The Mortality and the Risk of Aspiration Pneumonia Related with Dysphagia in Stroke Patients

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Background: Dysphagia may result in poor outcomes in stroke patients due to aspiration pneumonia and malnutrition. *Goal*: The aim of the study was to investigate aspiration pneumonia and the mortality rate in stroke patients with dysphagia in Taiwan. *Methods*: We selected 1220 stroke patients, divided them into dysphagia and nondysphagia groups, and matched them according to age; covariates and comedications from 2000 to 2005 were identified from the NHIRD 2000 database. The date of the diagnosed stroke for each patient was defined as the index date. All patients were tracked for 5 years following their index visit to evaluate mortality and the risk of aspiration pneumonia. We estimated the adjusted hazard ratio using Cox proportional hazard regression. *Results*: Within 1 year, the dysphagia group was 4.69 times more likely to develop aspiration pneumonia than the nondysphagia group (adjusted hazard ratio [aHR], 4.69; 95% confidence interval [CI] 2.83-7.77; $P < .001$). The highest significant risk of aspiration pneumonia was in the cerebral hemorrhage patients within 3 years of the index visit (aHR, 5.04; 95% CI 1.45-17.49; $P = .011$). The 5-year mortality rate in the dysphagia group was significantly higher than that in the nondysphagia group (aHR, 1.84; 95% CI 1.57-2.16; $P < .001$). *Conclusion*: Dysphagia is a critical factor in aspiration pneumonia and mortality in stroke patients. Early detection and intervention of dysphagia in stroke patients may reduce the possibility of aspiration pneumonia.

Key Words: Aspiration pneumonia—survival rate—stroke—dysphagia

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Introduction

Stroke and dementia may result in the high rates of dysphagia seen in diseases of elderly patients and health complications.[1] Poststroke dysphagia is a common complication of acute stroke and is associated with increased mortality, morbidity, and institutionalization due to aspiration pneumonia and malnutrition. Most stroke patients may recover swallowing spontaneously, but a significant minority still have dysphagia sequelae at 6 months.[2] Dysphagia is highly prevalent following a stroke attack, with an occurrence of 30%-65%.[3,4] In the USA, approximately 300,000-600,000 people experience dysphagia as a result of a stroke or other neurological deficit.[5]

Dysphagia could be secondarily associated with nutritional deficits, disability, an increased risk of pneumonia and death, and could result in a poor outcome in stroke patients.[6] Early dysphagia screening reduces stroke-related aspiration pneumonia and improves stroke outcomes, especially in recent ischemic stroke.[6] Pneumonia is one of the leading causes of mortality after a stroke, accounting for approximately 35% of poststroke deaths.[7] Most stroke-related pneumonia is due to dysphagia and the subsequent aspiration of oropharyngeal food material.

Rehabilitative management, together with appropriate nutrition, is recommended to improve clinical outcomes and prognosis, including improving the physical and swallowing functions in stroke patients with aspiration pneumonia. Dysphagia was associated with an increased risk of stroke-related pneumonia, case fatality during hospitalization, and disability at discharge.[6] However, there are no data on the long-term influence of the subtype of the stroke on aspiration pneumonia and the mortality rate. In the present study, we investigated the hazard ratio of aspiration pneumonia and mortality in stroke patients with or without dysphagia at 1, 3, and 5 years after stroke.

Material and Methods

Data Source

The study used claims data from Taiwan's National Health Insurance Research Database (NHIRD), which is managed by the National Health Research Institute (NHRI) in Taiwan. The National Health Insurance (NHI) program reimburses the healthcare costs of 99% of the population in Taiwan. The NHIRD contains comprehensive healthcare information for all of Taiwan's insured individuals, including demographic data, dates of clinical visits, diagnostic codes, and prescription details. In this study, we tapped the subset of the NHIRD known as the Longitudinal Health Insurance Database (LHID) 2000. This dataset contains ambulatory and inpatient care medical records for 1 million randomly sampled beneficiaries enrolled in the NHI system in the year 2000. The LHID 2000 database allows researchers to follow up on the medical service utilization of these 1 million subjects. According to the NHRI, there are no statistically significant differences in age, gender, or healthcare costs between the LHID 2000 and NHIRD.

Study Patients

We identified stroke patients (ICD-9 code: 430-438) between January 1, 2000 and December 31, 2005. The dysphagia group (ICD-9: 787.2) was compared with the nondysphagia group, which consisted of patients who had never diagnosed dysphagia, and the groups were matched (1:1) on the basis of age, sex, other covariates, propensity score, and index year. The date of the diagnosed stroke for each patient was defined as the index date. Subjects were excluded if they were less than 20 years old, more than 99 years old, or had incomplete follow-up insurance data.

Diagnosis of Aspiration Pneumonia

The outcome of interest was a diagnosis of ICD-9-CM 507 (pneumonitis due to solids and liquids). Patients were followed from the index date to the occurrence of aspiration pneumonia, death, disenrollment from the national health insurance, or the end of the study date (December 31, 2013), whichever came first.

Potential Confounders

Inpatient and outpatient files from the year prior to the index date were used to obtain information on comorbidities, including hypertension (ICD-9:401-405), diabetes (ICD-9:250.X), hyperlipidemia (ICD-9:272), cardiovascular disease (ICD-9: 411-414, 428), chronic kidney disease (ICD-9: 582, 583, 585, 586, 588), chronic liver disease (ICD-9: 571.2, 751.5, 571.6, 571.40-571.42, 571.49, 572.2-572.4, 572.8, 456.0-456.1, 456.20, 456.21), cancer (ICD-9: 140-208), dementia (ICD-9: 290.0-290.4, 291.1-291.2, 294.1, 331.0-331.2, and 331.82), and depression (ICD-9: 296.2, 296.3, 300.4, 311).

Statistics Analysis

Pearson's chi-squared test or Fisher's exact test was performed to evaluate differences in the categorical data between patients from the dysphagia and nondysphagia groups. An independent *t* test was performed to evaluate differences between the 2 groups in the continuous data. Cox proportional hazards regression analysis was performed to examine mortality, and the risk of aspiration pneumonia within 1, 3, and 5 years of the index date in the dysphagia group was compared with that in the nondysphagia group. In the subgroup analysis, we divided stroke subtypes as ischemic stroke (ICD-9 code: 433, 434, 436, 4378, 4379), cerebral hemorrhage (ICD-9 code: 430, 431, 432), and other types to compare the subtype relationship with dysphagia during the follow-up period. Several covariables, including age, gender, and comorbidities, were adopted in the statistical analysis model. Hazard ratios (HR) and 95% confidence intervals (CI), using the nondysphagia group as the reference, were calculated to show the risk of aspiration pneumonia and mortality in the stroke patients and in the subtype stroke analysis. A Kaplan-Meier curve was used to estimate the probability of aspiration pneumonia and mortality, and the log-rank test was used to evaluate the differences between the dysphagia group and the nondysphagia group. All statistical operations were performed using the SAS 9.3 statistical package; all P values were 2-sided, and P value $<.05$ was considered statistically significant.

Results

Demographic Data of the Recruited Stroke Population

The demographic data are shown in Table 1. From January 1, 2000 to December 31, 2005, we collected data from the LHID 2000 for 610 stroke patients as the dysphagia group and 610 stroke patients as the nondysphagia group. The mean age of the dysphagia group was 71.78 ± 11.7 years and 41% were female. The distribution of age, gender, and comorbidities, including diabetes, hypertension, hyperlipidemia, chronic kidney disease, cardiovascular disease, chronic liver disease, cancer, and dementia, were similar between the nondysphagia group and dysphagia group (Table 1). The dysphagia group was followed for an average of 2.96 years, and the nondysphagia group was followed for an average of 3.73 years (data not shown).

The Risk of Aspiration Pneumonia between the Dysphagia and Nondysphagia Groups in Stroke Patients

Table 2 shows the risk of aspiration pneumonia in stroke patients between the dysphagia and nondysphagia groups after 1, 3, and 5 years after the index date. Cox proportional hazard regression analysis revealed that aspiration pneumonia within the first year was significantly different between the dysphagia group and the nondysphagia group (adjusted hazard ratio [aHR] 4.69, 95% CI 2.83-7.77, $P < .001$). After age, gender, and comorbidities were adjusted for, some stroke subtypes had an increased risk of aspiration pneumonia. In the subgroup analysis, there was a significantly higher risk for aspiration pneumonia in patients with dysphagia than that in patients with nondysphagia, followed by ischemic stroke (aHR 5.64, 95% CI 2.82-11.28, $P < .001$) and other types (aHR 3.28, 95% CI 1.39-7.72, $P = .007$). The aspiration pneumonia risk within 3 years after the stroke episode was significantly statistically different between the dysphagia group and the nondysphagia group (aHR 3.49, 95% CI 2.43-5.01, $P < .001$); in the subgroup analysis, there was a significantly higher risk in patients with dysphagia than that in patients with nondysphagia, followed by ischemic stroke (aHR 3.66, 95% CI 2.27-5.89, $P < .001$), cerebral hemorrhage (aHR 5.04, 95% CI 1.45-17.49, $P = .011$), and other types (aHR 2.81, 95% CI 1.39-5.67, $P = .004$). Aspiration pneumonia risk within 5 years after the stroke episode was significantly different between the dysphagia group and the

Table 1. *Demographic data of the recruited stroke population*

	Nondysphagia group (Numbers = 610)		Dysphagia group (Numbers = 610)		
	numbers	(%)	numbers	(%)	P Value
Age, mean (standard deviation)	71.89	(10.7)	71.78	(11.7)	.859
<65 years old	129	(21.1)	134	(22.0)	.728
≥65 years old	481	(78.9)	476	(78.0)	
Gender					
Female	248	(40.7)	250	(41.0)	.907
Male	362	(59.3)	360	(59.0)	
Aspiration pneumonia history	79	(13.0)	74	(12.1)	.666
Subtype stroke					
Ischemic stroke	333	(50.1)	332	(55.2)	.001
Cerebral hemorrhage	73	(12.0)	115	(18.9)	
Other types	204	(33.4)	163	(26.7)	
Comorbidities					
Diabetes	281	(46.1)	278	(45.6)	.863
Hypertension	546	(89.5)	540	(88.5)	.583
Hyperlipidemia	226	(37.0)	221	(36.2)	.766
Chronic kidney disease	145	(23.8)	158	(25.9)	.389
Cardiovascular disease	89	(14.6)	99	(16.2)	.428
Cancer	40	(6.6)	48	(7.9)	.954
Dementia	160	(26.2)	161	(26.4)	.948
Depression	14	(2.3)	28	(4.6)	.028

Table 2. *The risk of aspiration pneumonia between the dysphagia and nondysphagia groups in the stroke patients*

	Nondysphagia group (N = 610)		Dysphagia group (N = 610)			
	n	(%)	n	(%)	Adjusted hazard ratio	*P* Value
Within 1 year						
Overall	19	(3.1)	77	(12.6)	4.69 (2.83-7.77)	<.001
Subtype stroke						
Ischemic stroke	10	(3.1)	46	(14.2)	5.64 (2.82-11.28)	<.001
Cerebral hemorrhage	1	(1.4)	10	(8.8)	6.78 (.83-55.25)	.074
Other types	8	(3.8)	21	(12.3)	3.28 (1.39-7.72)	.007
Within 3 years						
Overall	41	(6.7)	110	(18.0)	3.49 (2.43-5.01)	<.001
Subtype stroke						
Ischemic stroke	25	(7.7)	64	(19.7)	3.66 (2.27-5.89)	<.001
Cerebral hemorrhage	3	(4.1)	20	(17.5)	5.04 (1.45-17.49)	.011
Other types	13	(6.2)	26	(15.2)	2.81 (1.39-5.67)	.004
Within 5 years						
Overall	60	(9.8)	127	(20.8)	2.93 (2.15-3.99)	<.001
Subtype stroke						
Ischemic stroke	38	(11.7)	73	(22.5)	2.83 (1.89-4.24)	<.001
Cerebral hemorrhage	5	(6.8)	23	(20.2)	3.73 (3.37-10.13)	.010
Other types	17	(8.1)	31	(18.1)	2.94 (1.58-5.48)	.001

N: total numbers; n: case number of aspiratory pneumonia. Adjusted age, gender, aspiration pneumonia history, diabetes, hypertension, hyperlipidemia, chronic kidney disease, cardiovascular disease, cancer, dementia, depression.

nondysphagia group (aHR 2.93, 95% CI 2.15-3.99, $P < .001$); in the subgroup analysis, there was a significantly higher risk in patients with dysphagia than that in patients with nondysphagia, followed by ischemic stroke (aHR 2.83, 95% CI 1.89-4.24, $P < .001$), cerebral hemorrhage population (aHR 3.73, 95% CI 3.37-10.13, $P = .010$), and other types (aHR 2.94, 95% CI 1.58-5.48, $P = .001$).

The Mortality Rates in the Stroke Patients between the Dysphagia and Nondysphagia Groups

Table 3 shows the mortality risks of the dysphagia and nondysphagia groups after 1, 3, and 5 years of stroke episodes. There were 383 (58.8%) patients with dysphagia who expired within 5 years, and 268 (43.9%) patients with nondysphagia who expired within 5 years. Cox

Table 3. *The mortality between the dysphagia and nondysphagia groups in the stroke patients*

	Nondysphagia group (N = 610)		Dysphagia group (N = 610)			
	n	(%)	n	(%)	Adjusted hazard ratio	*P* Value
1-year survival						
Overall	82	(13.4)	151	(24.8)	1.90 (1.45-2.49)	<.001
Subtype stroke						
Ischemic stroke	47	(14.1)	79	(23.8)	1.72 (1.20-2.48)	.004
Cerebral hemorrhage	9	(12.3)	25	(21.7)	2.10 (.92-2.80)	.077
Other types	26	(12.7)	47	(28.8)	2.17 (1.32-3.56)	.002
3-year survival						
Overall	182	(29.8)	296	(48.5)	1.93 (1.60-2.32)	<.001
Subtype stroke						
Ischemic stroke	98	(29.4)	150	(45.2)	1.80 (1.39-2.23)	<.001
Cerebral hemorrhage	18	(24.7)	47	(40.9)	2.16 (1.21-3.86)	.010
Other types	66	(32.4)	99	(60.7)	2.32 (1.68-3.21)	<.001
5-year survival						
Overall	268	(43.9)	383	(58.8)	1.84 (1.57-2.16)	<.001
Subtype stroke						
Ischemic stroke	150	(45.0)	203	(61.1)	1.68 (1.36-2.09)	<.001
Cerebral hemorrhage	27	(37.0)	60	(52.2)	1.77 (1.09-2.87)	.021
Other types	91	(44.6)	120	(73.6)	2.30 (1.73-3.06)	<.001

N: total numbers; n: case number of expired. Adjusted age, gender, aspiration pneumonia history, diabetes, hypertension, hyperlipidemia, chronic kidney disease, cardiovascular disease, cancer, dementia, depression.

proportional hazard regression analysis revealed that the mortality risk in the first year was significantly different between the dysphagia group and the nondysphagia group (aHR 1.90, 95% CI 1.45-2-49, $P < .001$). After adjusting for age, gender, comorbidities, and some subtype stroke populations with an increased risk of aspiration pneumonia, the mortality risk in the first year after the stroke episode was significantly different between the dysphagia group and the nondysphagia group (aHR 1.90, 95% CI 1.45-2.49, $P < .001$); in the subgroup analysis, there was a significantly higher mortality risk in patients with dysphagia than that in patients with nondysphagia, followed by ischemic stroke (aHR 1.72, 95% CI 1.20-2.48, $P < .004$), cerebral hemorrhage (aHR 2.10, 95% CI .92-2.80, $P = .077$), and other types (aHR 2.17, 95% CI 1.32-3.56, $P = .002$). The mortality risk within 3 years after the stroke episode was significantly different between the dysphagia group and the nondysphagia group (aHR 1.93, 95% CI 1.60-2.32, $P < .001$); in the subgroup analysis, there was a significantly higher mortality risk in patients with dysphagia than that in patients with nondysphagia, followed by ischemic stroke (aHR 1.80, 95% CI 1.39-2.23, $P < .001$), cerebral hemorrhage population (aHR 2.16, 95% CI 1.21-3.86, $P = .010$), and other types (aHR 2.32, 95% CI 1.68-3.21, $P < .001$). The mortality risk within 5 years after the stroke episode was significantly different between the dysphagia group and the nondysphagia group (aHR 1.84, 95% CI 1.57-2.16, $P < .001$); in the subgroup analysis, there was a significantly higher mortality risk in patients with dysphagia than that in patients with nondysphagia, followed by ischemic stroke (aHR 1.68, 95% CI 1.36-2.09, $P < .001$), cerebral hemorrhage (aHR 1.77, 95% CI 1.09-2.89, $P = .021$), and other types (aHR 2.30, 95% CI 1.73-3.06, $P < .001$). Moreover, the survival curves comparing the dysphagia and nondysphagia groups in all stroke episodes (log-rank test: $P < .001$), ischemic stroke (log-rank test: $P < .001$), cerebral hemorrhage (log-rank test: $P < .001$), and other stroke types (log-rank test: $P < .001$) are shown in Figure 1.

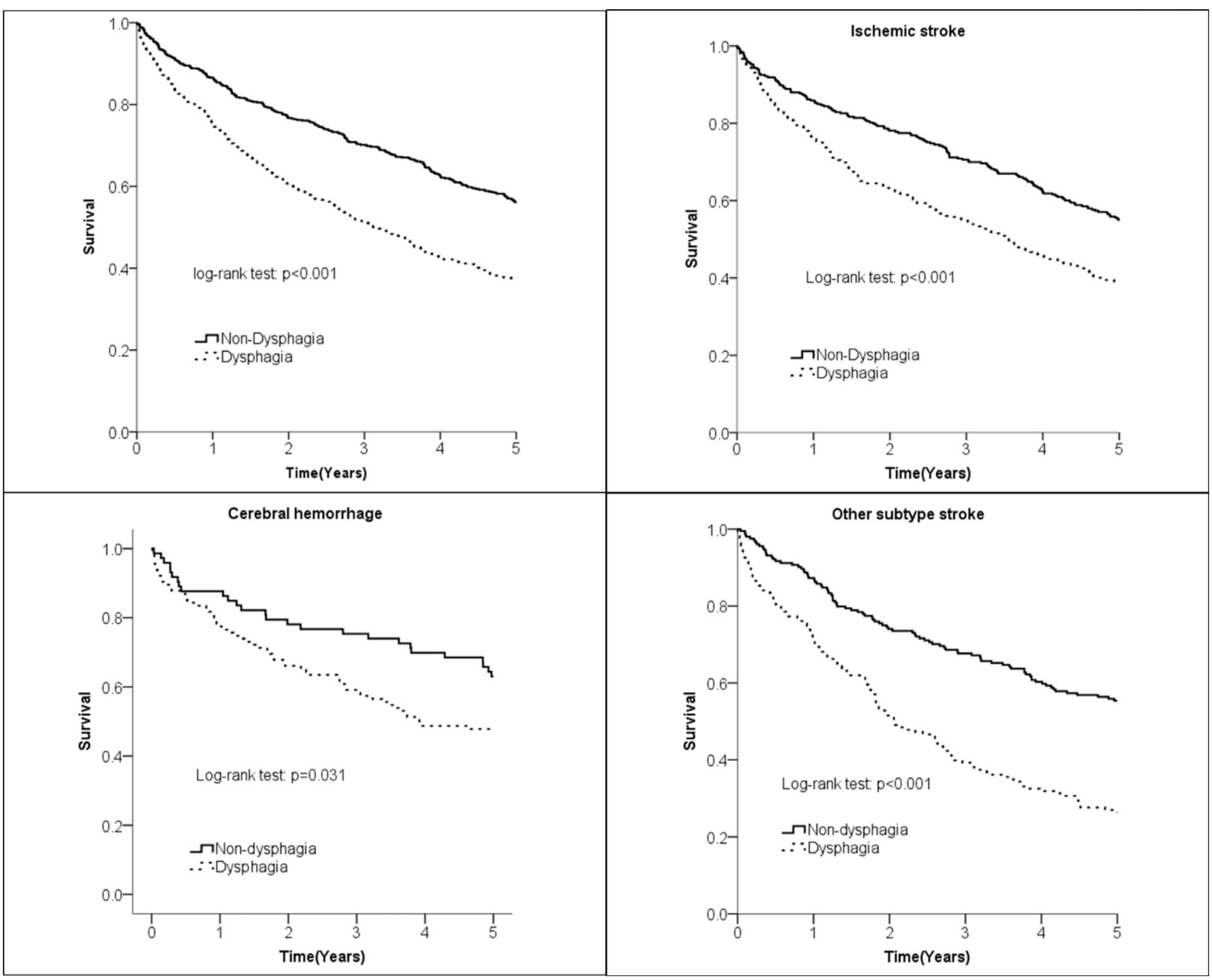

Figure 1. *Five-year survival curve between the dysphagia group and the nondysphagia group. There was statistical significance for the 5-year survival between the dysphagia group and the nondysphagia group in the overall stroke population (log-rank test: $P < .001$), in the ischemic stroke population (log-rank test: $P < .001$), in the cerebral hemorrhage population (log-rank test: $P = .031$), and in the subtype stroke population (log-rank test: $P < .001$).*

Discussion

Dysphagia has a higher prevalence following stroke, ranging from approximately 30%-65%.[4,8] Dysphagia exposes stroke patients to a higher risk of aspiration pneumonia, disability, malnutrition, and death. Poststroke pneumonia is a common adverse infection affecting up to one-third of acute stroke patients, especially when combined with dysphagia.[9,10] Patients with dysphagia had a higher rate of pneumonia than those without dysphagia, and stroke patients with dysphagia demonstrated a 3- to 11-fold increase in pneumonia risk.[11] However, there is still a lack of knowledge of the long-term relative risk for aspiration pneumonia. In our present study, we have demonstrated the longitudinally relative risk of aspiration pneumonia in stroke patients in relation to dysphagia to provide a more objective observation.

In the hemorrhage group, the difference of having aspiration pneumonia related to dysphagia was not significant in the first year because of the possibility of the high mortality of the hemorrhage group compared to the mortality of ischemic stroke patients in the general population, so there would be a small number of dysphagia with its secondary complication, aspiration pneumonia, in the hemorrhage group.[12] In following years, there would be a significant difference in the increased mortality and pneumonia rates in relation to having dysphagia. Other issues contributing to the increased risk of having aspiration pneumonia and mortality would be the white matter changes that are usually underestimated in patients after a stroke.[13,14] Importantly, these white matter changes could contribute to the subsequent cerebrovascular events[15] that would worsen clinical conditions to cause an increase in mortality or aspiration pneumonia.

The increasing differences in aspiration pneumonia and mortality in relation to dysphagia after a stroke could also result from the increased dementia after a stroke.[16] Dementia after a stroke could contribute to mortality and the occurrence of pneumonia due to the dementia itself making care difficult and increasing the care burden. Essentially, the economic burden of aspiration pneumonia in stroke patients is high. For example, the increased costs associated with longer hospitalization, greater disability, and poor nutritional status during hospitalization characterize aspiration pneumonia in stroke patients.[17,18] The increased care burden would not improve the quality of care for stroke patients, but vice versa.

In stroke patients with dysphagia, poor nutritional status and aspiration pneumonia appear to have strong interrelationships in the prognosis and mortality. Recent evidence suggests that successful swallowing rehabilitation and early preventions may reduce the frequency of both malnutrition and pneumonia in stroke patients with dysphagia. For example, acute stroke patients with dysphagia who receive an intensive exercise-based swallow rehabilitation program may have less malnutrition and aspiration pneumonia when compared to patients receiving diet modifications and compensations or those without intervention.[19]

The study has several strengths compared to other studies, including the use of a large data pool and a longer longitudinally follow-up to observe secondary dysphagia after stroke. Furthermore, there are still some limitations. Stroke is a critical and emergent disease. In Taiwan, the majority of patients with stroke episodes are sent to medical centers or large hospitals where neurologists there. Neurologists would perform neurological and physical examination including swallowing function to assess the patient's condition. The patients who have difficulty swallowing would be diagnosed as “dysphagia” through neurological and physical assessment. The definition of aspiration pneumonia is usually diagnosed by clinical symptoms and signs, laboratory tests, image findings, and the use of antibiotics. If a patient meets the above conditions, they will be diagnosed as aspiration pneumonia

(pneumonitis due to solids and liquids). However, the patient might not be examined thoroughly to ensure that he had dysphagia, and the physician might not report whether a stroke patient had dysphagia or aspiration pneumonia. These confounding factors would contribute to our study outcomes. A well-designed prospective study could be performed to minimize these confounding factors to provide more accurate and delicate information on these issues.

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