

# Gastroesophageal Reflux during Enteral Feeding in Stroke Patients: A 24-hour Esophageal pH-monitoring Study

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*Background:* Patients who are unable to eat or drink after stroke may receive percutaneous endoscopic gastrostomy (PEG) or nasogastric tube feeding. Although the most common serious complication is well known to be aspiration pneumonia, the role of gastroesophageal reflux (GER) has not been fully assessed. The aim of this study was to examine, by means of 24-hour esophageal pH monitoring, whether GER is related to aspiration pneumonia and whether the size and laterality of brain lesions influence GER. *Methods:* Sixteen stroke patients were examined using a Degitrappet pH400 (Medtronic Japan Co., Tokyo, Japan) and Zinetics 24ME multi-use pH catheter (Medtronic). All patients had stroke lesions in the territory of the left or right middle cerebral artery that were confirmed by magnetic resonance imaging (MRI) and were receiving PEG or nasogastric feeding. Stroke volume was measured with MRIcron software. *Results:* Nine patients (56%) were diagnosed with GER, and 10 (63%) developed aspiration pneumonia after enteral feeding. The rate of aspiration pneumonia was significantly higher in patients with GER (88.9%) than in those without GER (42.9%;  $P = .04$ ). Patients with left hemispheric lesions had a significantly higher incidence of acid reflux than those with right lesions ( $116 \pm 105$  vs  $13 \pm 17$ ;  $P = .04$ ). There were no significant differences in total time of acid reflux or mean pH value between patients with left and right hemispheric lesions. The lesion volume had no significant effect on any of 3 indices of GER. *Conclusions:* GER is associated with aspiration pneumonia and occurs more often in patients with stroke lesions in the left hemisphere. **Key Words:** Enteral feeding—gastroesophageal reflux—pH monitoring—poststroke pneumonia.

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Stroke is the major cause of neurogenic dysphagia, which is frequently complicated by the development of aspiration pneumonia.<sup>1,2</sup> Patients receiving nasogastric tube or percutaneous endoscopic gastrostomy (PEG)

feeding tend to have gastroesophageal reflux (GER).<sup>3</sup> James et al<sup>4</sup> reported that stroke patients with PEG had a high prevalence (18%) of aspiration pneumonia, and their median survival was only 10 months. Several mechanisms could be involved in the development of GER, including transient lower esophageal sphincter relaxation, excessive acid reflux, and gastric acid hypersecretion.<sup>5,6</sup> Nevertheless, the pathophysiology of GER after stroke has not been well documented. One previous study examined the relationship between GER and aspiration pneumonia in patients with various brain diseases,<sup>7</sup> but the influence of lateralization and size of brain lesions after stroke on GER remains unclear. This study was designed to examine, by means of 24-hour pH monitoring, the incidence of GER in stroke patients under enteral

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feeding and the effect of hemispheric lateralization or lesion volume on GER in those patients.

## Methods

We selected 16 stroke patients 57 to 95 years of age (mean  $83.2 \pm 9.2$  years) who had been admitted to Shimane University Hospital and who were receiving PEG or nasogastric tube feeding. Six patients had stroke lesions in the right middle cerebral artery (MCA) territory and 10 had lesions in the left MCA territory. Exclusion criteria were severe illness including malignancy, history of gastroesophageal surgery, and lack of informed consent. The diagnosis of stroke was made clinically and lesions were confirmed by magnetic resonance imaging (MRI; 1.5 T Magnetom, Siemens, Washington, DC). All patients had been treated with antiplatelet or antithrombin drugs in the acute stage of stroke. The diagnosis of aspiration pneumonia required 3 or more of the following characteristics: pulmonary infiltrates in chest radiography, fever, dyspnea, abnormal respiratory examination, and leukocytosis.<sup>7,8</sup> Aphasia was diagnosed on the basis of disruption of sentence comprehension, sentence production, naming, and reading.<sup>9</sup>

Twenty-four-hour esophageal pH monitoring was performed using the Degitrappher pH400 (Medtronic Japan Co, Tokyo, Japan), which was calibrated at pH 1 and pH 7 before use. The Zinetics 24ME multiuse external reference pH catheter (Medtronic) was inserted transnasally into the esophagus with the aid of 2% lidocaine jelly for gastroesophageal pH monitoring, and the pH electrode was positioned 5 cm above the lower esophageal sphincter. The mean duration between stroke onset and the start of PEG or nasogastric tube feeding was 59 ( $\pm 82$ ) days. Each patient was given liquid-type nutrition RACOL (pH 7.0, 360 mOsm/L, nitrogen 0.69 g/100 mL, and sodium 0.19 g/100 mL; EN Otsuka Pharmaceutical Co, Hanamaki City, Japan) 3 times a day during the study. The patients were kept in an upright position for 2 hours after each meal. The administration of H<sub>2</sub> blockers and/or proton pump inhibitors had been stopped 7 days before the study. The study was approved by the Ethics Committee of Shimane University Hospital. All recorded data were transferred to a personal computer for analysis using Polygram 98 Reflux Analysis software (Medtronic). A gastroesophageal acid reflux episode was defined as the time for which the pH was below 4.<sup>10,11</sup> We evaluated the number of acid reflux episodes, the total period (minutes) of acid reflux, and the mean pH values.

Lesion volume was measured on T2-weighted axial magnetic resonance images using MRIcron software (available at: <http://www.cabiatl.com/mricro/mricron/install.html>) with the intensity threshold used by Eckerström et al.<sup>12</sup> If the observation period about the occurrence of aspiration pneumonia differed among patients, there could be a significant bias; therefore, we

unified the observation period within 1 year after starting PEG or nasogastric tube feeding.

## Statistical Analysis

Descriptive statistics were used to quantify the degree and frequency of GER. The Mann-Whitney *U* test was used for nonparametric comparisons. The Chi-square test was used to analyze the relationship of aspiration pneumonia with GER and hemispheric lateralization of stroke lesion (right or left). It was also used to analyze the relationship of aphasia with GER and aspiration pneumonia. The Spearman correlation coefficient test was used to assess the correlation between GER indices, aspiration pneumonia, and stroke lesion volume.  $P < .05$  was considered statistically significant.

## Results

Four patients underwent PEG and 12 patients underwent nasogastric tube feeding (Table 1). Nine patients (56%) were diagnosed with GER, which was defined on the basis that the number of acid reflux episodes was  $>25$  per day and the cumulative reflux time was  $>4\%$ .<sup>6,11</sup> Ten patients (63%) developed aspiration pneumonia during enteral feeding. The rate of aspiration pneumonia was significantly higher in patients with GER (88.9%) than in those without GER (42.9%;  $P = .04$ ; Table 2). However, the rate of aspiration pneumonia revealed no significant difference between patients with left lesions (70.0%) and those with right lesions (50.0%). The incidence of aspiration pneumonia was not affected by age, gender, feeding method, or duration after stroke onset. The 3 pneumonia patients without GER were diagnosed with infectious pneumonia after sputum culture. *Staphylococcus aureus* was detected in cases 11 and 13, and *Klebsiella pneumoniae* was detected in case 14.

Table 2 shows the mean esophageal pH values over 24 hours, mean number of acid reflux episodes, and mean total time of acid reflux in 24 hours for all subjects. The 10 patients with left hemispheric lesions had a significantly higher incidence of acid reflux than the 6 patients with right hemispheric lesions ( $116 \pm 105$  vs  $13 \pm 17$ ;  $P = .04$ ). No significant difference was seen in total time (minutes) of acid reflux between left and right lesions ( $105.2 \pm 116.0$  vs  $23.8 \pm 9.7$ ). The mean pH value was also similar for left and right lesions ( $6.0 \pm 0.7$  vs  $6.2 \pm 0.7$ ). There was no difference in the rate of aphasia between patients with and without GER (55.5% vs 28.5%), or between patients with and without pneumonia (50.0% vs 33.3%).

There was no difference in lesion volume between patients with and without GER ( $47.8 \pm 49.3$  vs  $64.3 \pm 30.6$  cm<sup>3</sup>) or between patients with and without pneumonia ( $57.1 \pm 45.1$  vs  $50.4 \pm 38.0$  cm<sup>3</sup>; Table 1). The lesion volume was also similar between patients with left and right hemispheric stroke ( $60.9 \pm 45.4$  vs  $45.1 \pm 36.5$  cm<sup>3</sup>). The lesion volume was not correlated with any

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