Swallowing outcomes in patients with subcortical stroke associated with lesions of the caudate nucleus and insula

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Abstract

Objective: The present study was performed to investigate the relationships between swallowing outcomes and lesion location, bolus characteristics, and age in patients with subcortical stroke.

Patients: Patients with subcortical and insular stroke (mean age, 57.38 ± 12.71 years) were investigated. All patients (n = 21) completed both brain magnetic resonance imaging studies and videofluoroscopic swallowing studies.

Main Outcome Measures: The oral transit duration, pharyngeal transit duration (PTD), laryngeal response duration, and Penetration-Aspiration Scale (PAS) score were applied to examine the efficiency of propulsion and airway protection in three swallowing tasks. Path analyses were performed to assess the relationships between swallowing outcomes and lesion location, age, bolus viscosity, and bolus volume.

Results: Caudate nucleus (CN) lesions were associated with higher PAS scores. Insular lesions were associated with a longer PTD. Advanced age was associated with a longer PTD. Bolus viscosity significantly moderated the association between CN lesions and higher PAS scores.
Conclusions: In the present cohort, CN lesions impacted airway protection and insular lesions impacted pharyngeal transit. An increased bolus viscosity reduced the aspiration severity. These results suggest that lesion location is an important indicator to predict subsequent dysphagia in patients with subcortical stroke.

Keywords
Subcortical stroke, caudate nucleus, insula, pharyngeal transit duration, age, videofluoroscopic swallowing study

Introduction
Post-stroke dysphagia is characterized by a misdirection or delay in the transport of swallowed materials.\(^1\)\(^-\)\(^3\) Research of neurological swallowing dysfunction has implicated lesions in the anterior insula,\(^4\)\(^,\)\(^5\) the basal ganglia and internal capsule,\(^1\) and the periventricular white matter.\(^6\) Subcortical brain lesions may result in increased muscle tone or involuntary movements. Therefore, a plausible hypothesis is that patients with subcortical stroke may develop swallowing deficits secondary to an increase in the pharyngeal transit duration (PTD) and/or laryngeal response duration (LRD). A previous case-control study demonstrated an increased oral transit duration (OTD) and LRD in a small cohort of patients with subcortical stroke.\(^1\) Daniels and Foundas\(^7\) suggested that damage to subcortical structures, such as the thalamus and basal ganglia, may be more likely to increase the risk of aspiration in patients with stroke. Thus, damage to these subcortical structures is thought to not only delay the swallowing duration but also induce symptoms such as aspiration. However, although the neural network of subcortical structures is characterized by descending inputs from the cortical and subcortical regions to the cranial nerves and integration of inputs in both the cortical-subcortical and subcortical-bulbar regions,\(^8\) the neural control of swallowing is unclear. Indeed, the roles of specific subcortical structures are not fully understood. Identification of which subcortical lesions are dysfunctional is expected to provide clearer information regarding the neural network involved in swallowing control and the patient’s need for further evaluation or intervention.\(^9\)

Evaluation of swallowing dysfunction in patients with subcortical stroke may require the assessment of two parameters: the efficiency of propulsion and the airway protection ability. Videofluoroscopic swallowing study (VFSS) is the recognized gold standard for the diagnosis and management of oropharyngeal dysphagia.\(^10\)\(^,\)\(^11\) VFSS also detects laryngeal aspiration during swallowing; i.e., the accidental inhalation of swallowed materials into the trachea due to inadequate airway protection.\(^12\)\(^,\)\(^13\) In addition, temporal measurements using VFSS have been used to evaluate the efficiency of propulsion (increased OTD or/and LRD) and PTD.\(^14\)\(^-\)\(^16\) Given the fact that these swallowing outcomes using VFSS can be as measures of the key characteristics of dysphagia, we sought to determine what specific subcortical lesions could affect swallowing efficiency and function.
for airway protection. Therefore, we investigated swallowing dysfunction in patients with stroke presenting with subcortical lesions. Analyses were performed to determine the relationship between lesion location and swallowing outcomes, such as temporal measurements and laryngeal aspiration severity.

Methods

Patients

The patients in this study were drawn from a cohort of patients with subcortical stroke who were recruited from consecutive admissions to the Neurorehabilitation Unit of our institution from March 2011 to November 2013. The inclusion criteria were the presence of a subcortical lesion, no previous history of neurological disease, and aspiration or disorder of several components of swallowing (respiratory distress; harsh, wet, and or nasal voice; and oral intake ability). The lesion location was confirmed by brain magnetic resonance (MR) imaging. Two radiologists reviewed each MR image at different times. The initial MR image was clinically interpreted by a reviewer within a few hours after the patient underwent the MR imaging study, and another radiologist also reviewed the image in the same manner after several days. All discrepancies were resolved by consensus through a discussion involving both reviewers. Lesions in the following locations were classified as subcortical and insular: putamen, caudate nucleus (CN), globus pallidus, insula, periventricular white matter, thalamus, external capsule, lateral ventricle, frontal lobe white matter, parietal lobe white matter, and temporal lobe white matter (Table 1). All patients completed VFSS within 14 days after the MR imaging study. The study was approved by the institutional review board of Chonbuk National University Hospital. All participants provided written informed consent prior to inclusion.

VFSS procedure

VFSS was performed with a SONIALVISION VERSA 1001/DAR-8000 (SHIMADZU Corp., Kyoto, Japan) in a fluoroscopy suite by a clinician, radiology technician, and speech-language pathologist. The patient was positioned in the examination chair in a lateral position and asked to hold a bolus in their mouth until instructed to swallow. The patient was asked to swallow the following three substances: 2 mL of thin liquid [3.2 centipoise (cP)], 5 mL of thin liquid (3.2 cP), and 5 mL of curd-type yogurt (5500 cP) and a diet adjusted to the patient’s swallowing function (i.e., rice porridge or steamed rice). The viscosity of the three bolus types was measured at the Korea Testing & Research Institute using a Brookfield viscometer (LV3 spindle, 30 r/min, 25°C ± 1°C; Brookfield Engineering, Middleboro, MA, USA). The bolus doses were mixed with barium sulfate and water or barium sulfate and yogurt, the maximum contaminant level of which was set at 100 (100% w/v) in water. The anatomical boundaries in the lateral fluoroscopic view were the lips, nasopharynx, cervical spine, and cervical esophagus (Figure 1). Fluoroscopic images were stored frame-by-frame in a computer at a rate of 30 frames per second.

Outcome measures

Temporal measurements of oropharyngeal swallowing and scores on the 8-point Penetration-Aspiration Scale (PAS) were analyzed using Final Cut Pro X software for Macintosh (Apple Inc., Cupertino, CA, USA) (Figure 2). Temporal measurements were made for the OTD, PTD, and LRD. For each swallowing event, temporal measurements were made of the time from
onset to offset. For OTD, onset was defined as the time at which the bolus initiated a posterior movement in the oral cavity, and offset was defined as the time at which the bolus head reached the ramus of the mandible.\textsuperscript{10} For PTD, onset was defined as the time at which the bolus head reached the ramus of the mandible, and offset was defined as the time at which the tail of the bolus passed through the upper esophageal sphincter.\textsuperscript{19} For LRD, onset was defined as the time at which the bolus head reached the ramus of the mandible, and offset was defined as the time at which laryngeal elevation occurred as part of pharyngeal swallowing.\textsuperscript{10,16} These temporal measurements were evaluated by two speech-language pathologists. The main examiner analyzed all VFSS images. The second examiner analyzed a randomly selected 50% sample of the VFSS images to determine reliability.

### Statistical analysis

To investigate the relative effects of lesion location, temporal measurements, and PAS scores, path analysis was performed using AMOS (IBM Corp., Armonk, NY, USA). Simultaneous estimation and direct testing was performed for indirect and total effects. A multi-regression method was used to confirm causal relationships between independent variables. The chi-square value of the research model was 15.92 ($d f = 9$), the comparative fit index was 0.98, the goodness of fit index was 0.97, and the

| Patient no. | Age (y) | Subtype | Lesion side | Lesion site |
|-------------|---------|---------|-------------|-------------|
| 1           | 56      | Hemorrhage | Left        | O x O x x x x O x x x x x |
| 2           | 64      | Hemorrhage | Left        | O x x x x x x x x x x x |
| 3           | 43      | Hemorrhage | Left        | O x O x x O x x x x O |
| 4           | 44      | Hemorrhage | Left        | O x O x x O x x x x O x |
| 5           | 45      | Hemorrhage | Left        | O x x x x x x x x x x x |
| 6           | 53      | Infarction | Left        | O O O O x x x x x x O x |
| 7           | 77      | Infarction | Left        | O O x x x x x x x x x x x |
| 8           | 42      | Infarction | Left        | O O O x x x x x x x x x x |
| 9           | 49      | Infarction | Left        | O O O x x x x x x x x x x x |
| 10          | 49      | Infarction | Left        | O O O x x x x x x x x x x x x |
| 11          | 52      | Infarction | Left        | O x x x O x x x x O x |
| 12          | 61      | Infarction | Left        | O x x x O x x x x O x |
| 13          | 55      | Hemorrhage | Right       | O x O x x O x x x x x x x |
| 14          | 44      | Hemorrhage | Right       | O O O x x x x x x x x x x x |
| 15          | 54      | Infarction | Right       | O x x x x x x x x x x x x x |
| 16          | 69      | Infarction | Right       | O O O x x x x x x x x x x x |
| 17          | 81      | Infarction | Right       | O O O O O x O x x x x x |
| 18          | 49      | Infarction | Right       | O x x x O x x x x x x x |
| 19          | 63      | Infarction | Right       | O x x x O x x x x x x x |
| 20          | 74      | Infarction | Right       | O x x x O x x x x x x x x x |
| 21          | 81      | Infarction | Right       | O O O x O x x x x x x x x |

\(\text{x, present; }\text{O, absent; }\text{P, putamen; }\text{CN, caudate nucleus; }\text{GP, globus pallidus; }\text{I, insula; }\text{PVW, periventricular white matter; }\text{T, thalamus; }\text{EC, external capsule; }\text{LV, lateral ventricle; }\text{FW, frontal lobe white matter; }\text{PW, parietal lobe white matter; }\text{TW, temporal lobe white matter.}
critical ratio (CR) of the multivariate normality test was 1.49. Variables X15 and Y5 reduced the total model fit and were therefore removed.

The 0.05 significance level of the research model supported the null hypothesis, and the research was therefore considered valid. Multicollinearity between independent variables was not present as indicated by a correlation coefficient of <0.22. Use of multiple regression analysis was therefore appropriate. Multiple group factor analyses were carried out (p > 0.05) to compare measurements obtained during the 2- and 5-mL thin liquid tasks (difference in volume) and the 5-mL thin liquid and 5-mL curd-type yogurt tasks (difference in viscosity). The present study used swallowing outcomes according to three bolus-swallowing tasks. Statistical analyses were performed using IBM SPSS Statistics, version 20.0 for Windows (IBM Corp.).

Results

Patients

Twenty-one patients were included in this study. Their mean age was 57.38 years [standard deviation (SD) = 12.71 years]. The demographic characteristics of the cohort are shown in Table 2.

Interobserver and intraobserver agreement

Test–retest reliability was assessed using the intraclass correlation coefficient (ICC).
The ICC for interobserver agreement was excellent \[ \text{ICC} = 0.95, 95\% \text{ confidence interval (CI)} = 0.95–0.98 \]. Intraobserver agreement was also excellent \( \text{ICC} = 0.94, 95\% \text{ CI} = 0.94–0.98 \).

### Temporal measurements: OTD, PTD, and LRD

The mean OTD for the 2- and 5-mL thin liquids and the 5-mL yogurt was 0.87 s (SD = 0.63 s), 0.80 s (SD = 0.69 s), and 0.93 s (SD = 0.91 s), respectively. The mean PTD for the 2- and 5-mL thin liquids and the 5-mL yogurt was 0.83 s (SD = 0.50 s), 0.81 s (SD = 0.57 s), and 0.51 s (SD = 0.68 s), respectively. The mean LRD for the 2- and 5-mL thin liquids and the 5-mL yogurt was 0.40 s (SD = 0.61 s), 0.60 s (SD = 1.04 s), and 0.82 s (SD = 0.39 s), respectively.

### Effects of bolus viscosity

In the 5-mL thin liquid task, CN lesions were significantly associated with PAS scores \( (\beta = 0.72, \text{ CR} = 3.18, p = 0.001) \). Age was significantly associated with the LRD \( (\beta = 1.06, \text{ CR} = 2.62, p = 0.01) \). The PAS score was significantly associated with the PTD \( (\beta = 0.83, \text{ CR} = 4.32, p = 0.001) \). The LRD was significantly associated with the PTD \( (\beta = 11.05, \text{ CR} = 2.82, p = 0.001) \). In the 5-mL yogurt task, insular lesions were significantly associated with the PTD \( (\beta = 0.54, \text{ CR} = 2.23, p = 0.03) \) (Tables 3 and 4).

### Relationship among lesion location, PAS score, PTD, and bolus viscosity and volume

A significant moderating effect on the association between CN lesions and higher PAS scores was observed for bolus viscosity (CR = −2.48, over 95% CI). A significant moderating effect was also found for the relationship between insular lesions and the PTD (CR = 0.25, over 95% CI). The results of the path analysis are presented in Figure 3.

### Discussion

The present study used VFSS data to determine associations between lesion location and specific swallowing problems in patients with subcortical stroke, particularly the efficiency of swallowing function and airway protection. The results of the present study suggest that some subcortical lesions were associated with swallowing outcomes. Specifically, CN lesions were associated with increased PAS scores in the 5-mL thin liquid swallowing task. This suggests that patients with stroke-associated CN lesions are vulnerable to aspiration. However, because all 21 patients in the present study had lesions in the

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**Table 2.** Demographic characteristics of patients.

| Characteristics                        | Patients (n = 21) |
|----------------------------------------|------------------|
| Age, y                                 | 57.38 (12.71)    |
| Sex                                    | 13/8             |
| NIHSS score                            | 8.47 (5.57)      |
| Stroke type                            | Infarction/hemorrhage 7/14 |
| Lesion side                            | Left/right 12/9   |
| Lesion site                            | Putamen 21       |
| Caudate nucleus/globus/thalamus        | 8/10/3           |
| Periventricular white matter           | 7                |
| Insula                                 | 2                |
| External capsule/lateral ventricle     | 2/1              |
| Frontal/temporal/parietal white matter | 2/2/1            |

Data are presented as n or mean (standard deviation).

NIHSS, National Institutes of Health Stroke Scale.
Table 3. Results of path analysis in research model.

| Path analysis          | Dependent variables      | β      | CR     | p   | β       | CR     | p   | β       | CR     | p   |
|------------------------|--------------------------|--------|--------|-----|---------|--------|-----|---------|--------|-----|
| **Independent variables** | **Relationship** | **PAS score** | **Pharyngeal transit duration** | **Laryngeal response duration** |
| Caudate nucleus lesion | Thin liquid 2 mL →       | 0.25   | 0.86   | 0.39 | -0.36   | -1.15  | 0.25 | 0.49    | 1.05   | 0.30|
|                        | Thin liquid 5 mL →       | 0.72   | 3.18   | 0.001† | -0.01   | -0.29  | 0.77 | -0.75   | -1.96  | 0.06|
|                        | Yogurt 5 mL →           | 0.03   | 0.17   | 0.86 | -0.56   | -1.69  | 0.09 | -0.28   | -0.59  | 0.55|
| Insular lesion         | Thin liquid 2 mL →       | 0.29   | 1.18   | 0.24 | -0.05   | -0.23  | 0.81 | -0.13   | 1.02   | 0.30|
|                        | Thin liquid 5 mL →       | -0.15  | -0.74  | 0.46 | 0.01    | -0.03  | 0.98 | 0.41    | 1.62   | 0.10|
|                        | Yogurt 5 mL →           | 0.10   | 0.50   | 0.62 | 0.54    | 2.23   | 0.03†| 0.57    | 1.82   | 0.07|
| Age                    | Thin liquid 2 mL →       | 1.61   | 0.49   | 0.63 | -0.04   | -0.08  | 0.93 | 1.06    | 2.62   | 0.009†|
|                        | Thin liquid 5 mL →       | -0.19  | -0.50  | 0.62 | 1.06    | 2.62   | 0.009†| 0.04    | 0.07   | 0.94|
|                        | Yogurt 5 mL →           | 0.55   | 1.60   | 0.12 | 0.14    | 0.81   | 0.42 | 0.04    | 0.07   | 0.94|
| PAS score              | Thin liquid 2 mL →       | 0.14   | 0.81   | 0.42 | 0.86    | 4.32   | 0.00†| 1.06    | 2.62   | 0.009†|
|                        | Thin liquid 5 mL →       | -0.23  | -1.04  | 0.30 | -0.11   | -0.12  | 0.90 | 0.04    | 0.07   | 0.94|
|                        | Yogurt 5 mL →           | -0.92  | -0.71  | 0.48 | -0.11   | -0.12  | 0.90 | -0.23   | -1.04  | 0.30|
| Laryngeal response     | Thin liquid 2 mL →       | 6.33   | 1.428  | 0.158| 11.05   | 2.82   | 0.005†| 0.01    | 0.07   | 0.94|
|                        | Yogurt 5 mL →           | -1.07  | -1.06  | 0.29 | -0.01   | -0.07  | 0.94 | 0.04    | 0.07   | 0.94|

CR, critical ratio; PAS, Penetration-Aspiration Scale. *p < 0.05, †p < 0.01
putamen, a plausible hypothesis is that the observed insufficiency in airway protection was attributable to impaired striatum control. The CN and putamen are cytoarchitecturally similar structures with small neuronal cell bodies and are collectively referred to as the striatum. Previous MR imaging studies have demonstrated activation of both the CN and the putamen during swallowing. Thus, given the simultaneous activation of these structures, airway protection during swallowing appears to be under the control of the neurological unit that comprises the CN and the putamen. Moreover, another finding of the present study was the moderating effect of bolus viscosity on the relationship between CN lesions and the PAS score. Increasing viscosity was associated with a decrease in the PAS score. Previous studies

| Bolus type | Viscosity | Volume | Independent variables | Relationship | Dependent variables | β   | CR  | p    |
|------------|-----------|--------|----------------------|--------------|---------------------|-----|-----|------|
| 3.2 cP     | 5 mL      |        | Caudate nucleus lesion | →            | PAS score           | 0.72| 3.18| 0.001|
|            |           |        | Age                  | →            | LRD                 | 1.06| 2.62| 0.009|
|            |           |        | PAS score            | →            | PTD                 | 0.86| 4.32| <0.001|
|            |           |        | LRD                  | →            | PTD                 | 11.05| 2.82| 0.005|
| 5500 cP    | 5 mL      |        | Insular lesion       | →            | PTD                 | 0.54| 2.23| 0.03 |

CR, critical ratio; LRD, laryngeal response duration; PTD, pharyngeal transit duration; PAS, Penetration-Aspiration Scale. *p < 0.05, †p < 0.01.

Figure 3. Schematic diagram of path analyses for swallowing outcomes, age, and lesion location. The numbers are the standardized coefficients.
of patients with dysphagia have demonstrated that increasing the viscosity of a thin liquid bolus results in increased swallowing safety.\textsuperscript{22–24} Newman et al.\textsuperscript{25} also reported a significant decrease in the PAS score with an increase in viscosity from thin liquid to 1750 cP. The present findings thus support the results of previous research and suggest that increased viscosity could improve the airway protection aspect of swallowing function.

Insular lesions were associated with an increased PTD in the 5-mL curd-type yogurt swallowing task. This result should be interpreted with caution because of the small number of patients with insular lesions. Previous functional MR imaging studies in healthy subjects indicated activation of the insula during swallowing.\textsuperscript{20,26} Another study showed connections between the insula and the primary and supplementary motor cortices and revealed that these brain regions facilitate coordinated interaction between the oral and pharyngeal phases of swallowing.\textsuperscript{27,28} Other research has shown that patients with insula lesions exhibit pharyngeal swallowing problems.\textsuperscript{4,29} Therefore, it is possible that damage to the insula might delay transport during pharyngeal swallowing, but a large cohort study is need to provide more definitive results.

Age was significantly associated with the LRD. This result is unsurprising because several studies of healthy older adults have demonstrated an increase in the duration of pharyngeal triggering and oral and pharyngeal swallowing.\textsuperscript{14,25,30} Advanced age is associated with sensorimotor impairment, which frequently manifests as inefficient swallowing characterized by an increased LRD.\textsuperscript{31} Even in the presence of normal swallowing duration, older patients may be required to invest more effort in swallowing than younger adults, who recruit their neural networks more efficiently. Reduced swallowing efficiency by aging has been under discussion for a long time, and the present finding thus supports the hypothesis that patients with subcortical stroke display a tendency to develop inefficient pharyngeal swallowing.

Finally, the PTD was associated with an increased PAS score in the 5-mL thin liquid swallowing task. Previous studies have also shown that an increased PTD is associated with aspiration\textsuperscript{32,33} and that among patients with dysphagia, the PTD is longer in those with than without aspiration.\textsuperscript{32} Im et al.\textsuperscript{34} indicated that when the PTD was $>0.71$ s in patients with hemisphere stroke, laryngeal penetration occurred. Laryngeal aspiration/penetration is responsible for dysfunction of both pharyngeal and laryngeal movements.\textsuperscript{35,36} Because it is generally accepted that the mechanism of these movements involves transmission via the brain stem,\textsuperscript{21,37,38} damage to the sensory motor pathway that passes through the subcortical area from the cortical region to the brain stem may affect reduced swallowing efficiency and airway protection. Thus, damage to subcortical structures is thought to increase pharyngeal transit resulting from reduced sensory input, and aspiration may reflect an increased PTD.

The present study has several limitations. First, the cohort was small, which limits the generalizability of the results to other patients with subcortical stroke. Second, the time interval between MR imaging and VFSS varied. This may have impacted the results because swallowing outcomes are influenced by the stroke prognosis. Similarly, the analyses did not take stroke severity into account. Therefore, patient heterogeneity may have impacted the results. Future studies should control for stroke severity and the interval between MR imaging and VFSS. Third, the difference in the bolus volume evaluated via VFSS (2 mL versus 5 mL) was small. This may have led to the observed lack of association for this variable. A previous study
of patients with left basal ganglion/internal capsule lesions compared bolus volumes of 1 mL versus 10 mL and found an effect.1 Future research should therefore investigate larger differences in bolus volumes.

Conclusions

The present data suggest that in patients with subcortical stroke, CN lesions may impact airway protection while insular lesions may impact pharyngeal transit. CN and insular lesions may therefore predict aspiration and problems with pharyngeal swallowing, respectively. In addition, increasing the bolus viscosity may reduce the aspiration severity. A future study of the relationship between swallowing outcomes and lesion location may lead to the development of a sensitive index for predicting dysphagia associated with subcortical lesions.

Declaration of conflicting interest

The authors declare that there is no conflict of interest.

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