Observational Study

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Clinical characteristics of dysphagic stroke patients with salivary aspiration

A STROBE-compliant retrospective study

Kwang Jae Yu, MD, Donghwi Park, MD*

Abstract

The aim of this study was to evaluate the correlation between radionuclide salivagram findings and clinical characteristics in stroke patient with swallowing difficulty.

In this study, dysphagic stroke patients who had undergone both a radionuclide salivagram and videofluoroscopic swallowing study (VFSS) were included retrospectively. To evaluate the correlations between clinical parameters and salivary aspiration, clinical parameters, such as stroke lesion, the degree of paralysis, sex, age, onset duration of stroke, the score of the Mini-Mental State Examination (MMSE), the score of the Global Deterioration Scale (GDS), the total score of the Modified Barthel Index (MBI), and each sub-score of the MBI were collected and analyzed.

In the results of this study, the MMSE score was the only significant parameter for predicting positive findings in a salivagram in a multivariate logistic regression analysis in patients with supratentorial stroke. In patients with infratentorial stroke, however, the transfer sub-score of MBI was the only significant parameter for predicting positive findings in a salivagram in a multivariate logistic regression analysis.

In conclusion, care should be taken to prevent salivary aspiration when the MMSE score is less than eight in patients with supratentorial stroke, and the transfer sub-score of MBI score is less than three in patients with infratentorial stroke.

Abbreviations: AUC = area under the curve, GDS = Global Deterioration Scale, MBI = Modified Barthel Index, MMSE = Mini-Mental State Examination, PAS = penetration-aspiration scale, ROC = receiver operating characteristic, VFSS = videofluoroscopic swallowing study.

Keywords: deglutition, dysphagia, MMSE, radionuclide, salivagram, salivary aspiration, stroke

1. Introduction

Stroke is known to be the leading cause of death and disability worldwide and is associated with multiple medical complications that are potential barriers to proper recovery.[1–4] Among the complications, pneumonia is the most common respiratory complication, accounting for approximately one-third of all deaths after stroke, so early diagnosis and prevention of pneumonia is very important.[1,5] Post-stroke dysphagia, defined here as difficulty in swallowing after a stroke, is a common complication affecting many patients in the first few hours and days after ictus, and is associated with increased mortality and morbidity of aspiration, pneumonia, and malnutrition.

There are several methods to evaluate aspiration, such as fiber-optic endoscopic evaluation of swallowing, the videofluoroscopic swallowing study (VFSS), and the radionuclide salivagram. Among them, VFSS has become the most common method of assessing swallowing ability and aspiration due to the ability to evaluate the stages of swallowing of the oral pharyngeal and esophagus.[6] Previous studies using VFSS, however, have reported significant false-negative results when predicting aspiration pneumonia.[7,8] In previous studies, salivary aspiration has been suggested as one of the causes of significant false-negative results when predicting aspiration pneumonia because it cannot be detected with VFSS despite its contribution to aspiration pneumonia.[9]

In the diagnosis of salivary aspiration, the radionuclide salivagram may be useful for early detection of salivary aspiration that may induce aspiration pneumonia.[9–12] Despite the usefulness of the radionuclide salivagram in detecting salivary aspiration, its use as a routine diagnostic test for stroke patients with dysphagia has not gained wide acceptance because there is no accurate indication of when the radionuclide salivagram has to be performed.

In this study, therefore, use of a radionuclide salivagram with stroke patients with dysphagia was investigated by evaluating the correlation between the findings of the radionuclide salivagram and patients' clinical characteristics.

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2. Methods

2.1. Subjects

This study received Institutional Review Board approval. From January 2013 to May 2018, a retrospective analysis was performed with the medical records of 613 stroke patients in our hospital. The inclusion criteria for the study were adult stroke patients (≥18 years old) who had a swallowing difficulty and who had undergone both VFSS and a radionuclide salivagram. We excluded patients who had more than a one-week interval between the radionuclide salivagram and VFSS, and those who had not suffered a stroke but a brain lesion such as idiopathic Parkinson's disease, a traumatic brain injury, or hypoxic ischemic encephalopathy. Patients who did not have complete medical records were also not included.

2.2. Clinical parameters

To evaluate the correlations between clinical parameters and salivary aspiration, clinical parameters, such as stroke lesion (supratentorial or infratentorial stroke), the degree of paralysis (hemi or quadriplegia), sex, age, onset duration of stroke, the Mini Mental State Examination (MMSE), the Global Deterioration Scale (GDS), the total score of the Modified Barthel Index (MBI), and each sub-score of the MBI (hygiene, bathing, feeding, toilet, dressing, defecation, ambulation and chair/bed transfer) were collected and analyzed. Supratentorial stroke patients were defined as those who had stroke in the area located above the tentorium cerebelli; infratentorial stroke patients were defined as those who had stroke in the area located below the tentorium cerebelli.

2.3. Videofluoroscopic swallowing study (VFSS)

This study was performed with a fluoroscopic device and recorded as a video file. All studies were reviewed by two medical physicians at department of rehabilitation medicine. In VFSS, patients sequentially swallowed the following materials that had a phased consistency. The materials were mixed with liquid barium and were swallowed while sitting: water, nectar (51–350 cP), rice porridge (351–1750 cP), and boiled rice (greater than 1750 cP).[13,14] Dynamic fluoroscopic images were acquired as anterior-posterior and lateral images and were recorded at thirty frames per second.[15] The VFSS results were analyzed according to the penetration-aspiration scale (PAS) and considered positive for aspiration if the PAS score was higher than 5.

2.4. Radionuclide salivagram

Radionuclide salivagrams were conducted within one week of VFSS. All the salivagrams were performed in the Nuclear Medicine Department of our hospital. Patients were evaluated using a gamma camera while in a supine position. A Tc-99m sulfur colloid solution (0.5 mL of 0.3 mCi) was provided via a syringe into the patient's mouth. Sequential supine posterior images were acquired for 1 h at 1, 5, 10, 20, 30, and 60 min after the solution was administered, and images were taken with a gamma camera (102 Discovery NM630; GE Healthcare, Buckinghamshire, England).[12,16] Visual interpretation of the images was performed by a skilled physician of nuclear medicine. When radioactive drug activity was identified in the tracheobronchial fields, salivary aspiration was reported to be present.

2.5. Statistical analysis

Group comparisons of the results of the radionuclide salivagram were conducted using the Mann–Whitney *U* test, the Pearson chi-square test, and the Wilcoxon rank sum test. We also divided the patients into two groups according to stroke lesions: the supratentorial stroke group versus the infratentorial stroke group. For both groups, the Mann–Whitney *U* test and the Pearson chi-square test or the Wilcoxon rank sum test were also performed to compare clinical parameters according to the results of the radionuclide salivagram. To analyze the correlation between the clinical parameters and the results of the radionuclide salivagram according to stroke lesions, a multivariate logistic regression analysis was performed through forward stepwise selection to compare the positive findings for the salivagram and the variables with statistically significant differences between the two groups. We also performed a multivariate logistic regression analysis with forward stepwise selection for both the supratentorial and infratentorial stroke group. To evaluate the accuracy of predictive factors for positive findings on the salivagram, we performed a receiver operating characteristic (ROC) analysis in each group. Statistical analysis was conducted with the MedCalc program and the SPSS software version 22.0 (IBM, Armonk, NY).

3. Results

3.1. Patient characteristics

There are a total of 613 stroke patients with swallowing difficulties in our hospital. Among them, 252 patients who satisfied our criteria were included in this study. The mean time of the intervals between the radionuclide salivagram and VFSS was 3.95 ± 1.42 days. The mean time of the intervals between the measurement of clinical parameters and VFSS was 4.12 ± 1.63 days (Fig. 1).

The demographic data of the patients are presented in Table 1. We divided the subjects into two groups according to the presence or absence of salivary aspiration in the radionuclide salivagram. For 46 out of 252 patients there were positive findings of salivary aspiration in the radionuclide salivagram. To find out the correlations between salivary aspiration and the radionuclide salivagram and clinical parameters, the patients were also divided into two groups according to stroke lesions (supratentorial stroke group vs. infratentorial stroke group) and analyzed separately. The demographic data of the patients in these two groups are presented in Tables 2 and 3.

3.2. Comparison between whole stroke (both supratentorial and infratentorial stroke) patients with and without indications of aspiration on a radionuclide salivagram

Age, PAS, MMSE, GDS, total MBI, each sub-score of the MBI (hygiene, bathing, feeding, toilet, stair climbing, dressing, defecation, voiding, ambulation and chair/bed transfer), and duration of disease (months) were compared between the two groups by means of the Mann–Whitney test or the Wilcoxon rank sum test. Statistically significant differences were detected in PAS, total MBI score, and each sub-score of the MBI (Table 1, P-value $< .05$). The differences in feeding method and incidence of aspiration pneumonia between the two groups were analyzed by using Pearson's chi-squared test. There were statistically significant differences in the feeding method (P-value $= .033$) and

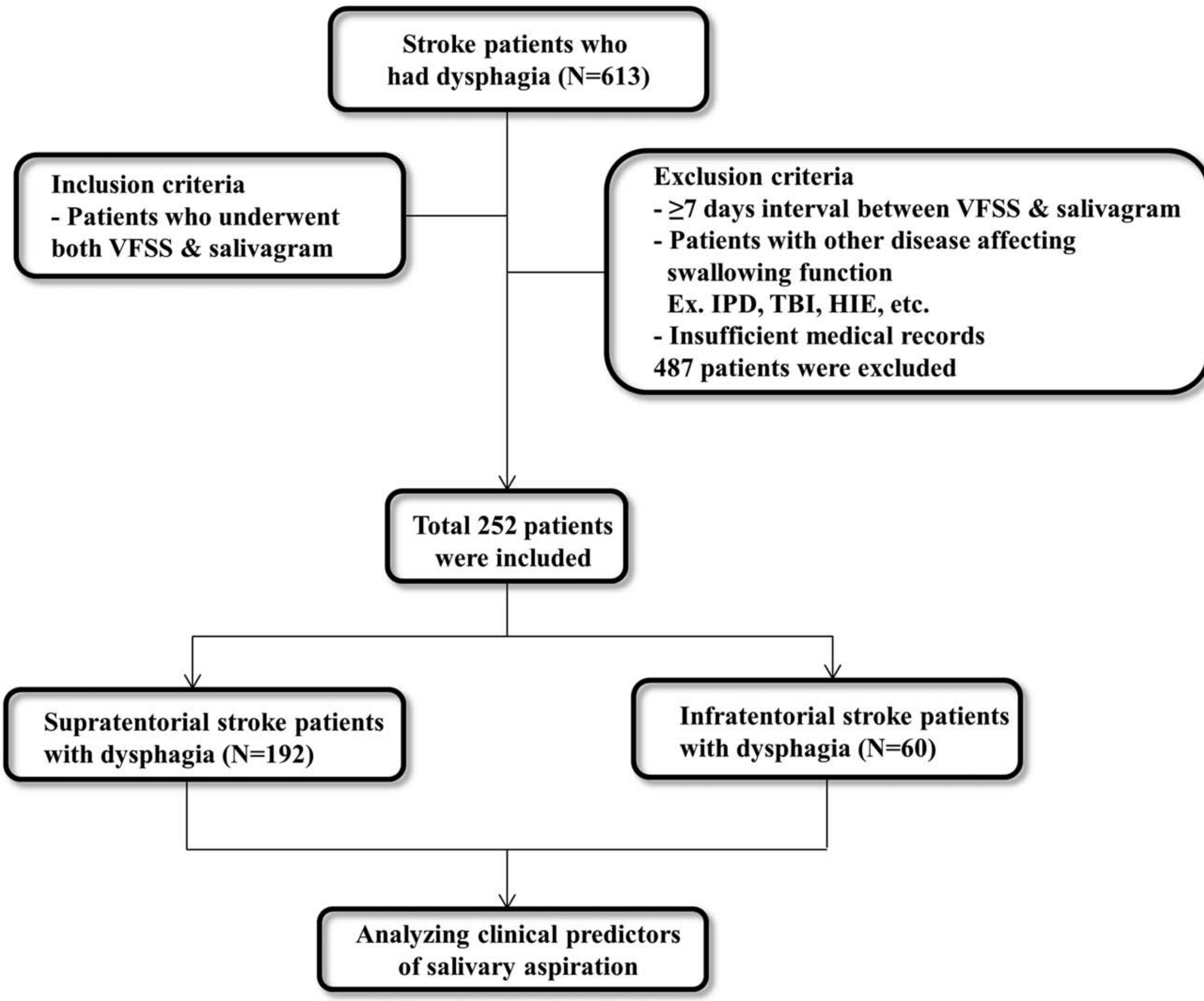

Figure 1. Flow chart of inclusion and exclusion criteria of the study sample. HIE=hypoxic ischemic encephalopathy, IPD=idiopathic Parkinson's disease, MBI=Modified Barthel Index, MMSE=Mini-Mental State Examination, TBI=traumatic brain injury, VFSS=videofluoroscopic swallowing study.

the incidence of aspiration pneumonia (P-value < .001) between the two groups. In addition, there was also a statistically significant difference in the distribution of hemiplegia and quadriplegia between the two groups (P-value < .001). There were more patients with quadriplegia in the group with salivary aspiration in the radionuclide salivagram.

3.3. Comparison between supratentorial stroke patients with and without indications of aspiration on a radionuclide salivagram (hygiene, bathing, feeding, toilet, dressing, and defecation)

Age, duration of disease, PAS, MMSE, GDS, total MBI, and sub-scores of MBI (hygiene, bathing, feeding, toilet, stair climbing, dressing, defecation, voiding, ambulation, and chair/bed transfer) were compared between the two groups, by means of the Mann–Whitney test or Wilcoxon rank sum test. Statistically significant differences were detected in PAS, MMSE, GDS, total MBI score, and sub-scores of MBI (hygiene, bathing, feeding, toilet, dressing, defecation, and chair/bed transfer) (Table 2, P-value < .05). Differences of incidence of aspiration pneumonia, degree of paralysis, and feeding method between the two groups were analyzed by Pearson's chi-squared test. There were no significant differences between the incidence of aspiration pneumonia (P-value = .259) and feeing method (P-value = .195) in the two groups. However, the distribution of patients with quadriplegia was significantly high among supratentorial stroke patients with salivary aspiration in the radionuclide salivagram ($P < .001$).

3.4. MMSE score for indications of aspiration on a radionuclide salivagram in patients with supratentorial stroke

In a multivariate logistic regression analysis using the forward stepwise method, the MMSE score was the only significant parameter for predicting positive findings in the salivagram in patients with supratentorial stroke. The area under the receiver operating characteristic (ROC) curve of the MMSE score was 0.784 in patients with supratentorial stroke for positive detection in salivagram (95% CI, 0.664–0.925; $P < .05$) (Table 4). The optimal cut-off value obtained from the maximum Youden index was 8 (sensitivity: 90.91%, specificity: 79.52%) when the radionuclide salivary gland was used (Fig. 2A).

Table 1

Patient characteristics and comparison of the patients with and without aspiration on radionuclide salivagram (whole stroke).

Characteristics	Aspiration (−)	Aspiration (+)	*P*-value
Age (years)	66.60±12.106	68.17±9.764	.569
Duration of disease (day)	86.77±375.970	91.04±165.365	.329
Duration of disease (month)	2.877±12.534	2.859±5.377	.300
Sex (M:F)	128:78	30:16	.490
PAS	5.07±2.170	6.61±1.877	**.001**
MMSE	16.73±8.488	13.61±11.823	.323
GDS	4.09±1.625	4.26±2.094	.607
MBI score			
Total	35.10±25.615	17.24±19.310	**.003**
Personal hygiene	2.10±1.481	0.80±1.322	<**.001**
Bathing	1.81±1.442	0.90±1.294	**.005**
Feeding	3.75±3.267	1.95±2.911	**.022**
Toilet	3.36±2.990	1.70±2.155	**.009**
Stair climbing	1.14±2.396	0.20±0.616	.190
Dressing	3.41±2.768	1.80±2.462	**.006**
Defecation	5.31±4.350	2.60±3.393	**.010**
Voiding	3.36±2.990	1.70±2.155	.201
Ambulation	3.83±4.739	0.30±0.923	<**.001**
Wheelchair	0.86±0.979	0.56±0.984	.109
Chair/bed transfer	6.10±4.304	1.85±2.540	<**.001**

Values are presented as mean±standard deviation or number (%).
GDS=Global Deterioration Scale, MBI=Modified Barthel Index, MMSE=Mini-Mental State Examination, PAS=penetration-aspiration scale.
Bold means $P<.05$ compared between two groups.

3.5. Comparison between infratentorial stroke patients with and without indications of aspiration on a radionuclide salivagram (hygiene, bathing, feeding, dressing, defecation, ambulation, and chair/bed transfer)

Age, duration of disease, PAS, MMSE, GDS, total MBI, and subscores of MBI (hygiene, bathing, feeding, toilet, stair climbing, dressing, defecation, voiding, ambulation, and chair/bed transfer) were compared between the two groups by means of the Mann–Whitney test or Wilcoxon rank sum test. A statistically significant difference was only observed in the total MBI score and subscores of MBI (hygiene, bathing, food, voiding, dressing, bowel, gait, and transfer MBI score) (Table 3, *P*-value<.05). Differences in the incidence of aspiration pneumonia, degree of paralysis, and feeding method between the two groups were analyzed by Pearson's chi-squared test. There were no significant differences in the feeding method (*P*-value=.232) and degree of paralysis (*P*-value=.154) between the two groups. However, there was a statistically significant difference in the incidence of aspiration pneumonia (*P*-value=.007) between the two groups.

Table 2

Patient characteristics and comparison of the patients with and without aspiration on radionuclide salivagram (supratentorial stroke).

Characteristics	Aspiration (−)	Aspiration (+)	*P*-value
Age (years)	66.86±11.739	72.36±5.372	.139
Duration of disease (day)	99.93±412.948	47.55±42.547	.319
Duration of disease (month)	3.31±13.767	1.58±1.418	.272
Sex (M:F)	104:66	10:12	.248
PAS	4.85±2.130	7.00±1.549	**.001**
MMSE	15.51±8.236	3.55±4.634	<**.001**
GDS	4.35±1.526	5.91±0.831	**.001**
MBI score			
Total	31.15±24.091	10.00±13.105	**.010**
Personal hygiene	1.84±1.451	0.33±1.000	**.001**
Bathing	1.60±1.396	0.56±1.014	**.017**
Feeding	3.16±3.058	1.00±1.732	**.038**
Toilet	3.00±2.834	0.67±1.000	**.004**
Stair climbing	0.97±2.203	0.00±0.000	.153
Dressing	2.97±2.618	1.33±2.179	**.034**
Defecation	4.85±4.371	1.33±2.179	**.023**
Voiding	4.13±4.452	1.33±2.179	
Ambulation	2.74±4.438	0.33±1.000	.103
Wheelchair	0.88±1.005	1.00±1.309	.953
Chair/bed transfer	5.03±3.938	2.22±2.635	**.047**

Values are presented as mean±standard deviation or number (%).
GDS=Global Deterioration Scale, MBI=Modified Barthel Index, MMSE=Mini-Mental State Examination, PAS=penetration-aspiration scale.
Bold means $P<.05$ compared between two groups.

Table 3

Patient characteristics and comparison of the patients with and without aspiration on radionuclide salivagram (infratentorial stroke).

Characteristics	Aspiration (−)	Aspiration (+)	*P*-value
Age (years)	65.39±14.017	64.33±11.436	.718
Duration of disease (day)	24.61±23.722	130.92±222.304	.539
Duration of disease (month)	0.81±0.791	4.02±7.27	.553
Sex (M:F)	24:12	20:4	.282
PAS	6.11±2.111	6.25±2.137	.645
MMSE	22.39±7.437	22.83±8.122	.899
GDS	2.89±1.568	2.75±1.712	.745
MBI score			
Total	51.33±25.943	22.67±21.865	**.007**
Personal hygiene	3.00±1.237	12.18±1.471	**.003**
Bathing	2.56±1.381	1.18±1.471	**.018**
Feeding	5.78±3.228	2.73±3.495	**.029**
Toilet	4.61±3.256	2.73±3.495	.075
Stair climbing	1.72±2.967	0.36±0.809	.385
Dressing	4.94±2.796	2.18±2.714	**.010**
Defecation	6.89±3.998	3.64±3.931	**.038**
Voiding	5.83±4.528	4.00±3.633	.317
Ambulation	7.06±4.179	0.27±0.905	<**.001**
Wheelchair	0.67±0.577	0.20±0.422	.140
Chair/bed transfer	9.78±3.457	1.55±2.544	<**.001**

Values are presented as mean±standard deviation or number (%).
GDS=Global Deterioration Scale, MBI=Modified Barthel Index, MMSE=Mini-Mental State Examination, PAS=penetration-aspiration scale.
Bold means $P<.05$ compared between two groups.

3.6. Transfer sub-score of MBI for indications of aspiration on a radionuclide salivagram in patients with infratentorial stroke

In a multivariate logistic regression analysis using the forward stepwise method, the transfer sub-score of MBI was the only significant parameter for predicting positive findings in a salivagram in patients with infratentorial stroke. In patients with infratentorial stroke, the area under the ROC curve of the transfer MBI score for positive detection in salivagram was 0.517 (95% CI, 0.332–0.804; $P<.05$) (Table 4). The optimal cut-off value obtained from the maximum Youden index was 3 (sensitivity: 90.91%, specificity: 88.89%) when the radionuclide salivary gland was used (Fig. 2B).

4. Discussion

Pulmonary aspiration can occur as a result of swallowing dysfunction, gastro-esophageal reflux, or an inability to adequately protect the airway from oral secretions.[6,17] Among these forms of

Table 4

Multivariate logistic regression analysis with forward stepwise method of clinical characteristics associated with salivary aspiration.

	Parameter	Beta coefficient	Standard error	OR (95% CI)	*P*-value
Supratentorial stroke patients	MMSE	−0.244	0.084	0.784 (0.664–0.925)	**.004**
Infratentorial stroke patients	Transfer sub-score of MBI	−0.660	0.226	0.517 (0.332–0.804)	**.003**

CI = confidence interval, MBI = Modified Barthel Index, MMSE = Mini-Mental State Examination, OR = odds ratio.
Bold means $P < .05$ compared between two groups.

aspiration, chronic salivary aspiration is the least-commonly recognized and there is currently no standard indication for performing a radionuclide salivagram for the detection and evaluation of salivary aspiration.

In salivary aspiration, the swallowing reflex is known to be an important defense against airway infection resulting from the aspiration of misdirected oropharyngeal or gastric contents into the larynx and lower airway.[18] The impairment of this reflex has been shown to be directly associated with an increased risk of silent aspiration and pneumonia in previous studies.[19,20] Moreover, it has been demonstrated that aspiration of pharyngeal secretions easily occurs in normal adults during deep sleep, presumably due to depression of pharyngeal reflexes, including the swallowing reflex.

The swallowing reflex consists of afferent pathways, central integration, and efferent pathways. The primary afferents pathway originates from the oropharyngeal mucosa, and it travels in the trigeminal (V), glossopharyngeal (IX), and vagus nerves (X). Then, the primary afferents pathway converges in the solitary tract destined for synaptic contact with second-order neurons in the nucleus tractus solitarius (NTS) of the brainstem.[21] In the NTS of the brainstem, which is known to control swallowing, interneurons perform a more complex level of swallowing control.[22] The control of the swallowing reflex in the brainstem is via the efferent pathways as follows: the trigeminal (V), facial (VII), ambiguous, and hypoglossal motor nuclei. In addition, it is well established that the swallowing center receives descending influences from the cerebral cortex and subcortical areas.[22,23] Therefore, there is no doubt that the cerebral cortex area and the subcortex areas, and their interaction with the brain stem can play an important role in the neural regulation of the swallowing reflex. Considering the importance of this swallowing reflex in salivary aspiration, any defect or disorder along the swallowing reflex arc can cause aspiration of saliva.

In this study, the clinical factors predicting salivary aspiration were totally different according to the lesion of the stroke. In infratentorial stroke, transfer sub-scores of MBI were significantly correlated with salivary aspiration. However, MMSE, which represents cognition, had a significant correlation with salivary aspiration in supratentorial stroke. On the other hand, in infratentorial stroke, MMSE did not show any significant correlation with salivary aspiration. This may be due to the fact that the degree of MMSE does not represent the degree of swallowing reflex damage in the infratentorial stroke, unlike the supratentorial stroke. On the contrary, in supratentorial stroke patients, the degree of MMSE reduction reflects a decrease in the supra-medullary swallowing reflex. These results can be explained by the suppression of the supra-medullary swallowing reflex, which may lead to a reduction in the swallowing reflex, even if there is no involvement of the swallowing reflex pathway at the brainstem level. On the other hand, in infratentorial strokes, the transfer sub-scores of MBI may be more indicative of brainstem damage than MMSE. Considering this fact, it is thought that the transfer sub-score of MBI in the infratentorial stroke reflects the severity of the swallowing pathway involvement. For that reason, the transfer sub-score of MBI seems to be correlated significantly with salivary aspiration.

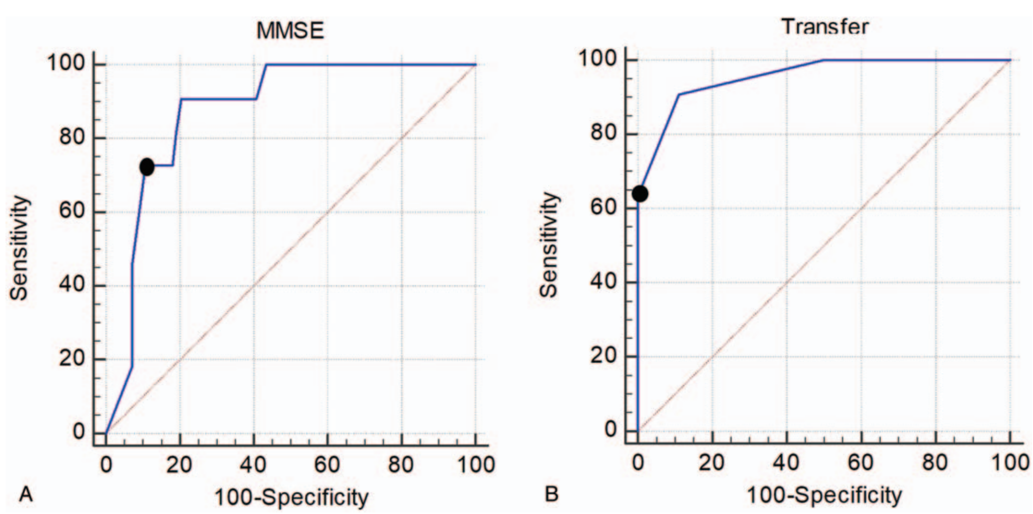

Figure 2. (A) ROC curve of MMSE score for developing salivary aspiration in supratentorial stroke patients with dysphagia. The optimal cut-off value (dots on the curves) for MMSE score, which was obtained from the maximal Youden's index, was a score of 8 or less for development of aspiration pneumonia (AUC, 0.784; 95% confidential interval, 0.664–0.925; $P < .05$; sensitivity: 90.91%, specificity: 79.52%). (B) ROC curve of transfer sub-score of Modified Barthel Index (MBI) for developing salivary aspiration in infratentorial stroke patients with dysphagia. The optimal cut-off value (dots on the curves) for total MBI score, which was obtained from the maximal Youden's index, was a score of 3 or less for development of aspiration pneumonia (AUC, 0.517; 95% confidential interval, 0.332–0.804; $P < 0.05$; sensitivity: 90.91%, specificity: 88.89%). AUC = area under the ROC curve, MMSE = Mini-Mental State Examination, ROC = receiver operating characteristic.

There are several limitations to our study. Firstly, the number of stroke patients with salivary aspiration was not large. For this reason, the power of the results of this study seems to be diminished. However, even with the small sample size we observed significant clinical predictors of salivary aspiration in stroke patients according to stroke lesions, and further well designed studies with larger patients group are warranted to extrapolate it. Secondly, this was a retrospective study; we excluded patients with insufficient medical records, which may have caused bias in the analysis. Therefore, further prospective studies should be performed to identify the important clinical predictors of salivary aspiration in stroke patients.

5. Conclusion

MMSE can be a clinical predictor of salivary aspiration in patients with supratentorial stroke, and the transfer sub-score of MBI can be a clinical predictor of salivary aspiration in patients with infratentorial stroke. Therefore, care should be taken to prevent salivary aspiration when the MMSE score is less than eight in patients with supratentorial stroke, and the transfer sub-score of the MBI score is less than three in patients with infratentorial stroke.

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Author contributions

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Writing – original draft: Kwang Jae Yu, Donghwi Park.
Writing – review & editing: Donghwi Park.

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