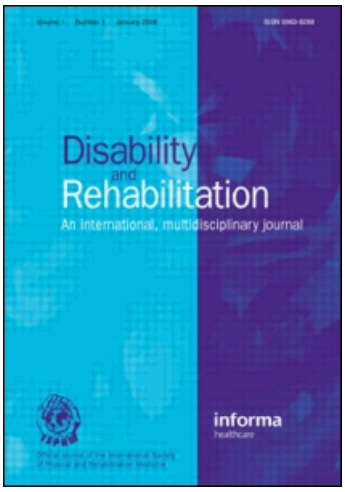

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Can the aspiration detected by videofluoroscopic swallowing studies predict long-term survival in stroke patients with dysphagia?

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Abstract

Purpose: This study aimed to evaluate whether the aspiration detected by videofluoroscopic swallowing study (VSS) could predict the long-term survival in stroke patients with dysphagia in the post-acute phase of stroke.
Methods: A cohort of 182 consecutive patients with stroke-related dysphagia referred for VSS from July 1994 to April 1999 was retrospectively constructed. VSS findings and clinical features in the post-acute phase of stroke were recorded. The records thus obtained were then linked to the National Death Register to track the occurrence of patient deaths until December 31, 2000.
Results: Of the 182 patients, 91 (50%) showed aspiration during VSS performed for a median duration of 8.4 weeks after stroke, and 76 (42%) had silent aspiration. In the post-acute phase of stroke (14.7 ± 8.7 weeks after stroke, mean ± standard deviation), 56 (31%) were tube-fed, and 88 (48%) were wheelchair-confined. A total of 65 patients died in a median follow-up duration of 30.8 months after VSS. Patients were classified into three groups based on the findings of VSS-detected aspiration or penetration, but no difference was noted in their survival curves. In the Cox stepwise regression analysis, only advanced age, recurrent stroke (hazard ratio 1.74, 95% CI 1.06–2.85), the need of tube-feeding (hazard ratio 2.07, 95% CI 1.19–3.59), and being wheelchair-confined (hazard ratio 2.83, 95% CI 1.54–5.19) during follow-up were independent predictors of long-term survival.
Conclusions: VSS-detected aspiration during the post-acute phase of stroke was not predictive for the long-term survival in stroke patients with dysphagia.

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Introduction

Dysphagia, a clinical diagnosis of impaired swallowing, is a common complication of acute stroke.[1–7] In stroke patients, dysphagia is associated with malnutrition, chest infections, long hospital stay, high mortality, and increased likelihood of discharge to institutional care.[6–11] Dysphagia can resolve quickly from an incidence of 30–50% at the onset of stroke, to around 11% at 6 months after stroke.[1, 2, 4–7, 9, 12] However, 31–66% of stroke patients residing in long-term care facilities have been reported to have dysphagia.[13–15] Many stroke patients with dysphagia face increased risk of aspiration pneumonia, high costs associated with tube-feeding, and disability owing to impaired swallowing. Consequently, early detection and appropriate management of aspiration in stroke patients is probably important to prevent pneumonia, malnutrition, and dehydration.[3, 6]

Videofluoroscopic swallowing study (VSS) is an established objective method for evaluating the swallowing process in a real-time mode.[16] The presence of stasis in the valleculae or pyriform sinus, and aspiration during the VSS can be clearly observed with acceptable inter-rater and intra-rater reliability.[17–19] During the acute phase of stroke, VSS-detected aspiration is associated with chest infections and malnutrition, but VSS

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added little to the value of bedside swallowing assessment to mortality prediction.[4, 10, 20] However, the clinical relevance of VSS is uncertain during the post-acute phase of stroke. The literature has rarely studied predictors of long-term survival in stroke patients with dysphagia.[21] This study aimed to evaluate whether the aspiration detected by VSS could predict the long-term survival in stroke patients with dysphagia in the post-acute phase of stroke.

Methods

STUDY POPULATION

A cohort of patients with stroke-related dysphagia was constructed by identifying 332 consecutive patients that were referred to the Department of Medical Imaging of a university hospital for VSS from July 1994 to April 1999. The cohort included patients suffering from stroke-related dysphagia that had received a complete VSS evaluation within 1 year of their stroke. Stroke patients were referred for VSS if they had one or more of the following conditions: (1) difficulties in swallowing or coughing associated with feeding, (2) persistent tube feeding, (3) requiring prolonged feeding time, and (4) suspicion of aspiration by the primary care physician, for example a history of pneumonia in the acute phase of stroke, severe dysphonia or dysarthria, abnormal gag reflex, or brainstem lesion. Fifty-two patients were excluded owing to death during their hospital stay ($n = 3$), lacking brain imaging studies (computed tomogram or magnetic resonance study, $n = 22$), incomplete VSS ($n = 17$), or incomplete feeding condition information upon discharge ($n = 10$). One foreign patient was excluded because his data could not be obtained from official mortality data. For patients who had received multiple VSS tests, only the last test during the hospital stay for index stroke was recorded and analysed. To relate the VSS findings in the post-acute phase of stroke and the participant's long-term survival, 97 patients whose VSS were performed within 4 weeks after stroke onset were excluded in the study. Finally, the study group enrolled 182 patients with stroke-related dysphagia in the post-acute phase of stroke. The medical charts of the entire study cohort were reviewed and abstracted by the authors who were blind to the patients' outcome. Furthermore, the clinical data and imaging study results of each patient were recorded on a specially designed form. No coexisting neurological diseases besides stroke or structural disorders that resulted in dysphagia were found in our study subjects. The study was approved by the Human Research and Ethics Committee of the hospital.

ASSESSMENT OF CLINICAL FEATURES AND RISK FACTORS

The diagnosis of stroke in each study subject conformed to the definition of World Health Organization.[22] Stroke type (cerebral infarct or cerebral haemorrhage) was classified based on brain imaging studies. According to the presenting clinical features and brain imaging studies, the brain lesions of each subject (including the index stroke and previous brain lesions if present) were classified into the following mutually exclusive categories: (1) supratentorium (unilateral), (2) infratentorium, and (3) multiple (combinations of two or three territories). Recurrent stroke was defined as that the index stroke that was not the first stroke experienced by the patient. A positive history of brain surgery was defined as the patient having received brain surgery for the index stroke. The following clinical variables were assessed upon discharge: (1) baseline characteristics: age, gender, history of smoking, hypertension, diabetes, heart disease, blood biochemistry, and socio-economic status; (2) severe motor impairment: Brunnstrom stage[23] of the worst involved limb of four or less; (3) aphasia: presence of difficulties in verbal expression, auditory comprehension, repetition, or naming; (4) the need of tube-feeding; and (5) confinement to a wheelchair, defined as the inability to walk even with moderate support from a helper.

ASSESSMENT OF DYSPHAGIA BY VSS

Standardized VSS was conducted using a remote controlled fluoroscope (KOX-850, Toshiba Corp., Tokyo, Japan; RSZ-2000, Shimadzu Corp., Kyoto, Japan) equipped with a high-resolution Super-VHS recorder (BR 1200, JVC, Japan). The videotape recorder had a frame rate of 33 frames per second and could display real-time dynamic images and frame-by-frame static images. Patients were instructed to sit on a specially designed chair (VESS chair, Vess Chairs Inc., Milwaukee, WI, USA) while both true lateral and frontal anterior-posterior views were recorded. Each patient swallowed three standardized formula (5 ml each of thin, thick and paste) of barium sulphate (E-Z-HD, E-Z-EM, Inc., Westbury, NY, USA) in sequence. The thin barium sulphate (suspension of 340 gram E-Z-HD and 65 ml of water) was used in routine gastrointestinal examinations, while the thick barium was prepared by adding extra 7.5 ml E-Z HD powder to 15 ml standard thin barium preparation, and the paste barium was

Table 1 Clinical features and VSS findings among 182 stroke patients with dysphagia

Variable	Findings of VSS in pharyngeal phase: *No penetration or aspiration* (n = 50) n (%)	*Penetration but no aspiration* (n = 41) n (%)	*Aspiration* (n = 91) n (%)	*p value*	*Total* (n = 182) n (%)
Age (yr)*	66.8 ± 13.0 (69.6)	68.0 ± 10.6 (67.2)	67.2 ± 9.9 (68.2)	0.869	67.2 ± 10.9 (68.2)
Duration from stroke onset to VSS (wk)*	9.8 ± 7.2 (7.6)	10.3 ± 8.0 (8.0)	11.4 ± 8.4 (9.6)	0.506	10.7 ± 8.0 (8.4)
Male in gender	28 (56.0)	29 (70.7)	54 (59.3)	0.321	111 (61.0)
Smoking ever	14 (28.0)	17 (41.5)	30 (33.0)	0.413	61 (33.5)
Hypertension	38 (76.0)	30 (73.2)	65 (71.4)	0.862	133 (73.1)
Diabetes mellitus	15 (30.0)	16 (39.0)	42 (46.2)	0.173	73 (40.1)
Heart diseases	18 (36.0)	15 (36.6)	32 (35.2)	1.000	65 (35.7)
Atrial fibrillation	12 (24.0)	9 (21.9)	18 (19.8)	0.840	39 (21.4)
Ischemic heart disease	3 (6.0)	5 (12.2)	11 (12.1)	0.508	19 (10.4)
Heart failure	6 (12.0)	1 (2.4)	4 (4.4)	0.146	11 (6.0)
Valvular heart disease	2 (4.0)	4 (9.8)	7 (7.7)	0.520	12 (7.1)
Hypercholesterolemia	17 (34.0)	8 (19.5)	31 (34.1)	0.202	56 (30.8)
Hypertriglyceridemia	9 (18.0)	5 (12.2)	18 (19.8)	0.584	32 (17.6)
Hyperuricemia	15 (30.0)	12 (29.3)	16 (17.6)	0.156	43 (23.6)
Low socioeconomic status	17 (34.0)	19 (46.3)	44 (48.4)	0.251	80 (43.9)
First-ever stroke	34 (68.0)	29 (70.7)	49 (53.8)	0.107	112 (61.5)
Type of stroke					
Infarct	37 (74.0)	28 (68.3)	69 (75.8)	0.650	134 (73.6)
Hemorrhage	13 (26.0)	13 (31.7)	22 (24.2)		48 (26.4)
Lesion of stroke					
Supratentorium (unilateral)	31 (62.0)	23 (56.1)	32 (35.2)	0.020†	86 (47.2)
Infratentorium	3 (6.0)	4 (9.8)	9 (9.9)		16 (8.8)
Multiple	16 (32.0)	14 (34.2)	50 (54.9)		80 (43.9)
Brain surgery due to stroke	12 (24.0)	3 (7.3)	12 (13.2)	0.074	27 (14.8)
Severe motor impairment	33 (66.0)	29 (70.7)	61 (67.0)	0.895	123 (67.6)
Wheelchair-confined during follow-up	23 (46.0)	23 (56.1)	42 (46.2)	0.543	88 (48.4)
Aphasia	19 (38.0)	12 (29.3)	25 (27.5)	0.437	56 (30.8)
VSS findings					
Abnormal oral phase	44 (88.0)	35 (85.4)	85 (93.4)	0.295	253 (90.1)
Stasis in valleculae or pyriform sinus	18 (36.0)	23 (56.1)	61 (67.0)	0.002†	157 (56.0)
Silent aspiration	0 (0)	0 (0)	76 (83.5)	< 0.001†	76 (41.8)
Need of tube-feeding during follow-up	8 (16.0)	16 (39.0)	32 (35.2)	0.022†	56 (30.8)
Follow-up duration after VSS (mo)*	36.0 ± 20.4 (34.0)	29.3 ± 17.4 (24.8)	37.2 ± 19.4 (34.6)	0.089	35.1 ± 19.4 (30.8)
Death during follow-up	19 (38.0)	13 (31.7)	33 (36.3)	0.825	65 (35.7)

VSS: videofluoroscopic swallowing studies.
*Data are presented as mean ± standard deviation (median).
†Significant in Fisher's exact test ($p < 0.05$).

prepared by adding an extra 12 ml E-Z-HD powder to 15 ml standard thin barium preparation. The three consistencies were physically distinguishable. All VSS results were reviewed by an experienced radiologist (Chang) based on the previously published criteria.[24] Briefly, stasis in valleculae or pyriform sinus was defined as a visible barium fluid level (more than trace coating) within the valleculae or pyriform sinus after swallowing, and aspiration was defined as misdirection of barium below the vocal cords[16, 25, 26] Based on the videotape review among 28 stroke patients with dysphagia, the intra-rater reliability for VSS measures of penetration and aspiration in the current work was determined by comparing the ratings from two different viewing with 2 weeks apart at least. The judge was unaware of ratings from the previous viewing.

ASSESSMENT OF END POINT

The primary endpoint of this study was the death from any cause, which occurred by Dec 31, 2000. The death of each patient was traced using citizen's ID

number, and confirmed using gender and birth date. This information was obtained from official mortality data provided by the National Death Register, and by the death records in medical charts at the hospital. The underlying cause of death was determined according to the National Death Register.

STATISTICAL ANALYSES

Group comparisons were conducted using Fisher's exact tests for proportions and general linear models for continuous variables. The intra-rater reliability for VSS measures was determined by calculation of kappa values.[27] Survival curves for all patients and for the various groups of interest were estimated using the Kaplan–Meier method. Moreover, the log-rank test was used to compare rate estimates among survival curves. The association between outcome predictors and time from VSS date to death was analysed with the Cox proportional hazards model. First, a univariate analysis of possible predictors of survival was performed. Then Cox proportional hazards multivariate regression analysis was used to assess the effects of age, gender, clinical features, risk factors, impairment and functional status, VSS findings, and tube-feeding status with a stepwise procedure. Entry into the model was determined based on the change in magnitude of the log likelihood. Possible effect modifiers were also evaluated for all regression models. Ties were handled according to Efron's method.[28, 29] Hazard ratios were calculated based on 95% confidence intervals. All analyses were performed by using the SAS System for Microsoft Windows (version 8.2, SAS Institute Inc., Cary, NC, USA) statistical software. A p value of less than 0.05 was considered statistically significant.

Results

The median age of the 182 study subjects was 68.2 years (range, 27–87) and the median duration from stroke onset to VSS was 8.4 weeks (range, 4–48). The clinical variables of study subjects were assessed 14.7 ± 8.7 weeks (mean $\pm$ standard deviation) after stroke. All subjects were separated into three groups (no penetration or aspiration, penetration but no aspiration, and aspiration) based on the VSS findings in the pharyngeal phase. The intra-rater kappa values for the VSS measures of penetration and aspiration were 0.826 and 1.000 among 28 stroke patients with dysphagia. The clinical features of the three groups are listed in table 1. Notably, a significantly higher proportion of patients with aspiration had multiple brain lesions compared with those without aspiration. The other demographic characteristics, clinical features, functional status at discharge, and results of brain imaging studies were similar among the three groups.

Most patients exhibited abnormal VSS findings during the oral phase of swallowing. Moreover, a significantly higher proportion of patients with penetration or aspiration displayed stasis in valleculae or pyriform sinus. Half of the patients had aspiration in VSS, and 41.8% had silent aspiration. Nearly 30% of the patients required tube-feeding during the follow-up period. Most of them were fed using nasogastric tube, and only 3 of the 56 were fed by percutaneous endoscopic gastrostomy. Patients without penetration or aspiration displayed a significantly lower proportion of tube-feeding during follow-up.

A total of 65 (35.7%) patients died by the end of this study. The median follow-up duration following VSS was 30.8 months (range, 2–78). No significant difference was observed among the three groups in the follow-up duration and proportion of deaths during follow-up. Of the 65 deceased subjects, the leading underlying cause of death was stroke (24 patients), followed by diabetes (14), non-stroke cardiovascular diseases (7), cancer (4), and miscellaneous (16). The distribution of underlying causes of death was similar among the three groups. The Kaplan–Meier estimates of the probabilities of survival at 1, 2, and 3 years after VSS were 87, 78, and 67%, respectively. As seen in figure 1, there was no difference in survival curves among the three groups.

Univariate analysis revealed that age, recurrent stroke, brain surgery due to stroke, hyperuricaemia, socioeconomic status, the need of tube-feeding, and being wheelchair-confined during follow-up were significantly associated with survival. As seen in table 2, only advanced age, recurrent stroke, the need of tube-feeding,

Table 2 Final multivariate model of survival in 182 stroke patients with dysphagia by Cox proportional hazards regression analysis

	Survival		
	HR	*95% CI*	*p value*
Age (every 10 years of increase)	1.46	1.13–1.89	0.0043*
Recurrent stroke vs. first-ever stroke	1.74	1.06–2.85	0.0284*
Need of tube-feeding during follow-up (Yes versus No)	2.07	1.19–3.59	0.0100*
Wheelchair-confined during follow-up	2.83	1.54–5.19	0.0008*

HR: hazard ratio; CI: confidence intervals; *$p < 0.05$.

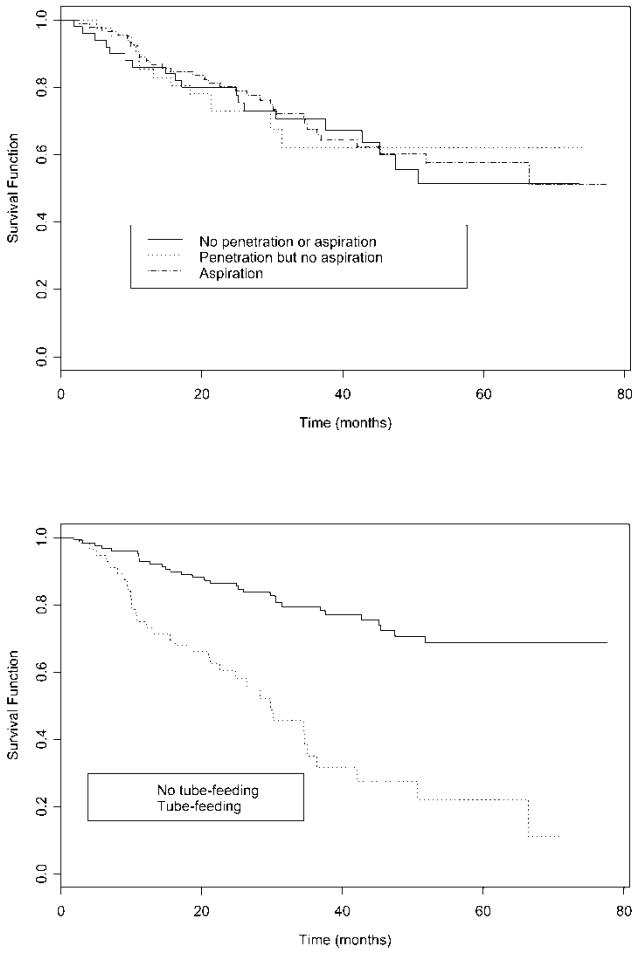

Figure 1 Kaplan–Meier survival curves of 182 stroke patients with dysphagia. Upper panel: grouped by VSS findings in pharyngeal phase ($p = 0.939$); Lower panel: grouped by the need of tube-feeding during follow-up ($p < 0.001$).

and being wheelchair-confined during follow-up were negatively associated with long-term survival in the stepwise regression analysis. VSS findings, including VSS-detected aspiration, were not predictive for the long-term survival in the study subjects.

Discussion

VSS is an established objective method for dysphagia evaluation and detection of aspiration, but our data show VSS-detected aspiration during the post-acute phase of stroke was not predictive for the long-term survival in stroke patients with dysphagia. However, advanced age, recurrent stroke, the need of tube-feeding, and being wheelchair-confined during follow-up predicted poor long-term survival. Stroke patients who required the long-term use of tube-feeding not only suffered from disability of dysphagia but also had higher mortality than those who resumed oral feeding.

Most previous studies have focused on the association between dysphagia in the acute phase of stroke and poor functional outcome or high mortality.[1, 7, 10, 30, 31] Since patients with stroke-related dysphagia may recover spontaneously to some extent, the association between acute-phase dysphagia and long-term survival is difficult to explain. The outcome may be influenced by large lesion size or overall stroke severity rather than the detrimental effects of dysphagia *per se*. On the contrary, this study only enrolled patients who had persistent dysphagia for at least 4 weeks after their stroke, and therefore may have been able to assess the effects of dysphagia on long-term survival.

Swallowing training in stroke patients aims to allow the safe resumption or maintenance of oral feeding through proper positioning, a modified-consistency diet, and appropriate feeding techniques.[32, 33] The question of how 'safe' it is for stroke patients with VSS-detected aspiration to resume or maintain oral feeding is very important. Previous studies showed that VSS-detected aspiration during the acute phase of stroke was associated with pneumonia and malnutrition but did not affect mortality.[4, 10, 20] This study also found no association between long-term survival and VSS-detected aspiration during the post-acute phase of stroke. In fact, aspiration pneumonia is not only caused by aspiration but also is influenced by the pH of the aspirate, the amount aspirated, and the immune defenses of the host.[34] VSS-detected aspiration might not lead to pneumonia since under certain circumstances it is also seen in 'normal' people.[35] To our knowledge, only one comparable study, with VSS performed an average of 2 months after stroke, revealed an association between aspiration and risk of pneumonia and death.[21] However, that study might be inconclusive because it involved a small sample size ($n = 59$) and univariate analysis.

The mechanism of how dysphagia resolves in stroke patients is unclear.[36] Clinically, treatment for dysphagia includes dietary manipulation (e.g. pureed or dental soft diets), and specific exercises and facilitation techniques (e.g. lip, tongue and jaw exercises and the use of chin tuck or head turning to facilitate swallowing).[32, 33, 36] Most our study subjects had been evaluated and trained by physiatrists or speech therapists. Therefore, our findings might imply that resume oral feeding through swallowing training can reduce disability of dysphagia and prolong lives for stroke patients with dysphagia. The question remains why tube-fed stroke patients had poor long-term survival. One possible mechanism is that

stroke patients with the need of tube-feeding during follow-up had more severe dysphagia and stroke severity. Another one possible mechanism is increased risk of infection and malnutrition associated with nasogastric feeding. Recurrent removal and resting of the nasogastric tube may have a risk of pulmonary aspiration, and frequent accidental removal of the nasogastric tube can disrupt nutritional intake.[37, 38] However, these possibilities were not confirmed in the present study because the role of chest infection or malnutrition played in each subject's death was unknown owing to limited information in death certificates. The official mortality data in our country provide the coding of underlying cause-of-death for each death certificate and the accuracy of underlying cause-of-death statistics is not ideal.[39]

The major limitation of this study is the referral bias, and therefore our findings cannot be generalized to all stroke patients with dysphagia. This referral bias led to the exclusion of certain patients, either because their dysphagia was too mild or because their general condition was too weak to receive standard VSS. The study subjects thus are likely to be a representative of stroke patients with moderate to severe dysphagia. The second limitation is the retrospective design of this study. Data were collected from medical records rather than being gathered prospectively and selectively. Moreover, factors such as urinary continent status and cognitive function, demonstrated to influence long-term survival in stroke patients,[1, 30, 31, 40, 41] were not considered owing to a lack of reliable data. Furthermore, since the medical records examined were limited to our hospital, it was impossible to obtain all information on the secondary prevention of recurrence stroke and the changes in feeding and swallowing status during follow-up if patients visited other hospitals. Dysphagia might resolve in some patients, in others it might worsen and tube-feeding is sometimes required again.[36] The potential non-differential misclassification will tend to underestimate the effect of need of tube-feeding during follow-up in our study.

Conclusion

VSS-detected aspiration during the post-acute phase of stroke was not predictive for the long-term survival in stroke patients with dysphagia in this study. The role of VSS in predicting long-term outcome in stroke patients needs further investigation. Age, recurrent stroke, the need of tube-feeding, and being wheelchair-confined during follow-up were independent predictors of long-term survival in post-acute phase of stroke patients with dysphagia. Stroke patients with dysphagia might benefit by swallowing training to reduce disability of dysphagia and resume oral feeding. Further randomized controlled trials are required to evaluate the effect of swallowing rehabilitation on long-term survival of stroke patients with dysphagia.

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