior to admission was obtained by mailed standardized questionnaires. If the questionnaire did not return within 6 weeks, a semiquantitative phone interview was

conducted with the patient, or the closest relatives, respectively. The telephone interviews were performed by two physicians (I.C.K. and J.B.K.) who were trained and certified for data acquisition on disability and quality of life. The collected data comprised pre-hospital body mass index, modified Rankin scale, history of ischemic or hemorrhagic stroke, use of nicotine, alcohol abuse (defined as >80 g ethanol/day), diagnosis of hypercholesterolemia (defined as >200 mg/dl), diagnosis of arterial hypertension (defined as $>140/90$ mm Hg), diagnosis of atrial fibrillation, prior myocardial infarction and diagnosis of diabetes mellitus (defined as HbA1c $>6.5\%$ or fasting plasma glucose >125 mg/dl). All patients or their relatives consented to the anonymous use of the data.

In-Hospital Treatment. These parameters [need and duration of ventilation, external ventricular drainage (EVD; for occlusive hydrocephalus [21]), or lumbar drainages (for posthemorrhagic communicating hydrocephalus [22]), respectively, intraventricular fibrinolysis [22], diagnosis of pneumonia, and sepsis, respectively, [23, 24]] were obtained by reviewing the patient's medical charts.

Outcome Findings. Primary outcome was defined as PEG placement within hospital stay or during rehabilitation until day 60.

Neuroradiologic Data. Diagnosis of ICH was made immediately after hospital admission by either CT (SIEMENS Somatom Volume zoom, Erlangen, Germany) or MRI (Siemens Sonata, 1.5 Tesla, Erlangen, Germany). The site of hemorrhage was defined as either lobar, deep (including thalamic hematomas), cerebellar or brainstem. Hematoma volume was calculated according to the formula of ellipsoids ($ABC/2$), which has been shown to estimate hemorrhage volume reliably [25]. Intraventricular hemorrhage (IVH) or subdural extensions were not taken into account for volume measurement. IVH was documented and scored using the Graeb score summation for each ventricle [26]. Hematoma growth was defined as an increase of intraparenchymal hemorrhage volume $>33\%$ as measured by image analysis on the follow-up CT or MRI 24 h after the baseline scan [27].

Clinical Management

All patients received standard medical treatment according to national and international guidelines [28]. Patients requiring mechanical ventilation during the course of the treatment were sedated with midazolam and fentanyl. Extraventricular drainage (EVD) was initiated in all patients showing evidence of occlusive hydrocephalus [22]. Pneumonia was diagnosed according to the criteria recommended by the American Thoracic Society [29]. Sepsis was diagnosed and treated according to national and international guidelines [30–32]. Acute kidney injury (AKI) was defined and treated according to the RIFLE classification for critically ill patients [33, 34].

PEG Tube Placement

In ventilated ICH patients enteral nutrition was started within 24 h after admission via nasogastric tubes according to international and national guidelines [35–39], or, as soon as further invasive procedures (e.g. delayed EVD placement or hematoma evacuation) had been carried out, respectively. PEG tube placement was initiated once it became apparent that the individual patient would not be able to consume sufficient oral intake to meet long-term metabolic demands within 30 days, but not earlier than 10 days after the initial event [20, 36, 40, 41]. The actual placement of the PEG tube was then accomplished within 3 days.

Table 1. Demographic data, past medical history, and neuroradiologic characteristics of the analyzed ICH patients

	With PEG (n = 51)	Without PEG (n = 157)	p value (p < 0.05)
Age, median (IQR)	71 (58–79)	70 (61–78)	0.920
Female sex, n (%)	22 (43.1)	76 (48.4)	0.284
<i>Pre-admission status</i>			
mRS ≤2, n (%)	34 (66.7)	117 (74.5)	0.180
Overweight (BMI ≥25), n (%)	24 (47.1)	76 (48.4)	0.498
Nicotine abuse, n (%)	16 (31.4)	52 (33.1)	0.480
Alcohol abuse (≥80 g/day), n (%)	11 (21.6)	33 (21.0)	0.538
<i>Past medical history</i>			
Hypertension, n (%)	29 (56.9)	103 (65.6)	0.169
Diabetes mellitus, n (%)	12 (23.5)	24 (15.3)	0.128
Hypercholesterolemia, n (%)	11 (21.6)	48 (30.6)	0.144
Atrial fibrillation, n (%)	5 (9.8)	6 (3.8)	0.101
Hemorrhagic stroke, n (%)	5 (9.8)	16 (10.2)	0.588
Ischemic stroke, n (%)	13 (25.5)	26 (16.6)	0.114
Prior cardiac infarction, n (%)	6 (11.8)	13 (8.3)	0.309
<i>Neuroradiologic data</i>			
<i>Localization</i>			
Lobar, n (%)	17 (33.3)	63 (40.1)	0.243
Lobar volume (ml), median (IQR)	34.8 (7.4–55.3)	16.8 (4.9–50.2)	0.047
Deep, n (%)	29 (56.9)	76 (48.4)	0.209
Deep volume (ml), median (IQR)	20.4 (4.6–41.1)	14.9 (5.7–36.6)	0.121
Cerebellar, n (%)	1 (2.0)	9 (5.7)	0.248
Cerebellar volume (ml), median (IQR)	16.3 (5.1–31.8)	12.4 (4.2–29.2)	0.543
Brainstem, n (%)	4 (7.8)	9 (5.7)	0.399
Brainstem volume (ml), median (IQR)	10.4 (2.7–16.3)	8.7 (3.7–14.1)	0.081
Hematoma growth within 24 h, n (%)	6 (11.8)	15 (9.6)	0.412
Intraventricular hemorrhage, n (%)	32 (62.7)	71 (45.2)	0.022
Occlusive hydrocephalus/EVD, n (%)	21 (41.2)	38 (24.2)	0.017
Graeb score, median (IQR)	4 (0–8)	0 (0–6)	0.062
ICH score, median (IQR)	3 (2–3)	2 (0–3)	0.001

Data are calculated as continuous or categorizes variables and are presented dichotomized for patients with or without PEG tube placement. Significant parameters are expressed in bold.

All spontaneously breathing patients underwent clinical swallowing evaluation by a speech therapist within 24 h after admission. If aspiration was assumed because of pathological water swallowing tests [42–45], fiberoptic endoscopic evaluation of swallowing was performed [46–51]. Patients with aspiration were monitored for at least fourteen days. Dysphagic patients were routinely re-evaluated on a daily basis, or at least every second day, as appropriate. If swallowing did not improve until day 14 after admission, PEG tube placement was initiated within the next 3 days [40, 52].

Because of varying capacity of rehabilitation institutions, some patients were transferred to rehabilitation within 2 weeks after admission. These patients were followed up until day 60 after the initial hospital admission (telephone interviews by I.C.K. and J.B.K.), and potential PEG tube placement during rehabilitation was recorded.

Statistical Analysis

Statistical analysis was performed with the SPSS 17.0 software package. The significance level was set at $\alpha = 0.05$. Statistical tests were two-sided. Distribution of the data was assessed with the Kolmogorov-Smirnov test. Normally distributed data is presented as mean $\pm$ SD and was compared using the Student's t test. Other data are presented as median with IQR (25–75th percentiles), or total range, respectively, and was compared using the Mann-Whitney U test. Pearson χ^2 or Fisher's exact tests were used for comparison of frequency distributions of categorized variables between the two groups (PEG vs. no PEG). One stepwise forward multivariate logistic regression analysis (that included all variables with $p < 0.5$) was carried out.

Table 2. Clinical parameters and laboratory findings at admission and during hospital stay

	With PEG (n = 51)	Without PEG (n = 157)	p value (p < 0.05)
<i>Clinical parameters at admission</i>			
Body temperature (°C), median (IQR)	36.6 (36.2–37.3)	36.9 (36.2–37.4)	0.439
GCS, median (IQR)	5 (3–10)	13 (3–15)	<0.001
NIHSS, median (IQR)	21 (18–38)	10 (5–28)	<0.001
APACHE II score, median (IQR)	19 (16–25)	13 (8–21)	<0.001
Mean arterial pressure (mm Hg), median (IQR)	123.3 (93.3–140)	113.3 (100–130)	0.881
<i>Characteristics during stay</i>			
Mechanical ventilation, n (%)	35 (68.6)	69 (43.9)	0.002
Duration of ventilation (days), median (IQR)	5 (0–27)	0 (0–6)	0.012
Hospital stay duration (days), median (IQR)	16 (10–29)	12 (6–9)	0.051
Pneumonia, n (%)	42 (82.4)	70 (44.6)	<0.001
Sepsis, n (%)	23 (45.1)	16 (10.2)	<0.001
ICP >20 mm Hg, n (%)	2 (3.9)	6 (3.8)	0.625
<i>Blood parameters at 72 h</i>			
White blood cells >12 × 10 ⁹ /l, n (%)	44 (86.3)	57 (36.3)	<0.001
CRP at 72 h (mg/l), mean ± SD (range)	117.9 ± 86.3 (0–308)	74.1 ± 69.9 (0–272)	0.004
HbA1c >6.5%, n (%)	4 (7.8)	16 (10.2)	0.428
Acute renal failure, n (%)	28 (54.9)	50 (31.8)	0.003

Significant parameters are expressed in bold.

Results

The initial screening showed dysphagia or inability to swallow due to mechanical ventilation in 129 patients. Twenty-four spontaneously breathing and all ventilated patients received nasogastric tubes. One ventilated patient died after PEG tube placement due to pulmonary complications.

Overall, 51 of 208 ICH patients (24.5%) received PEG tube placement. Thirty-one patients received PEG before hospital discharge and another 20 patients during rehabilitation. Of the 31 patients with PEG tube placement during hospital stay the mean duration until PEG tube placement was 17 days (range 15–22) in spontaneously breathing patients, and 18 days (range 13–28) in ventilated patients, respectively. Of the 20 patients who did not receive PEG tube placement before rehabilitation the mean duration until PEG tube placement was 31.5 days (range 21–48) in spontaneously breathing patients, and 30 days (range 16–51) in ventilated patients, respectively.

Table 1 provides information on demographic characteristics and past medical history. There were no significant differences between patients with and without PEG tube placement. When focusing on neuroradiological pa-

rameters, patients who received PEG placement showed significantly larger lobar hematomas, more frequent intraventricular hemorrhage and occlusive hydrocephalus, and an overall higher ICH score, as compared to patients without PEG placement (table 1).

The initial clinical presentation as well as parameters of the clinical course of all analyzed patients is given in table 2. Patients who received PEG tube placement were significantly more severely affected scoring worse on GCS, NIHSS, and APACHE. Moreover, necessity of mechanical ventilation, as well as its duration, was more frequently observed in those patients who received PEG tube placement. Furthermore, inflammatory serum markers and presence of pneumonia and sepsis, as well as occurrence of acute renal failure complicated the clinical course in patients with PEG tube placement significantly more often (table 2).

Table 3 shows the univariate analysis. All significant parameters were adjusted in the multivariate analysis that is given in table 4. The parameters (1) occlusive hydrocephalus, (2) GCS on admission, (3) necessity of mechanical ventilation, and (4) occurrence of systemic sepsis were independently predisposing for PEG tube placement.

Table 3. Univariate regression analysis for identification of parameters which were associated with PEG tube placement

	OR	95% CI	p value
<i>Demographic data</i>			
Age	1.026	0.967–1.132	0.9323
Female	0.861	0.400–1.853	0.7025
Prior mRS ≤2	1.125	0.211–1.304	0.1651
Prior BMI ≥25	0.966	0.886–1.052	0.4251
Prior hemorrhagic stroke	0.897	0.249–3.232	0.8677
Prior ischemic stroke	2.018	0.846–4.814	0.1136
Prior cardiac event	1.175	0.054–6.962	0.5261
<i>Neuroradiologic data</i>			
Localization			
Lobar volume	1.385	1.001–1.842	0.0361
Deep volume	1.223	0.601–1.268	0.4754
Cerebellar volume	0.999	0.984–1.014	0.9122
Brainstem volume	1.809	1.000–2.075	0.0419
Hematoma growth within 24 h	1.945	0.570–6.640	0.2848
Intraventricular hemorrhage	2.199	1.012–5.042	0.0149
Occlusive hydrocephalus	2.247	1.438–4.849	0.0027
Graeb score	1.565	0.498–2.763	0.8422
ICH score	8.938	5.593–12.372	0.0138
<i>Clinical parameters</i>			
At admission			
Body temperature	1.306	0.911–1.872	0.8017
GCS	0.857	0.790–0.931	0.0002
NIHSS	4.548	1.458–6.157	0.0001
APACHE II score	1.074	1.024–1.125	0.0003
Mean arterial pressure	1.823	0.707–4.701	0.2132
During stay			
Mechanical ventilation	2.439	1.744–3.911	0.0391
Duration of ventilation	1.597	0.968–6.485	0.0590
Hospital stay duration	1.132	0.109–1.904	0.1366
Pneumonia	3.719	1.272–4.526	0.0048
Sepsis	3.645	1.746–3.927	0.0027
ICP >20 mm Hg	1.567	0.904–2.945	0.8014
<i>Blood parameters at 72 h</i>			
White blood cells >12 × 10 ⁹ /l	2.855	1.155–5.471	0.0049
CRP at 72 h	2.192	1.178–12.701	0.0185
HbA1c >6.5%	4.347	0.336–5.630	0.2601
Acute renal failure	5.500	1.165–25.964	0.0314

Demographic characteristics and past medical history, neuro-radiologic data, clinical presentation, and laboratory data were included. Data are calculated as continuous or categorized variables. Significant parameters are expressed in bold.

Discussion

To the best of our best knowledge, the present study for the first time analyzed the incidence of PEG tube placement in spontaneous ICH patients and compared clinical

Table 4. Multivariate logistic regression model for prediction of PEG tube placement in spontaneous ICH patients

	OR	95% CI	p value
Prior mRS ≤2	1.013	0.872–1.433	0.8876
Prior BMI ≥25	0.948	0.754–1.651	0.7361
Prior ischemic stroke	1.875	0.948–2.844	0.1479
Lobar volume	0.879	0.784–1.056	0.1385
Deep volume	1.453	0.866–1.678	0.5481
Brainstem volume	0.854	0.301–2.145	0.6947
Occlusive hydrocephalus	1.471	0.184–2.697	0.0481
GCS	0.943	0.712–0.979	0.0072
Hospital stay duration	1.258	0.357–1.945	0.2473
Mechanical ventilation	1.395	1.021–3.183	0.0281
Sepsis	5.584	2.175–16.518	0.0014
HbA1c >6.5%	2.976	0.875–4.816	0.3477
Acute renal failure	2.184	0.914–6.491	0.0846

Significant parameters are expressed in bold.

and neuroradiological parameters between patients with and without PEG tube placement. Nearly 25% of ICH patients require PEG tube placement, and, as a key finding, disease severity (GCS), requirement of mechanical ventilation, presence of occlusive hydrocephalus and occurrence of sepsis were independently related to PEG tube placement. The following aspects emerge from the data.

An incidence of PEG tube placement of nearly 25% reflects that long-term dysphagia after ICH constitutes a relevant clinical complication [53]. At a second glance, however, and when interpreting the present data, one has to differentiate between ventilated patients who require neurocritical care, and those treated spontaneously on a stroke unit for breathing.

Similar to what has been suggested for ischemic stroke patients in whom mainly disease severity and clinical status – as displayed by the NIHSS – predisposed them for PEG tube placement [54], the baseline prognostic parameters (GCS, hematoma volume, presence of intraventricular hemorrhage and occlusive hydrocephalus [55]) represented the major driving factors necessitating PEG tube placement also in ICH patients who received neurocritical care. Hence, it appears plausible that secondary complications of intensive care medicine such as prolonged requirement of mechanical ventilation [22] or acute renal failure [56–59] were also significantly associated with PEG tube placement. In addition, the incidence of pneumonia (presumably based on aspiration in dysphagic patients), and related systemic sepsis, respectively, was significantly higher in patients who received PEG [54]. This

may reflect an epiphenomenon that PEG tube placement may have been initiated in such critically ill patients because of these severe systemic complications, rather than because of the disease and its symptoms itself [20].

On the other hand, spontaneously breathing ICH patients on stroke units may have a different risk profile, and probably clinical symptoms (e.g. dysphagia) and site of hemorrhage (e.g. brainstem) may rather represent independent risk factors, as previously suggested in ischemic stroke patients [54]. However, this is still some uncertainty about the timing of PEG tube placement in spontaneously breathing stroke patients [40, 52]. Besides the fact that lobar hemorrhages with increasing volume predicted PEG tube placement, there was no other hematoma site, and especially not hematoma volume, that was associated with PEG tube placement. On a general note, the incidence of PEG after ICH mainly seems to be related to overall disease severity (and subsequent complications) rather than to specific clinical symptoms alone.

Our study has several shortcomings mainly because of its retrospective design. The specific clinical stroke symptoms were not sufficiently re-assessable. Moreover, a sub-

stantial proportion of patients did not receive PEG before rehabilitation because the reason for PEG placement could not be verified as properly as in the clinical setting.

Taken together, disease severity – as expressed by GCS, occlusive hydrocephalus, mechanical ventilation, and sepsis – represents the major influencing factor for PEG tube placement in spontaneous ICH patients. Because of scarce data on the timing and method of enteral feeding in such patients, and until prospective studies will hopefully broaden the knowledge in this stroke field, the present analysis may help to guide stroke physicians in their decision-making process on PEG tube placement in ICH patients.

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