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의학박사 학위논문

Evaluation of swallowing function in infants with dysphagia

연하장애가 있는 영아에서 삼킴 기능의 평가

2020년 2월

서울대학교 대학원

의학과 재활의학 전공

이 유 경

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Evaluation of swallowing function in infants with dysphagia

by
You Gyoung Yi
(Directed by Prof. Hyung-Ik Shin)

A thesis submitted in partial fulfillment of requirements
for the degree of Ph. D of Science in Medicine
at Seoul National University College of Medicine
(Major in Rehabilitation Medicine)

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ABSTRACT

Evaluation of swallowing function in infants with dysphagia

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Interventions for dysphagia have been applied to infants and children with various conditions, such as cerebral palsy, neuromuscular disorders, and a wide range of other conditions, such as developmental disorders and tube-feeding dependency. There is a need for a tool that can aid clinicians in describing feeding status and measuring outcomes of the management of infants with dysphagia. Various evaluation tools have been developed for infants with feeding problem. However, most of these assessment tools are in the form of checklists and are often not validated or subjective.

The Neonatal Oral-Motor Assessment Scale (NOMAS) is a method of visual observation that is used to assess non-nutritive and nutritive sucking in an infant from birth to 48 weeks of postmenstrual age (PMA). The observational items

compatible with disorganization in the original NOMAS were divided into three groups according to the presence of arrhythmical, unable to sustain, and the incoordination items; cluster 2 (arrhythmical), 3 (unable to sustain), and 4 (incoordination). Although this cluster system grouped various NOMAS findings into categories, the clinical usefulness of each item has yet to be demonstrated.

The Functional Oral Intake Scale (FOIS) was initially developed for the clinical documentation of changes in the functional oral intakes by stroke patients. Despite the wide use of the FOIS to evaluate dysphagia in adults, it has not been validated for use in infants. The direct application of the FOIS to infants is challenging, as they are developing rapidly and will experience an expansion of the oral diet with age.

In this thesis, three individual studies were performed. First, we investigated whether specific items within the disorganized sucking patterns described by the NOMAS could estimate the time to full oral feeding (FOF) in preterm infants with feeding difficulty. Second, we investigated whether stress signals in NOMAS during bottle feeding in premature infants are a relevant factor for developmental outcomes at 10 months of age (corrected for prematurity). Finally, the reliability and validity of the Functional Oral Intake Scale (FOIS) for infants was analyzed.

In the first study, preterm infants diagnosed with a disorganized sucking pattern in the NOMAS evaluation before 50 weeks of postmenstrual age were included. Premature infants who exhibited disorganized sucking patterns (n = 109) were divided into three clusters (clusters 2–4) and further divided into incoordination-positive (cluster 4) and incoordination-negative groups (clusters 2 and 3).

In the study evaluating the association of stress signals with developmental outcomes at 8-12 and 18-24 months of age, NOMAS of 71 premature infants was obtained. The Bayley-III cognition composite scores for the incoordination-positive group and the incoordination-negative group were compared by independent t-test.

In the study assessing the reliability and validity of the FOIS for infants, infants who underwent a videofluoroscopic swallowing study (VFSS) were included in the analysis. Their nutrition records at the time of the VFSS were separately evaluated by two raters using the five-point FOIS for infants. Categorical swallowing and aspiration impairment scale data were also obtained from the VFSS.

In the first study, premature infants in the incoordination-positive group (cluster 4, which means stress signals) showed a median transition time of 22 days (range: 4–121 days) which was longer than that in the incoordination-negative group (median 6 days; range: 1–25 days). In a multivariate linear regression analysis, the variables revealed to be associated with the transition time were TPN duration, SGA, and the presence of stress signals (incoordination-positive group) among disorganized sucking patterns.

In the second study, seventy premature infants exhibited a disorganized sucking pattern according to the NOMAS. The average Bayley-III cognition composite scores at 18-24 months were higher in incoordination-negative group (n=46, 100.7±11.5) than incoordination-positive (n=21, 90.0±17.9) group (p=0.005). A multiple linear regression analysis indicated that the presence of uncoordinated sucking pattern, grade 3 or 4 germinal matrix hemorrhage–intraventricular

hemorrhage, and moderate to severe bronchopulmonary dysplasia were independently associated with cognitive development at 18-24 months of age.

In the third study, the inter-rater reliability of the FOIS for infants was high (95.5% absolute agreement) among the 201 evaluated infants, and this scale was correlated with aspiration severity in the VFSS. This analysis included 33 infants who were receiving both oral and tube feeding (i.e., POF). We also investigated whether infants with partial oral feeding (POF) at the FOIS evaluation had achieved full oral feeding within 1 year of the evaluation and used this information to estimate whether the caloric contribution, as well as consistency of oral feeding, affected the feeding outcomes. Among them, 26 infants achieved FOF without tube feeding after 1 year. Their initial contribution from oral feeding was higher than that in infants who still maintained POF after 1 year (28.46 ± 22.79 vs. 6.00 ± 5.45%, $p < 0.001$).

In summary, when selecting premature infants to be treated with swallowing therapy, it is reasonable to pay more attention to the incoordination-positive group described in the NOMAS to shorten the time to attain FOF and monitor the developmental milestones. Also, the five-point FOIS for infants, which reflected the expansion of their oral diet with growth, had adequate reliability and validity. These results suggest that both NOMAS and infantile FOIS can be used complementarily to assess swallowing function in infants.

Keywords: Neonatal Oral-Motor Assessment Scale (NOMAS), Functional Oral Intake Scale (FOIS), Evaluation tool, Infant, Swallowing, Deglutition, Deglutition

disorder, Oral feeding, Development

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LIST OF ABBREVIATIONS

BPD	bronchopulmonary dysplasia
BW	birth weight
CA	corrected age
FOIS	Functional Oral Intake Scale
FOF	full oral feeding
GA	gestational age
GMH-IVH	germinal matrix hemorrhage-intraventricular hemorrhage
ICC	intraclass correlation coefficient
IOF	initiation of oral feeding
IRB	institutional review board
NEC	necrotizing enterocolitis
NICU	neonatal intensive care unit
NIPPV	non-invasive positive pressure ventilation
NOMAS	Neonatal Oral-Motor Assessment Scale
PMA	post-menopausal age
POF	partial oral feeding
RDS	respiratory distress syndrome
SGA	small for gestational age
SNUH	Seoul National University Hospital
SSR	sucking, swallowing, and respiration
TPN	total parenteral nutrition
VFSS	videofluoroscopic swallowing study

BACKGROUND

Interventions for dysphagia have been applied to infants and children with various conditions, such as cerebral palsy (1), neuromuscular disorders (2), and a wide range of other conditions, such as developmental disorders (3,4) and tube-feeding dependency (5–7). Various interventions for infants with dysphagia, such as environmental modifications (8), oral-motor stimulation (9), altered feeding routines (10), and neuromuscular electrical stimulation (11,12), have attracted increased attention both in clinical and research perspectives.

Although infants with dysphagia often require tube feeding to achieve a satisfactory caloric intake, this practice may lead to later feeding difficulties (13). Especially, in the case of starting tube feeding during the first year of life, it has been reported that the feeding outcome was poor although the pharyngeal phase of swallowing function is well preserved. Therefore, oral feeding in this era of tube feeding is recommended and encouraged (6).

There is a need for a tool that can aid clinicians in describing feeding status and measuring outcomes of the management of infants with dysphagia. To describe swallowing ability of older children and adults with neuromuscular disease, the neuromuscular disease swallowing status scale (2,14) has been used. Additionally, an eating and drinking ability classification system (15–18) has been validated for children, aged 3 years and above, with cerebral palsy. However, these scales were developed for specific disease populations with older children, making it difficult to use them for infants with swallowing difficulty.

Various evaluation tools have been developed for infants with feeding problem; preterm infant breastfeeding behaviour scale (19), breast-feeding attrition prediction tool (20), bottle-feeding flow sheet (21), early feeding skills assessment for preterm infants (22), Bristol breastfeeding assessment tool (23), and analysis of feeding behaviour with direct linear transformation (24). However, most of these assessment tools are in the form of checklists and are often not validated or subjective.

Several dimensions exist to demonstrate the swallowing function of infants. Oromotor (25,26) or pharyngeal function (27,28), changes in oxygen saturation or heart rate (21,29,30) during feeding are frequently evaluated in infants with swallowing difficulty. The food the infant consume and factors associated with swallowing such as arousal or head control (31) could be also recorded. Among these dimensions, records for oromotor function (32) and the food the infant consume are widely used, particularly in the clinic, due to their noninvasiveness.

The Neonatal Oral-Motor Assessment Scale (NOMAS) is a method of visual observation that is used to assess non-nutritive and nutritive sucking in an infant from birth to 48 weeks of postmenstrual age (PMA) (33,34) (Table 1). The NOMAS consists of 28 items: 14 related to movements of the tongue and 14 related to movements of the jaw. Both movements are classified into three groups: normal, disorganization, and dysfunction (33–35). A dysfunctional sucking pattern in NOMAS is defined as abnormal jaw and tongue movements that result in the interruption of feeding, such as a flaccid tongue, excessive excursion of the jaw, or no movement. It is rarely observed (36), but frequently accompanied by congenital anomalies, severe brain lesions, and neuromuscular disease (33,37). Palmer, the developer of the NOMAS system, suggested that a dysfunctional sucking pattern is strongly associated with neurological dysfunction, rather than CNS immaturity (33). da Costa et al. reported that incoordination, under disorganization on the NOMAS, was more prevalent in preterm infants with bronchopulmonary dysplasia (BPD) than those without BPD (38). They further suggest that successful feeding is hindered by decreases in oxygen saturation during feeding, which deprives preterm infants of essential sensory and motor experiences (39,40), leading to the late achievement of full oral feeding (FOF).

The observational items compatible with disorganization in the original NOMAS were divided into three groups according to the presence of arrhythmical, unable to sustain, and the incoordination items (41): cluster 2 (disorganized: arrhythmical), 3 (disorganized: arrhythmical + unable to sustain), and 4 (disorganized: arrhythmical + incoordination ± unable to sustain) (Table 2). Although this cluster system grouped various NOMAS findings into categories, the clinical usefulness of each item (arrhythmical, unable to sustain, and incoordination) has yet to be demonstrated.

Observational findings of the "incoordination of SSR that results in stress signals" in the NOMAS include nasal flaring, head turning, and extraneous movements of the body or limbs during sucking, as the description in the study by Palmer et al. (42). The NOMAS working group in the Netherlands added further stress signs, such as choking, gagging, coughing, yelping, and grunting, to the findings of incoordination, and grouped these symptoms as cluster 4 (41). As the authors designated, these signs are essentially stress signals, and it is still unclear whether these clinical symptoms develop owing to lack of coordination in SSR. Furthermore, it has not yet been known whether these symptoms are more relevant than other symptoms of sucking difficulty to developmental outcome.

The Functional Oral Intake Scale (FOIS, Table 3) was initially developed for the clinical documentation of changes in the functional oral intakes of liquids and foods by stroke patients (43). This seven-point observer rating scale is considered a reliable and valid tool that can be applied without placing an additional burden on the patient. In adults with dysphagia, the FOIS has been reported to correlate significantly with the Food Intake Level scale (44), swallowing item of the Functional Assessment Measure (45), Mann Assessment of Swallowing Ability, modified Barthel Index, modified Rankin scale, and dysphagia and aspiration during a videofluoroscopic swallowing study (VFSS) (43). Additionally, Christiaanse et al. suggested a modified FOIS, which was used for investigating the effect of electrical stimulation in children with dysphagia in their study (11). They did not utilize the item involving a TOD with a single consistency (Level 4) in the FOIS for adults (Table 4). However, they did not report the validity and reliability of their modified FOIS for children. Despite the wide use of the FOIS to evaluate dysphagia and assess oral intake recovery in adults (46), it has not been validated for use in infants. The direct application of the FOIS to infants is challenging, as they are developing rapidly and will experience an expansion of the oral diet with age (47,48).

Table 2. Neonatal Oral-Motor Assessment Scale (NOMAS)

	Normal	Disorganization	Dysfunction
Jaw	__ consistent degree of jaw depression __ rhythmical excursions __ spontaneous jaw excursions occur upon tactile presentation of the nipple up to 30 minutes prior to feed __ jaw movement occurs at the rate of approximately one per second __ sufficient closure on the nipple during the expression phase to express fluid from the nipple	__ inconsistent degree of jaw depression __ arrhythmical jaw movements __ difficulty initiating movements: __ inability to latch __ small, tremor-like start-up movements noted __ does not respond to initial cue of nipple until jiggled __ persistence of immature suck pattern beyond appropriate age __ under 40 weeks	__ excessively wide excursion that interrupt the intra-oral seal on the nipple __ minimal excursion; clenching __ asymmetry; lateral jaw deviation __ absence of movement (% of time) __ lack of rate change between NNS and NS (NNS=2/sec; NS=1/sec)
Tongue	__ cupped tongue configuration (tongue groove) maintained during sucking __ extension-elevation-retraction movements occur in anterior-posterior direction __ rhythmical movements __ movements occur at the rate of one per second __ liquid is sucked efficiently into the oro-pharynx for swallow	__ excessive protrusion beyond labial border during extension phase of sucking without interrupting rhythm __ arrhythmical movements __ unable to sustain suckle pattern for two minutes due to: __ habituation __ poor respiration __ fatigue __ incoordination of suck/swallow and respiration which results in nasal flaring, head turning, extraneous movement	__ flaccid; flattened with absent tongue groove __ retracted; humped and pulled back into or-pharynx __ asymmetry; lateral tongue deviation __ excessive protrusion beyond labial border before/after nipple insertion with out/down movement __ absence of movement

Table 2. Cluster system of the Neonatal Oral-Motor Assessment Scale

Cluster	Diagnoses and items
1	Normal
2	Disorganized: Arrhythmical
3	Disorganized: Arrhythmical + unable to sustain
4	Disorganized: Arrhythmical + incoordination +/- unable to sustain
5	Dysfunctional

Table 3. Functional Oral Intake Scale

Levels	Oral Intake Functionality
1	No oral intake
2	Tube dependent with minimal/inconsistent oral intake
3	Tube supplements with consistent oral intake
4	Total oral intake of a single consistency
5	Total oral intake of multiple consistencies requiring special preparation
6	Total oral intake with no special preparation, but must avoid specific foods or liquid items
7	Total oral intake with no restrictions

Table 4. Functional Oral Intake Scale and pediatric example

Levels	Oral Intake Functionality
1	Nothing by mouth
2	Tube dependent with minimal attempts of food or liquids. Pediatric example: Pacifier dips, 1 oz. puree 3*/day, 15 cc's of honey consistency 2*/day
3	Tube supplements with consistent oral intake of food or liquids. Pediatric example: One or more texture ad lib, but continues to be tube dependent
4	Total oral intake of a single consistency. Pediatric example: Not utilized
5	Total oral intake with multiple consistencies, but requiring special preparation or compensations. Pediatric example: Purees with nectar consistency liquid; Mechanical soft with honey consistency liquids; Formula thickend using 1 Tablespoon rice cereal: 2 oz
6	Total oral intake with multiple consistencies, but with specific food limitations. Pediatric example: No mixed consistencies
7	Total oral diet with no restrictions

OBJECTIVES

The thesis aimed to evaluate the clinical significance of the NOMAS and to apply the modified FOIS in infants younger than 1 year. In specific, it aimed

- To investigate whether specific items within the disorganized sucking patterns described by the NOMAS could estimate the time to full oral feeding (FOF) in preterm infants with feeding difficulty
- To investigate whether stress signals during bottle feeding in premature infants are a relevant factor for developmental outcomes at 8-12 and 18-24 months of age (corrected for prematurity)
- To evaluate the reliability and validity of the Functional Oral Intake Scale (FOIS) for infants

1. Transition Time in Premature Infants

Achieving full oral feeding (FOF) early in preterm infants can shorten hospitalization time, reduce hospital costs, and enable greater interaction between the mother and child (29,49). Strategies, such as non-nutritive sucking using a pacifier, sensorimotor stimulation, and actively pacing suck–feeds, have been used to facilitate suck–swallow function and have been reported to be effective in reducing the time to reach FOF in premature infants (25,50–53). Therefore, at the moment of transition from tube feeding to oral feeding, predicting the time to reach FOF could be useful in choosing candidates who may require additional facilitation techniques. In this study, we investigated whether the stress signals during bottle feeding were associated with a longer time to FOF in preterm infants who showed feeding difficulty at the beginning of the oral feeding.

2. Developmental Outcome at 8-12 and 18-24 months in Premature Infants

Feeding skills in a newborn requires complex functions that are directed by the central nervous system (CNS), including the coordination of sucking, swallowing, and respiration (SSR) (53–55). Preterm infants often have difficulty in coordinating SSR (30,34,40,53–57). It is reported that incoordination of SSR is associated with a longer transition time to full oral feeding in premature infants with tube feeding. Additionally, lack of muscle strength and/or endurance could precipitate the inability to sustain sucking in premature infants (58).

Two hypotheses exist regarding the difficulty in sucking encountered by neonates: (i) CNS immaturity that is self-limiting as the child ages and (ii) neurologic dysfunction due to disruption of the CNS (29,37,54,55,59,60). Distinguishing between these two potential causes of sucking difficulty is important to adequately counsel parents and commence early intervention to address developmental issues. However, it has not yet been known whether incoordination of SSR that results in stress signals are more relevant than other symptoms of sucking difficulty to developmental outcome.

The aim of this study was to investigate if the incoordination of SSR that results in stress signals during bottle feeding observed during the preterm period has relevance to developmental outcomes evaluated at 8-12 and 18-24 months of age (corrected for prematurity).

3. Functional Oral Intake Scale for Infants

Despite the wide use of the FOIS to evaluate dysphagia and assess oral intake recovery in adults (43), it has not been validated for use in infants. The direct application of the FOIS to infants is challenging, as they are developing rapidly and will experience an expansion of the oral diet with age. Additionally, it can be difficult to distinguish FOIS level 2 (tube feeding with minimal attempts of oral feeding) from FOIS level 3 (tube feeding with consistent oral feeding) because consistent but very small amounts of oral feeding are possible during the period of tube feeding (7). Accordingly, Coppens et al. modified the FOIS (Table 6) for the evaluation of infants subjected to esophageal atresia repair by reducing the FOIS levels from seven to five stages to reflect the food expansion status (7). However, the authors did not report the validity or reliability of this modified scale.

Therefore, the third objective of the thesis was to investigate the reliability and validity of this modified FOIS for infants. Additionally, we evaluated whether the oral feeding amount and frequency could be used to distinguish FOIS levels 2 and 3.

MATERIALS AND METHODS

1. Transition Time in Premature Infants

1.1 Participants

Between May 2014 and March 2017, 148 infants in Neonatal Intensive Care Unit (NICU) were referred for consultation to the Division of Pediatric Rehabilitation for sucking difficulty during the transition period from enteral tube feeding to oral feeding. Regarding all infants who were referred, a video recording was done for over 2 min, which was a necessary preparation for the NOMAS evaluation (34,41). Infants were eligible for inclusion if they were born preterm (<37 weeks), video recordings of oral feeding were obtained for more than 2 min for the NOMAS evaluation before 50 weeks of PMA, and if they were diagnosed with a disorganized sucking pattern in NOMAS. Premature infants were excluded if the NOMAS assessment point was more than 72 h after oral feeding initiation or if the infant received postnatal surgery resulting in the interruption of oral feeding. The result of the NOMAS evaluation was integrated into the electronic medical record, which the authors analyzed retrospectively. Medical records, as well as video-recordings, were retrospectively reviewed by the authors. This study was conducted in compliance with the Declaration of Helsinki, International Conference on Harmonization Guidelines for Good Clinical Practice. The final protocol was approved by the Seoul National University Hospital Institutional

Review Board (IRB) No. 1705-122-855.

1.2 Clinical Characteristics

The following parameters were investigated by retrospective medical records analysis: birth weight (BW), gestational age (GA) at birth, sex, Apgar score at 1 and 5 min after birth, total parenteral nutrition (TPN) duration, and PMA at the time of the NOMAS assessment. We also investigated the history of BPD, germinal matrix hemorrhage, intraventricular hemorrhage (IVH), periventricular leukomalacia, invasive ventilator use after birth, the duration of non-invasive positive pressure ventilation (NIPPV) including high-flow nasal cannula and nasal continuous positive airway pressure, small for gestational age (SGA), sepsis, necrotizing enterocolitis (NEC), respiratory distress syndrome (RDS), and pulmonary hypertension.

1.3 Neonatal Oral-Motor Assessment Scale

Regarding all infants who were referred, a video recording of bottle feeding was done for over 2 min, which was a necessary preparation for the NOMAS evaluation. The caloric density of breast milk was variable and known to be about 57–65 kcal/100 ml (61). Premature infant powdered milk had a calorie density of 75–85 kcal/100 ml, depending on the preparation concentration (62). Video recordings within 72 h of commencement was assessed using the NOMAS (34) by a rehabilitation doctor (one of the coauthors of this paper) who has been certified by

Marjorie Meyer Palmer, the original developer of the NOMAS. Video recordings included a close-up lateral view of the mouth, jaw, and neck, and only the bottle feeding was recorded. The videotaping was initiated before the lips reached the bottle nipple, and the recording was stopped after more than 2 min of the oral feeding had occurred. During the recordings, feeding was performed by an NICU nurse. To investigate interrater reliability at the cluster level, an occupational therapist, who had more than 5 years of experiences in oromotor and swallowing training for infants admitted to the NICU, also blindly assessed the NOMAS cluster using the same video recordings. The first rater (rehabilitation doctor) was blinded to clinical factors but not to GA and PMA, and the second rater (an occupational therapist) was blinded to all clinical factors. Findings from the 28 items in the NOMAS were categorized into five clusters according to the suggestions of the Dutch NOMAS working group. An arrhythmic sucking pattern in isolation was classified as cluster 2. The NOMAS cluster 3 was defined as adding the "unable to sustain" item to cluster 2, which was defined by at least one of the following findings: (1) the infant stops sucking completely in the first 2 min of nutritive sucking; (2) the pause is longer than the burst; or (3) the bursts are shorter than three sucks. Cluster 4 refers to the addition of at least one of the "incoordination" items to cluster 2 or 3. Incoordination items defined by the Dutch group include stress signals, such as head bobbing, extraneous movements of the body or limbs during sucking, choking, gagging, coughing, yelping, and grunting (41). Disorganized sucking patterns were further divided into incoordination-positive (cluster 4, which means stress signals) and incoordination-negative groups (clusters 2 and 3).

1.4 Outcome Measures

The primary outcome was the transition time from the initiation of oral feeding (IOF) to FOF according to the presence of the incoordination item among the disorganized sucking patterns. FOF was defined as the ability to feed three or more times only by bottle feeding, which corresponds to the time of removing the nasogastric tube (39).

1.5 Statistical Analysis

We analyzed the data from the presence of the stress signals (incoordination-positive vs. incoordination-negative group, cluster 4 vs. clusters 2 and 3) among disorganized sucking patterns in terms of transition time to FOF and baseline characteristics. The continuous variables, including transition time, were compared between the two groups (cluster 4 vs. clusters 2 and 3) using the Mann–Whitney U test. For the analysis of the categorical variables, the chi-square test or Fisher's exact test was performed. A p-value < 0.05 was considered statistically significant. Cohen's kappa was obtained for the interrater reliability of the two evaluators in the cluster level and the presence of the incoordination item. Univariate linear regression analysis was performed with the transition time to FOF as the dependent variable. Afterward, the multivariate linear regression was carried out through a stepwise selection (entry condition $p < 0.05$, removal condition $p > 0.15$). Analyses were performed using the IBM SPSS 20 software (IBM Corporation, New York, NY, USA).

Table 5. Scoring instructions and interpretation for each Neonatal Oral-Motor Assessment Scale cluster

Cluster	Interpretation	Scoring instruction
1	Normal sucking pattern	
2	Disorganized sucking pattern	Only an arrhythmical sucking pattern, without the observation of "unable to sustain" or "incoordination of suck/swallow and respiration" sucking patterns
3	Disorganized sucking pattern	An arrhythmical and "unable to sustain" suckle pattern The "unable to sustain" suckle pattern includes the following: 1. The infant ceases sucking completely during the first 2 min of nutritive sucking, or 2. The pauses are longer than the burst, or 3. The bursts are shorter than three sucking phases
4	Disorganized sucking pattern	An arrhythmical and "incoordination of suck/ swallow and respiration" sucking patterns that cause stress signals; the "unable to sustain" suckle pattern may or may not be present "Incoordination of suck/swallow and respiration" includes all the following stress signals: nasal flaring, head turning, head bobbing, extraneous movements of the body or limbs, gagging, choking, coughing, yelping, and grunting
5	Dysfunctional sucking pattern	The interruption of sucking activity owing to abnormal movements of the tongue and jaw which includes the following: 1. Excessively wide excursions of the jaw or 2. Minimal excursions: clenching or 3. Flaccid tongue with absent tongue groove or 4. Retracted tongue with posterior humping

2. Developmental Outcome at 8-12 and 18-24 months in Premature Infants

2.1 Subjects

We performed a retrospective review of the medical records of premature infants born between January 2014 and December 2016 at Seoul National University Hospital (SNUH) and referred for consultation to the Division of Pediatric Rehabilitation for sucking difficulty. The results of the NOMAS evaluation were incorporated into the electronic medical records, which were analyzed retrospectively by the authors. We included those infants who were: (i) born very premature (< 32 weeks) or very low birthweight (< 1500 g); (ii) assessed as having a disorganized sucking pattern in the NOMAS before 40 weeks postmenstrual age (PMA); and (iii) evaluated using the cognitive domain of the Bayley Scale of Infant Development, third edition (Bayley-III), at both 8-12 and 18-24 months of age. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards. Ethical approval was obtained from the SNUH Institutional Review Board No. 1711-128-901.

2.2 NOMAS Evaluation

NOMAS evaluation was performed within 72 hours from commencement of feeding on all neonates referred to the division of pediatric rehabilitation consultation regarding sucking difficulty. The evaluation was done by analyzing the video recording of sucking activity (34). Video recording included a close-up lateral view of the mouth, jaw, and neck. Only bottle feeding was analyzed. The videotaping started before the lip reached the bottle nipple, and was stopped after recording for more than 2 minutes since the initiation of the oral feeding. Bottle feeding was performed by a neonatal intensive care unit (NICU) nurse during the video recordings. Sucking difficulties were categorized into normal, disorganized, and dysfunctional sucking pattern according to the classification of original version of NOMAS (42).

2.3 Conversion to NOMAS Cluster System

For this study, disorganized sucking pattern was divided into three clusters (cluster 2, 3, or 4) according to the cluster system presented by the Dutch group as shown in Table 5 (41). The existing NOMAS video recordings were re-evaluated and reclassified according to the cluster system by a rehabilitation doctor (one of the co-authors of this paper) who has been certified by Marjorie Meyer Palmer, the original developer of the NOMAS. The occupational therapist, who had more than 5 years of experience in rehabilitative interventions for swallowing function in infants at the NICU, also blindly evaluated the NOMAS cluster using the same video recordings. The first evaluator (rehabilitation physician) was blinded to clinical factors, but not to diagnosis, gestational age (GA), and PMA. The second evaluator (occupational therapist) was blinded to all clinical factors.

2.4 Medical Records Acquisition

Premature infants included in this study were evaluated using the Bayley Scales of

Infant Development, third edition (Bayley-III), cognition composite score at 8-12 and 18-24 months of age (corrected for prematurity). In addition to 18-24 months of corrected age, 8 to 12 months corrected age was chosen because it is known to be a good time to identify the suspicion or presence of cerebral palsy or other neurologic abnormality. It is also known to be an appropriate time for the first developmental assessment to be performed, usually the Bayley Scales of Infant Development, because the children show little stranger anxiety at this age and most are cooperative (63).

Through a retrospective electrical medical record review, GA; sex; brain sonographic finding, such as germinal matrix hemorrhage-intraventricular hemorrhage (GMH-IVH); PMA at initiation of oral feeding (IOF, defined as oral consumption of at least 5 ml of milk); PMA at the time of NOMAS evaluation; small for gestational age (SGA) or appropriate for gestational age (AGA); severity of bronchopulmonary dysplasia (BPD); total parenteral nutrition (TPN) duration; birth weight (BW); development of sepsis; and 5 minute Apgar score were obtained.

2.5 Statistical Analysis

Cohen's kappa was obtained for the interrater reliability of the two evaluators. The cognitive domain of Bayley-III was compared between the incoordination-positive (cluster 4) and incoordination-negative groups (clusters 2 and 3) at 8-12 and 18-24 months of age using the independent t-test. Pearson's correlation coefficient r was calculated between continuous variables (GA and BW) and cognition composite score at 18-24 months. Multiple linear regression was performed with the Bayley-III cognition composite score at 18-24 months as the dependent variable. Analyses were performed using IBM SPSS version 20 software (IBM Corp., Armonk, NY, USA). A probability value <0.05 was considered significant in all analyses.

3. Functional Oral Intake Scale for Infants

3.1 Participants

The following inclusion criteria were applied to potential subjects: (1) participation in the VFSS to evaluate a swallowing disorder at ≤1 year of age between 2011 and 2017 and (2) recording of the dietary status at the time of the VFSS by a nutritionist. All study-related procedures were performed in accordance with the ethical standards of the institutional and/or national research committee and the 1964 Declaration of Helsinki. Ethical approval for the study was obtained from the Seoul National University Hospital Institutional Review Board (IRB) (No. 1807-189-963), which waived the requirement for informed consent due to the retrospective nature of the study.

3.2 FOIS for Infants

A seven-point ordinal FOIS has been validated in adults (Table 3) (43). As noted in the Introduction, a modified five-point version of the FOIS was developed to account for normal infant development (Table 6) (43). At FOIS levels 1, 2, and 3, the same criteria as those for adults were used in this study. However, we divided full oral feeding (FOF) into two categories: (1) achievement of oral diet expansion, the initiation of pureed foods before 9 months, and the initiation of mashed foods and those with soft lumps before 12 months as normal developmental stages; and (2) no achievement of this oral diet expansion

3.3 Inter-rater Reliability

The infants' caregivers were interviewed by a nutritionist, who recorded the type, amount, and consistency of food and liquid intakes, tube dependency, and total nutrient intake. Two occupational therapists with >2 years of experience in swallowing therapy retrospectively reviewed the nutritionist's medical records and assigned FOIS levels.

3.4 Validity

Cross-validity was determined by comparing the infantile FOIS scores with the categorical ratings of swallowing impairment/aspiration severity and on the basis of the presence of swallowing impairment/aspiration determined by the VFSS (43). These tools were also used to validate the original FOIS (43). The swallowing impairment scale score was rated as 5 (normal) in the absence of a swallowing abnormality and as 1 (complete) if there was no response to a food stimulus. The aspiration impairment scale score was rated as 5 (normal) if the contrast material did not enter the true vocal cord and as 1 (complete) if the infant showed frank aspiration without reflex coughing (Table 7).

3.5 Nutritional Contribution of Oral Feeding in Infants with Partial Oral Feeding

For infants with partial oral feeding (POF), the calorie contribution of oral feeding to the total caloric intake was estimated based on the same records used for the FOIS evaluation. Calories were calculated using the web version of CAN-Pro 5.0

software (http://www.kns.or.kr/English/index.asp, The Korean Science and Technology Center, Gangnam-gu, Seoul, Korea), which was developed by the Korean Nutrition Society for the nutritional evaluation of individuals or groups. If any food was not registered in the program, calories were calculated from the information printed on the product container. We also investigated whether infants with POF at the FOIS evaluation had achieved FOF within 1 year of the evaluation and used this information to estimate whether the caloric contribution, as well as consistency of oral feeding, affected the feeding outcomes.

3.6 Statistics

For the five-point FOIS for infants, Cohen's κ and Cronbach's α coefficient were calculated as measures of the inter-rater reliability between the two evaluators. To assess cross-validity, Spearman's ρ-test was used to assess correlations between the FOIS for infants with swallowing impairments and aspiration severity ratings. We used Cramer's V (dichotomized data) to determine the association between the FOIS for infants and the presence or absence of swallowing impairment and aspiration. Infants with POF were stratified according to whether they achieved FOF or not at 1 year after the evaluation, as determined by the caloric contribution of the oral intake at the time of the initial FOIS evaluation. Differences between these two groups were analyzed using an independent ttest. $P < 0.05$ was considered statistically significant. Analyses were performed using SPSS ver. 23.0 (IBM Corporation, Armonk, NY, USA).

Table 6. Modified Functional Oral Intake Scale (FOIS): children <1 year

Levels	Oral Intake Functionality
1	Nothing by mouth
2	Tube dependent with minimal attempts of food or liquids
3	Tube dependent with consistent oral intake of food or liquids
4-6	Expansion of oral diet not reached[1]
7	Expansion of oral diet reached[1]

[1] Normal expansion of oral diet was considered reached when introduction of solid foods in pureed form started before 9 months of age and the introduction of mashed foods and soft lumps started before 12 months of age

Table 7. Videofluoroscopic diagnostic criteria for dysphagia and aspiration

Swallowing impairment (dysphagia)	
Normal	No swallowing abnormality detected
Mild	Slight delay in bolus control initiation of the swallow or transport, resulting in some stasis of material without laryngeal penetration
Moderate	Moderate delay in bolus control, initiation of the swallow or transport, resulting in coating or stasis of materials within the oral cavity and/or pharynx, slight laryngeal penetration or trace aspiration of thin liquid only
Severe	Substantial delay in bolus control, initiation of swallow and bolus transport; significant (>10% of bolus) penetratio and/or aspiration of one or all consistencies
Complete	No response to food stimulus; the initiation of a swallow sequence is not obtained over several trials
Aspiration	
Normal	No entry of contrast material through the true vocal cords
Mild	Trace of contrast materials through the vocal cords
Moderate	Entry of <10% of bolus through the true vocal cords
Severe	Entry of >10% of bolus through the true vocal cords
Complete	Frank aspiration of materials through the vocal cords without observable reaction by the patient

RESULTS

1. Transition Time in Premature Infants

1.1 Subjects

From 148 infants with the NOMAS assessments, 14 infants with oromotor disorganization (lack of rhythm of total sucking activity), and 5 infants with oromotor dysfunction (interruption in the feeding process due to abnormal movements of the tongue and jaw) were excluded because the PMA at the time of the NOMAS assessment exceeded 50 weeks, or because GA exceeded 37 weeks. Of the remaining 129 NOMAS evaluation records, 18 cases were further excluded because the infants received postnatal surgery resulting in the interruption of oral feeding (n = 6) or because the NOMAS assessment point was more than 72 h after oral feeding initiation (n = 12). Of these 111 preterm infants, 109 preterm infants belonged to the disorganization group and were included in our study: incoordination-negative group (clusters 2 and 3) and incoordination-positive group (cluster 4, presence of stress signals) (Figure 1). A total of 109 premature infants were included in the analysis.

1.2 Clinical Characteristics

The baseline characteristics and the differences according to the presence of an incoordination item (stress signals) among the disorganized sucking patterns are summarized in Table 8. Subjects in the incoordination-positive group, showed a younger GA, and a lower BW compared with those in the incoordination negative group, among the disorganized sucking pattern preterm infants. However, there were no differences between these two groups in PMA during the NOMAS evaluation. The NOMAS cluster according to PMA is shown in figure 2.

1.3 Interrater Reliability for NOMAS Clustering

The two evaluators agreed on the cluster level for 103 out of the 109 recordings (Cohen's $\kappa = 0.825$). Disagreement occurred between clusters 3 and 4 (three infants) and clusters 2 and 3 (three infants). The reliability of the two evaluators on the presence of the incoordination items (cluster 4 vs. cluster 2 or 3) was higher with the Cohen's κ of 0.933, with only three disagreements occurring.

1.4 Time to FOF according to Presence of Incoordination Item among Disorganized Sucking

The median [range] transition time to FOF of 109 preterm infants was 9 days [1–121 days]. As shown in Figure 3, there were differences in the transition time to FOF between the incoordination-positive and -negative groups. The incoordination positive group (cluster 4, presence of stress signals) had a longer transition time of 22 days [4–121 days] compared with those of the incoordination-negative group (cluster 2 or 3, median 6 days; range: 1–25 days).

1.5 Factors related to Transition Time to FOF

A univariate analysis was performed to estimate factors related to the transition time (Table 9). In the univariate analysis, the presence of incoordination items (NOMAS cluster 4 vs. clusters 2 and 3), BW, TPN duration, NIPPV duration and the presence of moderate to severe BPD, pulmonary hypertension, sepsis, SGA, and NEC were determined to represent factors affecting the transition time. In the multivariate analysis, the R value of the final model was 0.699, and the included variables were TPN duration, SGA, and the presence of incoordination items (NOMAS cluster 4 vs. clusters 2 and 3) (Table 10).

Table 8. Subjects' characteristics with disorganized sucking pattern in the NOMAS

Characteristic	Total (n=109)	Incoordination negative group (n=77)	Incoordination positive group (n=32)	P-value
GA at birth (days)	209.23(20.47)	213.58(18.74)	198.75 (20.94)	<0.001
Females/Males	57/52	42/35	15/17	0.465
Birthweight (kg)	1.27 [0.42,3.05]	1.3 [0.48,3.05]	1.02 [0.42,2.45]	0.002
TPN duration (days)	9 [0,73]	7 [0,59]	17 [0,73]	<0.001
Days on non-invasive ventilation	18 [0,88]	12 [0,75]	36 [0,88]	<0.001
PMA at NOMAS evaluation (days)	241 [203,347]	242 [224,300]	240 [203,347]	0.984
Apgar score (1 min)	4 [0,9]	5 [0,9]	3 [0,7]	0.001
Apgar score (5 min)	7 [0,10]	7 [0,10]	6 [2,9]	<0.001
Moderate to severe BPD	27 (24.8)	14 (18.18)	13 (40.63)	0.020
Ultrasonic finding, n (%)				0.593
Normal	52 (47.71)	42 (54.55)	10 (31.25)	
Grade 1–2 GMH or IVH	52 (47.71)	32 (41.56)	20 (62.50)	
Grade 3-4 GMH or IVH	5 (4.59)	3 (3.90)	2 (6.25)	
Invasive ventilator use	56 (51.38)	32 (41.56)	24 (75.0)	0.001
Sepsis	8 (7.34)	1 (1.30)	7 (21.88)	<0.001
Necrotizing enterocolitis	4 (3.67)	0 (0)	4 (12.5)	0.002
Respiratory distress syndrome	75 (68.81)	49 (63.64)	26 (81.25)	0.071
Small for gestational age	13 (11.93)	8 (10.39)	5 (15.63)	0.442
Pulmonary hypertension	7 (6.42)	4 (5.19)	3 (9.38)	0.418

Continuous variables following the normal distribution are denoted by mean (SD), while continuous variables which did not follow the normal distribution are denoted by Median [range]. Categorical variables are denoted by n (%).

Abbreviations: GA, gestational age; TPN, total parenteral nutrition; PMA, postmenstrual age; NOMAS, Neonatal Oral-Motor Assessment Scale; BPD, bronchopulmonary dysplasia; GMH, germinal matrix hemorrhage; IVH, intraventricular hemorrhage.

Table 9. Univariate linear regression analysis for the transition time to FOF in preterm infants with disorganized sucking patterns

Variable	B	95% CI for B		P-value
Presence of stress signals (NOMAS cluster 4 *versus* cluster 2,3)	19.351	16.704	21.998	<.0001
Male *versus* female	1.890	-3.958	7.738	0.523
Gestational age	-0.131	-0.273	0.010	0.069
Birth weight	-9.187	-14.790	-3.584	0.002
TPN duration	0.626	0.443	0.809	<.0001
NIPPV duration	0.309	0.188	0.431	<.0001
Moderate/severe BPD *versus* none/mild BPD	11.454	5.040	17.868	0.001
Grade 3/4 GMH, IVH *versus* none, grade 1/2 GMH, IVH	0.165	-6.891	7.221	0.981
Sepsis yes vs. no	21.835	11.423	32.248	<.0001
NEC yes *versus* no	10.233	-5.208	25.674	0.192
RDS yes *versus* no	4.481	-1.777	10.739	0.159
SGA yes *versus* no	12.546	3.843	21.250	0.005
Pulmonary hypertension yes *versus* no	13.817	2.176	25.457	0.021
Apgar 1	-0.690	-1.995	0.614	0.297
Apgar 5	-1.209	-2.565	0.148	0.080

Abbreviations: FOF, full oral feeding; NOMAS, Neonatal Oral-Motor Assessment Scale; BPD, bronchopulmonary dysplasia; TPN, total parenteral nutrition; NIPPV, non-invasive positive pressure ventilation; GMH, germinal matrix hemorrhage; IVH, intraventricular hemorrhage; NEC, necrotizing enterocolitis; RDS, respiratory distress syndrome; SGA, small for gestational age.

Table 10. Multiple linear regression analysis for transition time to FOF in preterm infants with feeding difficulty

Variable	B	95% CI for B	Beta	t	P value
Presence of stress signals (NOMAS cluster 4 *versus* cluster 2 and 3)	14.063	11.507-16.619	0.419	7.310	<0.001
TPN duration (days)	0.407	0.320-0.494	0.357	4.658	<0.001
SGA yes *versus* no	9.065	2.048-16.082	0.192	2.562	0.012

Abbreviations: FOF, full oral feeding; NOMAS, Neonatal Oral-Motor Assessment Scale; TPN, Total parenteral nutrition; SGA, small for gestational age

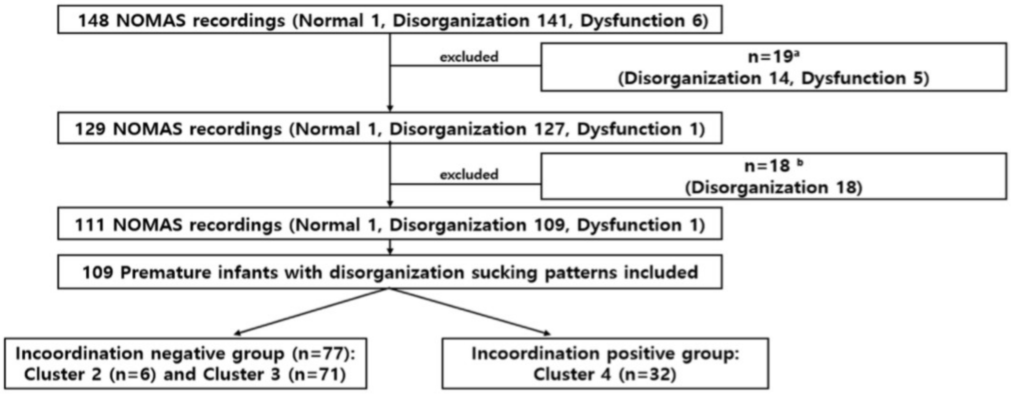

Figure 1. Study flowchart. Of the 148 infants evaluated, time to full oral feeding was compared in 109 preterm infants with disorganized sucking patterns. a Excluded if assessment of the NOMAS was performed at >postmenstrual age 50 weeks or GA ≥ 37 weeks. b Excluded if the infant received postnatal surgery resulting in the interruption of oral feeding (n = 6) or the NOMAS assessment point was later than 72 h after oral feeding initiation (n = 12).

Abbreviations: NOMAS, Neonatal Oral-Motor Assessment Scale;

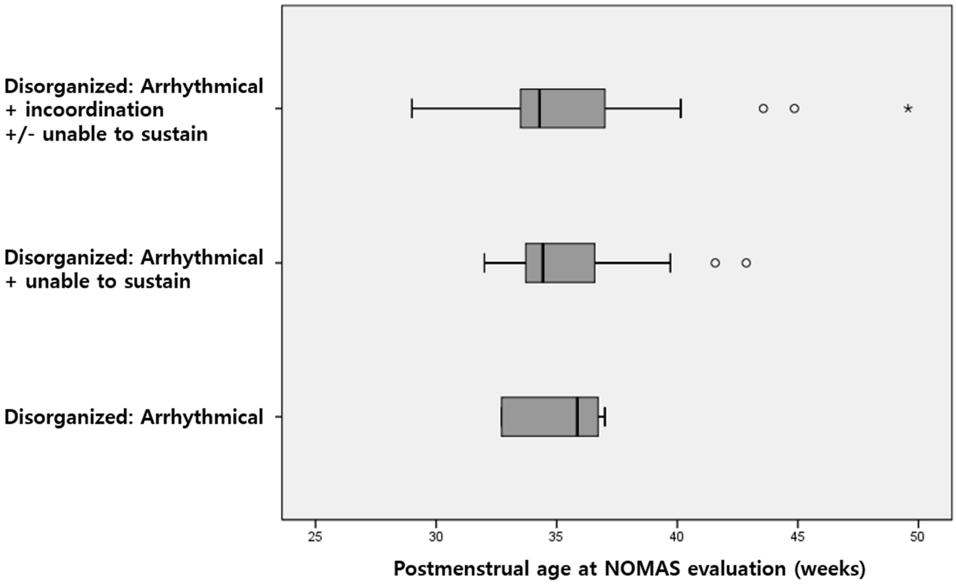

Figure 2. NOMAS cluster according to PMA.

No differences in PMA among the three clusters with disorganized sucking patterns (p=0.564).

Abbreviations: NOMAS, Neonatal Oral-Motor Assessment Scale; PMA, postmenstrual age

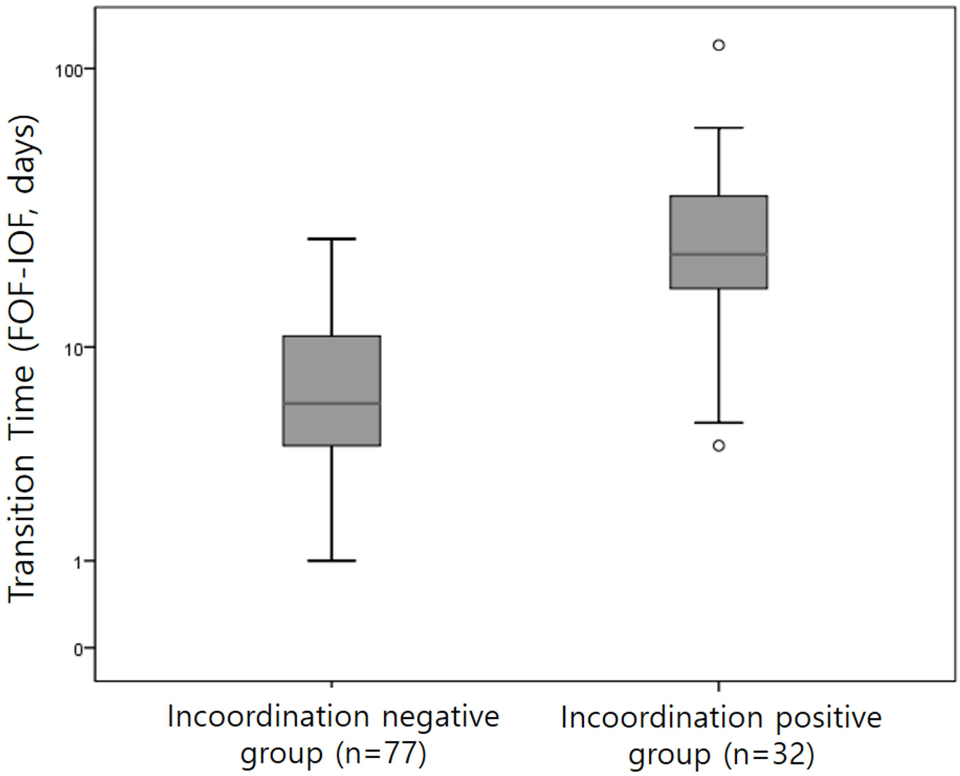

Figure 3. The transition time from the initiation of oral feeding (IOF) to full oral feeding (FOF) between the two groups

$p < 0.001$ by the Mann–Whitney U test.

2. Developmental Outcome at 8-12 and 18-24 months in Premature Infants

2.1 Subjects

A total of 71 premature infants had both a Bayley-III cognitive domain and NOMAS score. One premature infant belonging to cluster 5, who had a grade III GMH-IVH and was a cardiopulmonary resuscitation survivor, showed delayed cognitive development at 8-12 months of age and was excluded from the analysis since the infant did not belong to the disorganized sucking pattern in the NOMAS cluster system. Clinical characteristics of the premature infants included in the analysis (n=70) are shown in Table 11. Among the premature infants with a disorganized sucking pattern in NOMAS, there were four premature infants in cluster 2, 44 premature infants in cluster 3, and 22 premature infants in cluster 4.

2.2 Interrater reliability for the NOMAS cluster system

The two evaluators agreed on the cluster levels for 65 of 70 recordings (Cohen's K = 0.853). Disagreement occurred between clusters 2 and 3 (1 infants) and Clusters 3 and 4 (4 infants). The reliability of the two evaluators on the presence of incoordination items (cluster 4 vs. clusters 2 or 3) was higher with a Cohen's K value of 0.864, with four disagreements being documented.

2.3 Bayley-III cognition composite score at 8-12 and 18-24 months according

to the incoordination findings in NOMAS

The average Bayley-III cognition composite scores were higher in incoordination-negative groups (n=48, 103.0±11.3) than the incoordination-positive group (n=22, 92.5±15.6) at 8-12 months (p=0.002; Figure 4a). The average Bayley-III cognition composite scores at 18-24 months were higher in incoordination-negative groups (n=46, 100.7±11.5) than the incoordination-positive (n=21, 90.0±17.9) groups (p=0.005; Figure 4b).

2.4 Baseline characteristics related to cognitive development at 18-24 months

Independent t-test was performed to investigate the baseline characteristics related to the Bayley-III cognition composite score at 18-24 months (Table 12). The Bayley-III cognition composite scores at 18-24 months were different according to the presence of SGA, moderate to severe BPD, uncoordinated sucking pattern (incoordination-positive group vs. incoordination-negative group; cluster 4 vs. clusters 2 or 3), and grades 3 or 4 GMH-IVH. GA (R=0.312, p=0.010) and 5-minute Apgar score (R=0.333, p=0.006, for Spearman's correlation test) were found to be significantly correlated with Bayley-III cognition composite score at 18-24 months. All clinical variables were included in the multiple linear regression analysis model with stepwise selection to control multicollinearity between independent variables. In the multiple linear regression analysis, the R^2 value of the final model was 0.331, and the variables included in this model were the presence of uncoordinated sucking pattern, grades 3 or 4 GMH-IVH, and moderate to severe BPD (Table 13).

2.5 Bayley-III Motor Composite Score at 8-12 Months According to the Presence of Incoordination Findings in NOMAS

Among 70 subjects, 18 infants did not perform motor evaluation and were excluded from the analysis. The average Bayley-III motor composite score was 92.59 (SD 15.56) for the incoordination-positive group (n=17) and 96.86 (SD 13.85) for the incoordination-negative group (n=35). Although incoordination-negative group showed higher motor composite score than the incoordination-positive group, this was not significant at 8-12 months (p=0.344 by independent t-test, figure 5a). However, average Bayley-III motor composite scores at 18-24 months were higher in incoordination-negative groups (n=46, 100.0±8.9) than the incoordination-positive (n=21, 89.5±18.2) groups (p=0.020; Figure 5b).

Table 11. Characteristics of premature infants (n = 70) included in the final analysis for cognitive development

Variable	Total (n=70)	Incoordination-positive group (n=22)	Incoordination-negative group (n=48)	p value
Male/female	33/37	13/9	20/28	0.175
GA at birth (weeks)	29.0 (2.3)	27.6 (2.1)	29.6 (2.1)	0.001
Birth weight (g)	1124.7 (344.5)	952.3 (346.1)	1203 (316.9)	0.006
PMA at NOMAS evaluation (weeks)	34.8 (1.5)	34.9 (1.7)	34.8 (1.5)	0.757
Apgar score (5 min)	6.6 (1.9)	5.9 (1.8)	6.9 (1.9)	0.032
SGA, n (%)	8 (11.4)	4 (18.2)	4 (8.3)	0.229
Moderate to severe BPD, n (%)	23 (32.9)	12 (54.5)	11 (22.9)	0.009
GMH-IVH grade 3-4, n (%)	4 (5.7)	1 (4.5)	3 (6.3)	0.775
Sepsis, n (%)	8 (11.4)	7 (31.8)	1 (2.1)	<0.001

Abbreviations: GA, gestational age; PMA, postmenstrual age; NOMAS, Neonatal Oral-Motor Assessment Scale; SGA, small for gestational age; BPD, bronchopulmonary dysplasia; GMH-IVH, germinal matrix hemorrhage-intraventricular hemorrhage.

Table 12. Bayley-III cognition composite score at 18-24 months of corrected age according to baseline characteristics of the premature infants (n=67).

		n	mean	SD	p value
Respiratory distress syndrome	Yes	49	95.2	15.3	0.049
	No	18	103.1	10.7	
Small for gestational age	Yes	8	85.0	13.9	0.010
	No	59	99.0	13.9	
Moderate to severe BPD	Yes	23	89.1	16.5	0.001
	No	44	101.6	11.5	
Necrotizing enterocolitis	Yes	4	88.8	4.8	0.240
	No	62	97.6	14.8	
Sepsis	Yes	8	90.0	17.3	0.131
	No	59	98.3	14.0	
Pulmonary hypertension	Yes	6	95.8	21.8	0.796
	No	61	97.5	13.9	
Incoordination findings in NOMAS	Yes	21	90.0	17.9	0.005
	No	46	100.7	11.5	
Grades 3 or 4 GMH-IVH	Yes	3	71.7	14.4	0.001
	No	64	98.5	13.5	

Abbreviations: SD, standard deviation; BPD, bronchopulmonary dysplasia; NOMAS, Neonatal Oral-Motor Assessment Scale; GMH-IVH, germinal matrix hemorrhage–intraventricular hemorrhage.

Table 13. Multiple linear regression analysis: Bayley-III cognition composite score at 18-24 months of corrected age

Variable	B	95% CI for B	Beta	t	P value
Incoordination-positive group on NOMAS	-7.737	-14.521 to -0.952	-0.249	-2.528	0.026
Grade 3 or 4 GMH-IVH	-23.818	-38.371 to -9.265	-0.341	-3.271	0.002
Moderate to severe BPD	-8.477	-15.178 to -1.775	-0.279	-2.528	0.014

Abbreviations: CI, confidence interval; NOMAS, Neonatal Oral-Motor Assessment Scale; GMH-IVH, germinal matrix hemorrhage–intraventricular hemorrhage; BPD, bronchopulmonary dysplasia.

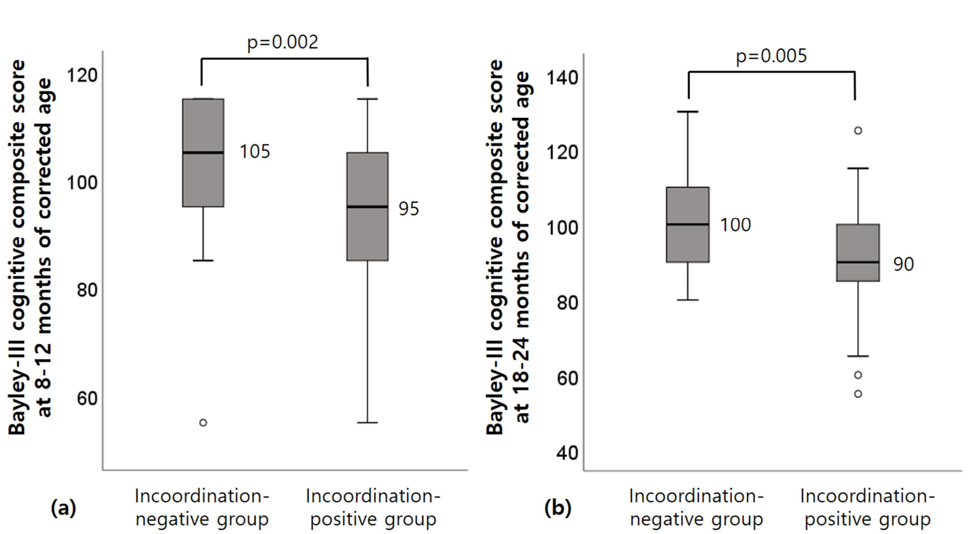

Figure 4. Bayley-III cognition composite score based on incoordination findings on the Neonatal Oral-Motor Assessment Scale

(a) At 8-12 months of age (corrected for prematurity). (b) At 18-24 months of age (corrected for prematurity). The median Bayley-III cognition composite score of each group is represented.

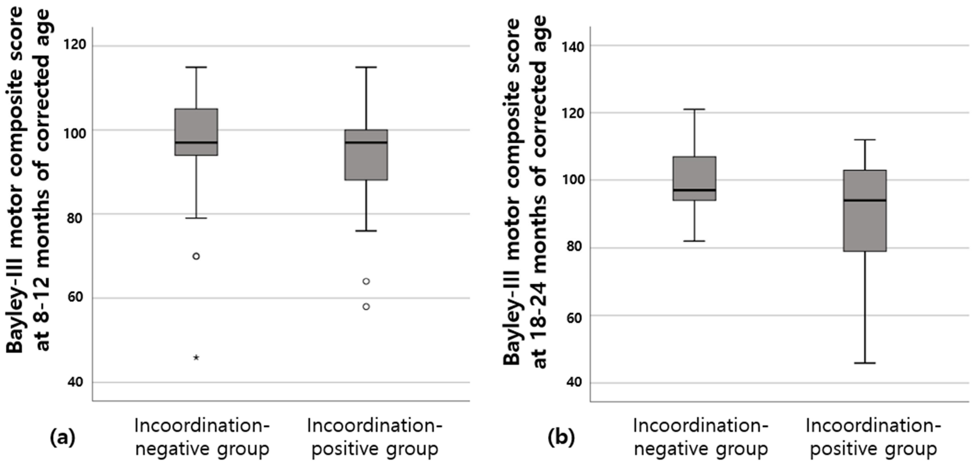

Figure 5. Bayley-III motor composite score based on incoordination findings on the Neonatal Oral-Motor Assessment Scale

(a) At 8-12 months of age (corrected for prematurity). (b) At 18-24 months of age (corrected for prematurity).

*Among 70 subjects, 18 infants did not perform motor evaluation at 8-12 months of age and were excluded from the analysis.

3. Functional Oral Intake Scale for Infants

3.1 Subjects

Data were obtained from 201 infants (mean age: 199 days, range: 22–364 days) who underwent a VFSS between 2011 and 2017. The baseline characteristics and main diagnoses of the subjects are presented in Table 14. Brain lesions were found in 63 infants, which included hypoxic ischemic encephalopathy, encephalitis, intracerebral hemorrhage, brain tumor, corpus callosal dysgenesis, and hydrocephalus. Myopathy/motor neuron disease including spinal muscular atrophy, mitochondrial myopathy, myotubular myopathy, Fukuyama congenital muscular dystrophy, and congenital muscular dystrophy was found in 21 infants. The non-oral feeding, POF, and FOF groups did not differ significantly in age at the time of FOIS evaluation. VFSS findings with aspiration of liquid were found in 61 infants among 201 infants. The swallowing impairment scale (Table 7) scores ranged from 1 to 5 with a median of 4 (interquartile range: 3–4) with 38 infants having a score of 5, 78 with a score of 4, 53 with a score of 3, 31 with a score of 2, and 1 with a score of 1.

3.2 Inter-rater Reliability of the FOIS for Infants

The two occupational therapists achieved a high level of absolute agreement (95.5%) when applying the FOIS for infants (Table 6), as shown in Table 15 (κ = 0.935; intraclass correlation coefficient [ICC] = 0.996; 95% confidence interval [CI]: 0.995–0.997). The main disagreements were observed between FOIS levels 2 and 3 (n = 3) and levels 4 and 5 (n = 5).

3.3 Validity

This study identified significant associations between the subject's level on the FOIS for infants and the presence ($p = 0.014$, $V = 0.249$) and severity ($p = 0.001$, $r = 0.229$) of aspiration during the VFSS. The infantile FOIS ratings correlated significantly with the severity ($p = 0.040$, $r = 0.145$), but not the presence of dysphagia ($p = 0.188$, $V = 0.175$).

3.4 Nutritional Contribution of Oral Feeding in Infants with POF

This analysis included 33 infants who were receiving POF at the time of the VFSS and for whom nutritional records at 1 year after the VFSS were available (Figure 6). Among them, 26 infants achieved FOF after 1 year, and their mean nutritional contribution from oral feeding at the time of VFSS was 28.46 ± 22.79%, which was higher than 6.00 ± 5.45% in the seven infants who maintained a POF status ($p < 0.001$, Figure 7).

3.5 Oral Feeding Outcome in Infants with NOF

Among 80 infants with NOF at the time of the VFSS (Figure 6), records about the dietary status after one year was obtained in 60 infants. Among them, 13 infants achieved FOF and 17 infants achieved POF after 1 year. However, 30 infants maintained NOF.

Table 14. Characteristics of subjects at the time of the videofluoroscopic swallowing study

Characteristics	Eating abilities in infants		
	Non-oral feeding (n = 80)	Partial oral feeding (n = 44)	Full oral feeding (n = 77)
Female sex (%)	38 (47.5)	21 (47.7)	36 (46.8)
Age (range), days	171 (22–364)	233 (65–349)	210 (53–364)
Main diagnosis, n (%)			
Brain lesion	25 (31.3)	8 (18.2)	30 (39.0)
Myopathy/motor neuron disease	10 (12.5)	5 (11.4)	6 (7.8)
Gastrointestinal	6 (7.5)	6 (13.6)	7 (9.1)
Cardiac	4 (5.0)	3 (6.8)	5 (6.5)
Otolaryngology	7 (8.8)	4 (9.1)	10 (13.0)
Metabolic	6 (7.5)	0 (0)	1 (1.3)
Pulmonary	4 (5.0)	3 (6.8)	4 (5.2)
Immunologic	0 (0)	0 (0)	2 (2.6)
Unknown	1 (1.3)	0 (0)	1 (1.3)
Syndrome	17 (21.3)	15 (34.1)	11 (14.3)
Pierre Robin Syndrome	1	2	2
Kabuki syndrome	1	1	
Zellweger syndrome	1		
Beckwith-Weidemann syndrome			1
Schinzel-Giedion syndrome			1
VACTERL syndrome	1		
Cornelia de lange syndrome		2	
Patau syndrome	1		
Sotos syndrome			3
Noonan syndrome	1		
Down syndrome		1	1
Miller-Dieker syndrome	1		1
Mobius syndrome		1	
CHARGE syndrome	2	2	
Treacher Collins syndrome	1	1	1
Russel Silver syndrome	1		
Prader Willi syndrome	2		
Goldenhar syndrome	1	2	
CATCH 22 syndrome	3	1	
Smith-limli-opitz syndrome		1	
Wolf Hirschhorn syndrome			1
Mosaic 22q13 deletion		1	

syndrome

Table 15. Inter-rater reliability of the FOIS for infants

	Rater 2					
Rater 1	1	2	3	4	5	Total
1	79	1[a]	0	0	0	80
2	0	2	1	0	0	3
3	0	2	39	0	0	41
4	0	0	0	7	3	10
5	0	0	0	2	65	67
Total	79	5	40	9	68	201

Shaded values indicate agreement between the evaluators.
Abbreviations: FOIS, functional oral intake scale; TPN, total parenteral nutrition
[a] TPN was performed without tube or oral feeding at the time of the examination. Rater 2 misinterpreted the meaning of TPN and classified it as FOIS level 2.

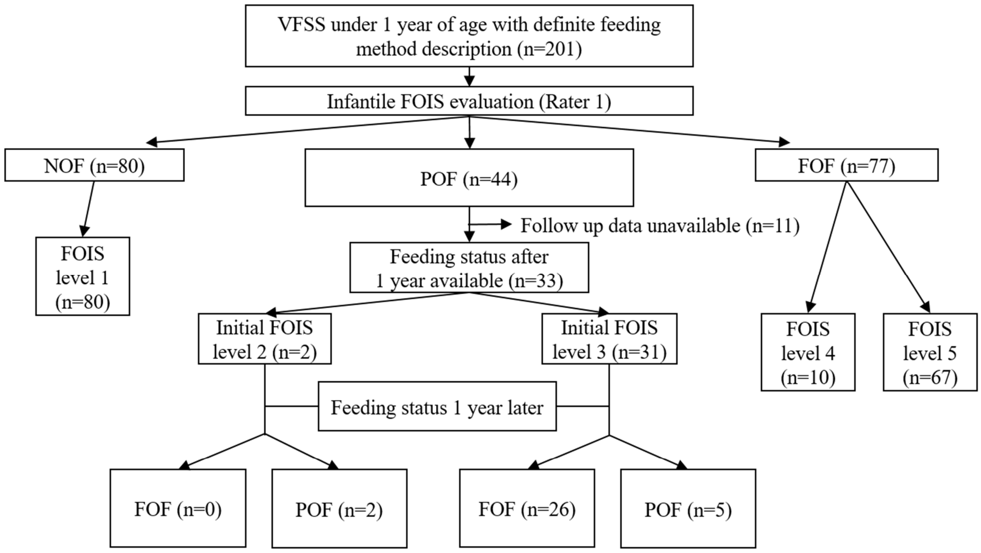

Figure 6. Acquisition of data relevant to the FOIS for infants and the feeding status after 1 year.

Abbreviations: FOIS, functional oral intake scale; VFSS, videofluoroscopic swallowing study; NOF, non-oral feeding; POF, partial oral feeding; FOF, full oral feeding.

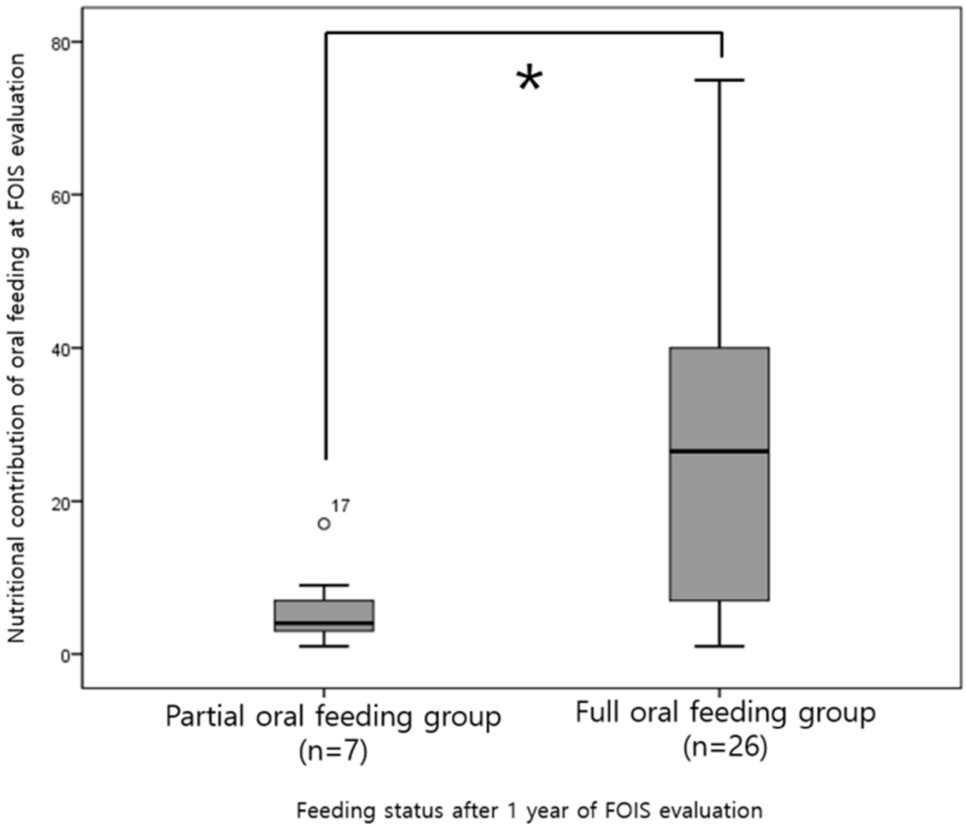

Figure 7. Comparison of the caloric contributions of oral intake among POF infants stratified according to the achievement or non-achievement of FOF after 1 year

*p < 0.001. Abbreviations: POF, partial oral feeding; FOF, full oral feeding.

DISCUSSION

1. Summary of the Results

In premature infants, incoordinated sucking patterns observed before 50 weeks of PMA might delay time to full oral feeding and are also associated with cognitive development evaluated at both 8-12 and 18-24 months (corrected for prematurity). In infants under 1 year of age, it is feasible to use FOIS to assess the eating ability.

1.1 Transition Time in Premature Infants

In the first subject of the thesis, premature infants with feeding difficulties corresponding to NOMAS cluster 4, which means the presence of stress signals (Arrhythmical + incoordination ± unable to sustain), showed a longer transit time to FOF than did those of the incoordination-negative group (clusters 2 and 3).

1.2 Developmental Outcome at 8-12 and 18-24 months in Premature Infants

The results of the second subject of the thesis suggest that incoordination of SSR sucking pattern could be more relevant factor to the development in the cognitive domain at both 8-12 and 18-24 months than arrhythmical sucking or inability to sustain pattern.

1.3 Functional Oral Intake Scale for Infants

In the last subject of the thesis, we selected the modified FOIS that is specific to infants, proposed by Coppens et al. (43), and verified the validity and reliability of the scale. The FOIS for infants, which reflects the expansion of oral diet in infants, showed adequate reliability and validity.

2. Interpretation

2.1 Transition Time in Premature Infants

An interesting finding is that patients with SSR coordination reached early FOF quicker than did those with incoordination. For successful oral feeding, premature infants should achieve maturity with developments in the central and enteric nervous system-mediated reflexes involved in the activation, control, coordination, and adaptation of oromotor, aerodigestive, and peristaltic functions (64–66). In coordination-positive patients, these reflexes might be activated in the critical window of the maturational timeline, leading them to ultimately reach early FOF. These findings suggest that preservation of neuromuscular and pattern generator functions could be augmented with feeding therapies. Clusters 2 and 3 may also require therapy, but the transition time is much shorter than cluster 4, which is likely to be less prominent in terms of reducing the transition time.

The stress signals observed in the premature infants may be due to incomplete maturation of the aerodigestive system. Jadcherla et al. reported that swallow-integrated esophageal motility is an important factor in distinguishing between a primary oral feeder and a chronic tube feeder (65). Swallow frequency, swallow propagation, presence of adaptive peristaltic reflexes, oral feeding challenge test results, and upper esophageal sphincter tone were also reported to be important factors in feeding outcomes (65), demonstrating that swallowing is a complex task that requires close regulation and coordination between aerodigestive reflexes and respiratory status. The regulation of swallowing and aerodigestive pathways involves vagal and supranuclear neural pathways and is influenced by perinatal events, prematurity, and inflammatory state. Therefore, if stress signals are observed in a premature infant, the period until FOF is considered to be somewhat delayed.

2.2 Developmental Outcome at 8-12 and 18-24 months in Premature Infants

Premature infants frequently experience difficulty in sucking, thereby delaying the transition from tube to full oral feeding (67–69). According to the NOMAS cluster system, sucking difficulty can be classified as arrhythmical sucking pattern, inability to sustain sucking pattern, incoordination of SSR sucking pattern, and dysfunctional sucking pattern. Although the dysfunctional sucking pattern is known to be associated with poor developmental outcome, the relationship with developmental outcome is not well known in other patterns. The results of this study suggest that incoordination of SSR sucking pattern could be more relevant factor to the development in the cognitive domain at both 8-12 and 18-24 months than arrhythmical sucking or inability to sustain pattern.

Premature infants need time for the maturation of central and enteric nervous system-mediated reflexes involved in the activation, control, coordination, and adaptation of oromotor, aerodigestive, and peristaltic function. Also, pharyngo-esophageal stimulus causes regional (pharyngo-esophageal reflex within the upper digestive tract), and extraregional (pulmonary and cardiac systems), and neurocognitive responses [64]. Interaction between the aerodigestive system and the neurocognitive response might explain the association between the uncoordinated sucking pattern and cognitive development.

2.3 Functional Oral Intake Scale for Infants

Modified FOIS versions for the pediatric population have never been validated and tested for reliability. Additionally, the scales proposed before were used for young children as well as infants. Since oral diet expansions occur during the infantile period, the functional oral intake of infants should be assessed separately from that of young children. In this study, we observed a high level of inter-rater reliability for the FOIS for infants, which was similar to that in other studies. In the present study, the FOIS for children was associated with aspiration and dysphagia severity identified from the VFSS. This was similar to the results of a previous study, which evaluated the FOIS in stroke patients (43). Accordingly, the FOIS for infants may be appropriate for documenting feeding abilities and evaluating the e□ectiveness of interventions. In the NOF group, 13 among 60 infants reached FOF after one year. However, 26 out of 33 infants achieved FOF after one year in POF group. This finding suggests that oral feeding outcome in infants with some calorie contribution by mouth was better than NOF group.

3. Comparison with Previous Studies

3.1 Transition Time in Premature Infants

Neonatal Oral-Motor Assessment Scale defines incoordination as an observational finding, while Lau et al. objectively evaluate these findings through a catheter with a pressure sensor (70). During oral feeding, respiration is disrupted, resulting in reduced ventilation and tidal volume and increased apneic episodes. This change in breathing is not caused by sucking alone but also by the interruption of airflow during swallowing. Lau et al. (59,69) quantitatively measured nutritive sucking (suction and expression), swallowing events (as identified by hyoid upward movement), and respiration to simultaneously monitor the SSR. In their study, suction was defined as the intraoral negative pressure that draws liquid into the mouth and the expression is defined as compression and/or stripping of the tongue against the hard palate to eject liquid into the mouth. By contrast, NOMAS has the advantage of being able to evaluate these factors without specific measuring equipment and with high interrater reliability among incoordination items.

Lau and Smith (71) also evaluated fatigue and endurance by measuring the proficiency (PRO, % volume taken during the first 5 min/total volume prescribed) and the rate of milk transfer (RT, ml/min) during the entire feeding event. They reported that there are four different levels of oral feeding skills, with different feeding duration and transition time depending on the level. Although this approach has the advantage of being able to conduct evaluations through the entire duration of the feeding event, it may not reflect the intermittent stress signs of the infant during feeding, nor is it possible to distinguish between unable to sustain (cluster 3) and incoordination (cluster 4) items.

Previous studies have reported that GA, BW, and medical conditions, such as BPD, cardiac, gastrointestinal, and neurological conditions were factors which could affect the time to reach FOF (56,72,73). However, there is a distinct paucity of research targeting the oromotor function itself as a predictive factor for time to FOF. Bingham et al. reported that the NOMAS was a poor predictor (74) and noted that feeding efficiency, such as volume consumed in the first 5 min of bottle feeding, consumption rate (ml/min), and other baseline traits were better predictors of feeding skills in premature infants. The authors in the study used subscores of the NOMAS which consisted of 12 dichotomous assessments of nutritive suck organization (suck rhythm) and 8 assessments of nutritive suck function (lip seal, tongue, and jaw movement). However, without selecting critical items such as incoordination, they counted the number of items checked in the NOMAS, which might have influenced their results. In their study, the dysfunction subscore did not change over time, but the disorganization score improved. In contrast, our present results showed that specific items, especially when an incoordination item is observed among the disorganized sucking pattern, were a strong predictor in the multivariate models. In this study, only preterm infants with disorganization sucking patterns were included, with all of these infants successfully reaching FOF. Jadcherla et al. reported an aerodigestive protective mechanism of respiratory support in infants with severe BPD and reported delayed feeding milestones, including longer gavage feeding duration in the non-invasive respiratory support group than in the control group. Notably, incoordination was more frequent in patients with longer NIPPV duration in this study. The potential reason for this finding is that the severity of BPD was different between the two groups or the NIPPV duration may be shortened due to early surfactant administration in the group with a coordinated sucking pattern.

3.2 Developmental Outcome at 8-12 and 18-24 months in Premature Infants

Previous studies have attempted to predict developmental delay through neonatal oromotor function. In a study of 27 premature infants without brain lesions, the risk of developmental delay increased when the premature infants exhibited a disorganized sucking pattern at 37 weeks PMA (75). However, this study only examined the presence of disorganized sucking pattern and did not distinguish between specific patterns among disorganized sucking pattern.

The results of this study are compatible with those of the study by Nieuwenhuis et al (76), who classified the disorganized sucking patterns in the NOMAS into two categories: disorganized due to arrhythmic sucking and disorganized due to lack of coordination of SSR. They concluded that uncoordinated sucking patterns, but not arrhythmic sucking patterns, were associated with abnormal fidgety movement at 14 weeks post-term (76). However, in the previous study, they did not discern dysfunctional sucking pattern from incoordination sucking pattern in the NOMAS. Additionally, the study did not distinguish the inability to sustain sucking pattern separately.

Regarding brain ultrasound finding, GMH-IVH grades III and IV are widely considered predictors of developmental delay, while the implications of GMH-IVH grades I and II still being controversial (77). In concert with previous studies, GMH-IVH grades III and IV were identified as predictors of the cognition composite score in a multiple linear analysis in the present study. In the present study, BPD was also analyzed as a statistically significant predictor of developmental delay. Mizuno et al. reported that infants with BPD demonstrated not only poorer feeding coordination, but also poorer feeding endurance and performance (78), which might have affected development (79).

3.3 Functional Oral Intake Scale for Infants

Dodrill et al. modified the FOIS to describe the swallowing function of infants/toddlers by replacing the levels. indicating single/multiple consistency (level 4 and 5, respectively, in the adult version of the FOIS) with levels indicating requirement of modified liquids/solids (level 4 and 4.5, respectively, in the modified FOIS for infants). Strychowsky et al. utilized this version of the FOIS to describe the swallowing dysfunction among toddlers with laryngeal cleft (80). Christiaans et al. (11) also modified the original version of the FOIS by removing the level 4: total oral diet of a single consistency, in their report regarding the e□ectiveness of neuromuscular electrical stimulation in children with dysphagia. Later on, Baxter et al. applied the scale in children with esophageal atresia and tracheoesophageal fistulas (11). However, these modified FOIS versions for the pediatric population have never been validated and tested for reliability.

Among adult stroke patients, Crary et al. reported a high interrater reliability of the FOIS (absolute agreement, 85%) (43), and McMicken et al. reported ICC values of 0.975 and 0.964 at the time of admission and discharge, respectively (45).

4. Clinical Significance

The NOMAS and FOIS for infants presented in this study cover many areas of the international classification of functioning, disability and health: children and youth version (ICF-CY) related to swallowing function in infants (Figure 8). However, those two tools did not cover digestive functions (b515) and environmental factors (Figure 8). Also they did not include other neurodevelopmental domains such as head control and consciousness level which could affect swallowing function. Therefore, for a more comprehensive assessment, appropriate additional assessments should be made for each infant.

In the NOMAS, stress signals, including nasal flaring, head turning, and extraneous movement, are regarded as the symptoms of incoordination of SSR, as described in Palmer et al (81). However, the relationship between incoordination of SSR and stress signals was suggested by clinical observation and not by direct measurement of SSR. To demonstrate the incoordination of SSR, recordings of intraoral pressure (rhythmic alternation of suction and expression/compression) (59), pharyngeal pressure (67,69), nasal thermistor flow (68,82), and thoracoabdominal plethysmography (69) have been used although these methods are not widely used, particularly in the clinic, due to its complexity and invasiveness. However, in terms of research, the relationship between SSR incoordination and clinically observed stress symptoms could be investigated by directly measuring SSR. There might be certain stress signals which are more relevant to SSR incoordination than other signals.

Although there might be a relationship between the incoordination of the SSR and the NOMAS cluster 4 (stress signals regarded as the results from incoordination of SSR), the meaning of these two items is different. Therefore, the results of this study could be interpreted as follows: the stress signals in the NOMAS during nutritive sucking in preterm infants are more associated with a longer transition time and delayed cognitive development at both 8-12 and 18-24 months (corrected for prematurity).

Lastly, the FOIS for infants may be appropriate for documenting feeding abilities and evaluating the e□ectiveness of interventions.

4.1 Transition Time in Premature Infants

If sucking patterns in premature infants are compatible with the NOMAS cluster 4 (stress signals regarded as the results from incoordination of SSR), active oromotor facilitation and swallowing training, such as applying pacifier, non-nutritive oral-motor stimulation, massage therapy, and direct tactile stimulation on specific oral structures, could be considered as supplemental oral sensory and motor experiences, and as a result, shorten the transition time to FOF. Also, giving the infant time for maturation could be considered.

4.2 Developmental Outcome at 8-12 and 18-24 months in Premature Infants

Most of the preterm infants with an immature sucking pattern can successfully bottle feed as the SSR matures, and the sucking pattern of term infants is characterized by the rhythmic alternation of suction and expression/compression (59). In the arrhythmical or inability to sustain pattern group, it could be assumed that SSR coordination has already been formed in preterm period, but sucking difficulty has occurred due to lack of oromotor strength and endurance (59). And this group showed a faster development at both 8-12 and 18-24 months of correctional age compared to the group with less developed SSR coordination.

4.3 Functional Oral Intake Scale for Infants

Both FOIS levels 2 and 3 could be categorized as concurrent tube and oral feeding, and our observers reported three disagreements between these levels when evaluating patients in our study. One patient was an 11-month-old infant with myotonic dystrophy who received a total tube feeding volume of 700 cc per day in five or six doses, as well as 20–40g of puree once per day. One evaluator regarded once-daily feeding as a consistent oral intake (i.e., FOIS level 3), whereas the other considered it a minimal attempt at oral intake (i.e., FOIS level 2). The second patient was a 9-month-old infant with CHARGE syndrome who received a total tube feeding volume of 700 cc per day in four or five doses and attempted to consume minimal amounts of puree orally with every meal. The last patient was a 7-month-old infant with Pierre–Robin syndrome who received a total tube feeding volume of 800 cc per day in six or seven doses, together with a soft blended oral diet (～40 cc per day) at least once per day. In our study, infants with POF who received a higher nutritional contribution from oral feeding were more likely to achieve FOF. This suggests that both the oral feeding amount and consistency should be considered when distinguishing FOIS levels 2 and 3. For example, eight out of 14 infants with <10% POF achieved FOF after 1 year, whereas 18 out of 19 infants with ≥10% POF achieved FOF after 1 year. Based on these results, we have revised the criteria for distinguishing FOIS levels 2 and 3 to consider both the oral intake amount and consistency, as shown in Table 16.

According to Pridham et al. infants can begin to consume semisolid food from a spoon between 5 and 7 months of age and complete this type of consumption at approximately 8 months of age (83). A 2001 guideline from the World Health

Organization recommended the initiation of complementary feeding at 6 months of age and a concurrent and gradual solidification of foods (47). According to this guideline, the consumption of pureed, mashed, and semi-solid foods generally begins at 6 months of age, followed by the consumption of finger foods at 8 months and an adult-like diet at 12 months (84). In 2017, the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition Committee on Nutrition in 2017 recommended that complementary foods should be introduced between 4 and 6 months of age (47). From the neurodevelopmental point of view, lumpy (semisolid) food can be consumed between 6 and 12 months, and after 9 months, most infants can eat finger food and are able to chew their food (47). Northstone et al. reported a tendency toward feeding di□culties and the avoidance of certain foods if solid foods are not introduced until 9–10 months of age (48). Consistent with those studies, we defined the normal expansion of oral diet as the introduction of pureed foods before 9 months of age and of mashed foods and soft lumps before 12 months of age.

Among the 77 infants with FOF at the time of the VFSS in our study, the two raters reported five disagreements between FOIS levels 4 and 5. One such infant was assessed at 270 days of age and was consuming bottled milk. One examiner considered 270 days to be older than 9 months and evaluated the infant at FOIS level 4, whereas the other rater considered the infant younger than 9 months and evaluated him at FOIS level 5. Another infant was mainly consuming bottled milk at 305 days of age and had been attempting a 50-cc volume of pureed food 1 week before the evaluation. In this case, one examiner rated the feeding status as FOIS level 5 because she considered a pureed diet to be normal, whereas the other examiner assigned a rating of FOIS level 4 because the pureed diet had been initiated after 9 months of age. To improve the inter-rater reliability, it could be recommended to give a clear instruction that the FOIS for infants is based on the diet at the time of the evaluation.

5. Limitation

In this thesis, NOMAS was assessed in premature infants and FOIS was assessed in infants with various disease conditions. The correlation between NOMAS and FOIS could not be analyzed because the populations assessed for each scale were not identical. In fact, almost all infants who underwent NOMAS did not have records of VFSS.

5.1 Transition Time in Premature Infants

Since instrumental evaluation was not included and measurements were only made through video recordings, it is possible that the process of sucking was not objectively evaluated. If manometry, pulse oximetry, and plethysmography had been added through a multidisciplinary approach, a more integrated interpretation might have been possible. This study examined the time to reach FOF from the IOF but did not evaluate the long-term feeding performance or neurodevelopment outcome of preterm infants. In this study, the stress signals of the incoordination-positive group included head bobbing, extraneous movements of the body or limbs, choking, gagging, coughing, yelping, and grunting. However, each stress signal is thought to be different. For future studies, incoordination symptoms could be further classified into different subcategories and investigated for their relative implications upon oral feeding and development.

5.2 Developmental Outcome at 8-12 and 18-24 months in Premature Infants

First, we did not include more objective signs that could be assessed in premature infants with sucking difficulty, including episodes of desaturation, apnea, and bradycardia. Those measurable signs might complement NOMAS, which is composed of observational findings. Second, we only evaluated the sucking pattern before 40 weeks PMA since most premature infants are discharged from the NICU before term age. In our study, clusters 2 and 3 (i.e., arrhythmia and inability to sustain sucking without stress signals) were less relevant to neurodevelopmental outcomes. However, if those symptoms persist during the post-term period, the clinical relevance could be changed. For example, Wolthuis-Stigter et al. (48) reported that the inability to sustain sucking at 46 weeks significantly increased the odds of abnormal neurodevelopmental outcomes at two years of age. Therefore, a longitudinally designed study would improve our understanding of the clinical significance of sucking difficulties that are observed in premature infants.

5.3 Functional Oral Intake Scale for Infants

We were unable to evaluate the correlation between the FOIS for infants and developmental assessments. Future studies could potentially apply the Bayley Scales of Infant and Toddler Development (48) in conjunction with the FOIS assessment. Additionally, this was a single-center study, which may have led to selection bias. Moreover, the validity and reliability of the FOIS for infants were assessed with a heterogeneous disease group. Crary et al. (43) originally suggested the adult FOIS for stroke patients. Afterwards, other researchers expanded the FOIS for patients with traumatic brain injury (85,86), head and neck cancer (87,88), vocal fold immobility (89), vagal schwannoma resection (90), cerebral palsy (91), postsurgical dysphagia (92), neurodegenerative diseases, postextubation dysphagia in children (93), and neurogenic dysphagia (94). The FOIS for infants suggested in the present study was a simplified scale with levels reduced from 7 to 5, without taking into account the concepts of single/multiple consistency food, special preparation or compensation, and food restriction. Therefore, the variation in applicability according to disease groups might be less than that in the adult population. However, the scale proposed in this study might be more appropriate for certain disease groups than other groups, and in some groups, this scale would not be applicable. For example, the FOIS suggested in this study could be inappropriate for infants who require continuous total parenteral nutrition because of gastrointestinal problems.

6. Future direction

There have been inconsistent results from studies regarding the implication of feeding difficulty on the neurodevelopmental outcomes in preterm infants (52,75,95). This might have at least partially contributed to the differences in interpreting the findings of the NOMAS. Some authors simply divided the NOMAS findings into three groups: normal, disorganization, and dysfunction (52,75,95), while others summed up entire items, which were checked dichotomously (74). Since these interpretive methods have still not been established as being useful in predicting the neurodevelopmental outcome, the presence of incoordination, defined by the Dutch group, could be another option for interpreting the findings of the NOMAS and utilizing this scale in an appropriate manner. Further studies are needed to identify which items of the NOMAS represent a delayed attainment of the maturational process or are indicative of neurological dysfunction. Although there was no statistically significant difference in PMA between the three NOMAS clusters, the distribution range was wider in cluster 4. Therefore, it is necessary to observe the change of NOMAS cluster according to PMA longitudinally for each premature infant in the future. Also, a longitudinally designed study would improve our understanding of the clinical significance of sucking difficulties that are observed in premature infants.

Also, investigating correlation between the FOIS for infants and developmental assessments including the Bayley Scales of Infant and Toddler Development is needed in the future.

Table 16. The Functional Oral Intake Scale for infants considering both attempts and amounts of oral intake at level 2

	Intake
Level 1	Nothing by mouth
Level 2	Tube-dependent with minimal oral intake[a]
Level 3	Tube and oral feeding in parallel[b]
Level 4	Expansion of oral diet not reached[c]
Level 5	Expansion of oral diet reached[c]

[a] "Minimal oral intake" indicates minimal attempts of or a very small amount of oral intake.

[b] "In parallel" indicates consistent oral intake with significant caloric contribution.

[c] Normal expansion of oral diet is defined as the introduction of solid foods in pureed form before 9 months of age and the introduction of mashed foods and soft lumps before 12 months of age.

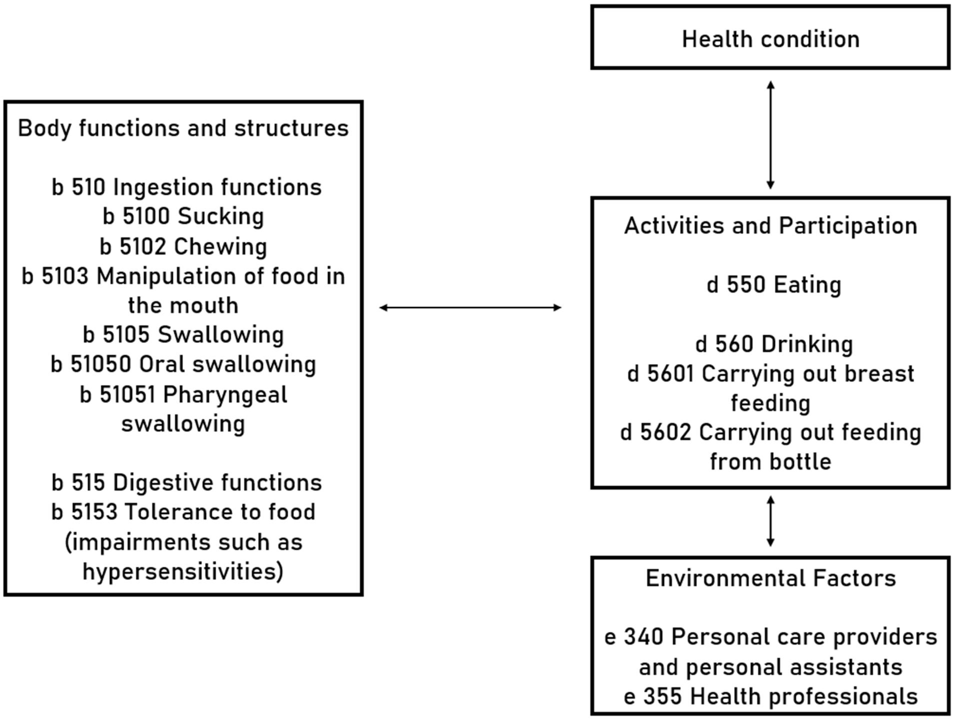

Figure 8. Various factors affecting the swallowing function of children based on International classification of functioning, disability and health: children and youth version.

CONCLUSION

The stress signals reflecting incoordination of SSR among disorganized sucking pattern are associated with the transition time to FOF in preterm infants with feeding difficulties. Stress signals during sucking activity were also associated with developmental delay in the cognitive domain of the Bayley-III at both 8-12 and 18-24 months. When selecting premature infants to be treated with swallowing therapy, it is reasonable to perform treatment to shorten the time to attain FOF with an incoordination-positive group in the NOMAS, that is, premature infants with stress signals. Additionally, there may be a need for periodic follow-up and early intervention for developmental delay when incoordination of SSR that results in stress signals on the NOMAS is observed before 40 weeks postmenstrual age.

The five-point FOIS for infants, which reflected the expansion of their oral diet with growth, had adequate reliability and validity. The caloric contribution as well as consistency of oral feeding could be used to distinguish FOIS levels 2 and 3, which correspond to the POF status in infants.

REFERENCES

1. Byars KC, Burklow KA, Ferguson K, O'Flaherty T, Santoro K, Kaul A. A multicomponent behavioral program for oral aversion in children dependent on gastrostomy feedings. J Pediatr Gastroenterol Nutr. 2003 Oct;37(4):473–80.

2. Audag N, Goubau C, Toussaint M, Reychler G. Screening and evaluation tools of dysphagia in children with neuromuscular diseases : a systematic review. Dev Med Child Neurol. 2017 Jun;59(6):591-6.

3. Somerville H, Tzannes G, Wood J, Shun A, Hill C, Arrowsmith F, et al. Gastrointestinal and nutritional problems in severe developmental disability. Dev Med Child Neurol. 2008 Sep;50(9):712-6.

4. Goh YR, Choi JY, Kim SA, Park J, Park ES. Comparisons of severity classification systems for oropharyngeal dysfunction in children with cerebral palsy: Relations with other functional profiles. Res Dev Disabil. 2018 Jan;72:248-56.

5. Senez C, Guys JM, Mancini J, Paz Paredes A, Lena G, Choux M. Weaning children from tube to oral feeding. Child's Nerv Syst. 1996;12(10):590–4.

6. Dello Strologo L, Principato F, Sinibaldi D, Appiani AC, Terzi F, Dartois AM, et al. Feeding dysfunction in infants with severe chronic renal failure after long-term nasogastric tube feeding. Pediatr Nephrol. 1997 Feb;11(1):84-6.

7. Mason SJ, Harris G, Blissett J. Tube feeding in infancy: Implications for the development of normal eating and drinking skills. 2005 Winter;20(1):46-61.

8. Erasmus CE, Van Hulst K, Rotteveel JJ, Willemsen MAAP, Jongerius PH. Clinical practice: swallowing problems in cerebral palsy. Eur J Pediatr. 2012 Mar;171(3):409-14.

9. Davis AM, Dean K, Mousa H, Edwards S, Cocjin J, Almadhoun O, et al. A randomized controlled trial of an outpatient protocol for transitioning children from tube to oral feeding: no need for amitriptyline. J Pediatr. 2016 May;172:136-41.e2.

10. Bell HR, Alper BS. Assessment and intervention for dysphagia in infants and children: Beyond the neonatal intensive care unit. Semin Speech Lang. 2007 Aug;28(3):213-22.

11. Christiaanse ME, Mabe B, Russell G, Simeone TL, Fortunato J, Rubin B. Neuromuscular electrical stimulation is no more effective than usual care for the treatment of primary dysphagia in children. Pediatr Pulmonol. 2011 Jun;46(6):559-65.

12. Marcus S, Friedman JN, Lacombe-Duncan A, Mahant S. Neuromuscular electrical stimulation for treatment of dysphagia in infants and young children with neurological impairment: a prospective pilot study. BMJ Paediatr Open. 2019 Jan 23;3(1):e000382.

13. Abithol CL, Zilleruelo G, Montane B, Strauss J. Growth of uremic infants on forced feeding regimens. Pediatr Nephrol. 1993 Apr;7(2):173-7.

14. Wada A, Kawakami M, Liu M, Otaka E, Nishimura A, Liu F, et al. Development of a new scale for dysphagia in patients with progressive neuromuscular diseases: the Neuromuscular Disease Swallowing Status Scale (NdSSS). J Neurol. 2015 Oct;262(10):2225-31.

15. Sellers D, Mandy A, Pennington L, Hankins M, Morris C. Development and reliability of a system to classify the eating and drinking ability of people with cerebral palsy. Dev Med Child Neurol. 2014 Mar;56(3):245-51.

16. Tschirren L, Bauer S, Hanser C, Marsico P, Sellers D, van Hedel HJA. The Eating and Drinking Ability Classification System: concurrent validity and reliability in children with cerebral palsy. Dev Med Child Neurol. 2018 Jun;60(6):611-617.

17. Scott S. Classifying eating and drinking ability in people with cerebral palsy. Dev Med Child Neurol. 2014 Mar;56(3):201.

18. Benfer KA, Weir KA, Ware RS, Davies PSW, Arvedson J, Boyd RN, et al. Parent-reported indicators for detecting feeding and swallowing difficulties and undernutrition in preschool-aged children with cerebral palsy. Dev Med Child Neurol. 2017 Nov;59(11):1181-1187.

19. Nyqvist KH, Rubertsson C, Ewald U, Sjödén PO. Development of the Preterm Infant Breastfeeding Behavior Scale (PIBBS): a study of nurse-mother agreement. J Hum Lact. 1996 Sep;12(3):207-19.

20. Gill SL, Reifsnider E, Lucke JF, Mann AR. Predicting breast-feeding attrition: adapting the breast-feeding attrition prediction tool. J Perinat Neonatal Nurs. 2007 Jul-Sep;21(3):216-24.

21. Bache M, Pizon E, Jacobs J, Vaillant M, Lecomte A. Effects of pre-feeding oral stimulation on oral feeding in preterm infants: a randomized clinical trial. Early Hum Dev. 2014 Mar;90(3):125-9.

22. Thoyre SM, Shaker CS, Pridham KF. The early feeding skills assessment for preterm infants. Neonatal Netw. 2005 May-Jun;24(3):7-16.

23. Dolgun G, İnal S, Erdim L, Korkut S. Reliability and validity of the Bristol Breastfeeding Assessment Tool in the Turkish population. Midwifery. 2018 Feb;57:47-53.

24. Mizuno K, Aizawa M, Saito S, Kani K, Tanaka S, Kawamura H, et al. Analysis of feeding behavior with direct linear transformation. Early Hum Dev. 2006 Mar;82(3):199-

204.

25. Greene Z, O'Donnell CP, Walshe M. Oral stimulation for promoting oral feeding in preterm infants. Cochrane Database Syst Rev. 2016 Sep 20;9:CD009720.

26. Sjögreen L, Gonzalez Lindh M, Brodén M, Krüssenberg C, Ristic I, Rubensson A, et al. Oral sensory-motor intervention for children and adolescents (3-18 years) with dysphagia or impaired saliva control secondary to congenital or early-acquired disabilities: a review of the literature, 2000 to 2016. Ann Otol Rhinol Laryngol. 2018 Dec;127(12):978-85.

27. Leonard R, Rees CJ, Belafsky P, Allen J. Fluoroscopic surrogate for pharyngeal strength: The pharyngeal constriction ratio (PCR). Dysphagia. 2011 Mar;26(1):13-7.

28. Abraham SS, Wolf EL. Swallowing physiology of toddlers with long-term tracheostomies: a preliminary study. 2000 Fall;15(4):206-12.

29. Lima AH, Côrtes MG, Bouzada MC, Friche AA. Preterm newborn readiness for oral feeding: systematic review and meta-analysis. Codas. 2015 Jan-Feb;27(1):101-7.

30. Kirk AT, Alder SC, King JD. Cue-based oral feeding clinical pathway results in earlier attainment of full oral feeding in premature infants. J Perinatol. 2007 Sep;27(9):572-8.

31. Kamide A, Hashimoto K, Miyamura K, Honda M. Assessment of feeding and swallowing in children: validity and reliability of the Ability for Basic Feeding and Swallowing Scale for Children (ABFS-C). Brain Dev. 2015 May;37(5):508-14.

32. Barton C, Bickell M, Fucile S. Pediatric oral motor feeding assessments: a systematic review. Phys Occup Ther Pediatr. 2018 May;38(2):190-209.

33. Palmer MM, Heyman MB. Developmental outcome for neonates with dysfunctional and disorganized sucking patterns: preliminary findings. Infant-Toddler Intervention. 1999;9:299–308.

34. da Costa SP, van den Engel-Hoek L, Bos AF. Sucking and swallowing in infants and diagnostic tools. J Perinatol. 2008 Apr;28(4):247-57.

35. Pados BF, Park J, Estrem H, Awotwi A. Assessment tools for evaluation of oral feeding in infants younger than 6 months. Adv Neonatal Care. 2016 Apr;16(2):143-50.

36. Da Costa SP, van der Schans CP, Boelema SR, van der Meij E, Boerman MA, Bos AF. Sucking patterns in fullterm infants between birth and 10 weeks of age. Infant Behav Dev. 2010 Feb;33(1):61-7.

37. Hawdon JM, Beauregard N, Slattery J, Kennedy G. Identification of neonates at risk of developing feeding problems in infancy. Dev Med Child Neurol. 2000 Apr;42(4):235-9.

38. Da Costa SP, Van Der Schans CP, Zweens MJ, Boelema SR, Van Der Meij E,

Boerman MA, et al. Development of sucking patterns in pre-term infants with bronchopulmonary dysplasia. Neonatology. 2010;98(3):268–77.

39. Jackson BN, Kelly BN, McCann CM, Purdy SC. Predictors of the time to attain full oral feeding in late preterm infants. Acta Paediatr. 2016 Jan;105(1):e1-6.

40. Bingham PM. Deprivation and dysphagia in premature infants. J Child Neurol. 2009 Jun;24(6):743-9.

41. da Costa SP, Hübl N, Kaufman N, Bos AF. New scoring system improves inter-rater reliability of the Neonatal Oral-Motor Assessment Scale. Acta Paediatr. 2016 Aug;105(8):e339-44.

42. Palmer MM. Identification and management of the transitional suck pattern in premature infants. J Perinat Neonatal Nurs. 1993 Jun;7(1):66-75.

43. Crary MA, Mann GD, Groher ME. Initial psychometric assessment of a functional oral intake scale for dysphagia in stroke patients. Arch Phys Med Rehabil. 2005 Aug;86(8):1516-20.

44. Kunieda K, Ohno T, Fujishima I, Hojo K, Morita T. Reliability and validity of a tool to measure the severity of dysphagia: the Food Intake LEVEL Scale. J Pain Symptom Manage. 2013 Aug;46(2):201-6.

45. McMicken BL, Muzzy CL, Calahan S. Retrospective ratings of 100 first time-documented stroke patients on the Functional Oral Intake Scale. Disabil Rehabil. 2010;32(14):1163-72.

46. Kjaersgaard A, Nielsen LH, Sjölund BH. Factors affecting return to oral intake in inpatient rehabilitation after acquired brain injury. Brain Inj. 2015;29(9):1094-104.

47. Fewtrell M, Bronsky J, Campoy C, Domellöf M, Embleton N, Fidler Mis N, et al. Complementary feeding: a position paper by the European Society for Paediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN) committee on nutrition. J Pediatr Gastroenterol Nutr. 2017 Jan;64(1):119-132.

48. Northstone K, Emmett P, Nethersole F. The effect of age of introduction to lumpy solids on foods eaten and reported feeding difficulties at 6 and 15 months. J Hum Nutr Diet. 2001 Feb;14(1):43-54.

49. Glass RP, Wolf LS. A global perspective on feeding assessment in the neonatal intensive care unit. Am J Occup Ther. 1994 Jun;48(6):514-26.

50. Dodrill P, McMahon S, Donovan T, Cleghorn G. Current management of transitional feeding issues in preterm neonates born in Queensland, Australia. Early Hum Dev. 2008 Oct;84(10):637-43.

51. Howe TH, Sheu CF, Hsieh YW, Hsieh CL. Psychometric characteristics of the Neonatal Oral-Motor Assessment Scale in healthy preterm infants. Dev Med Child Neurol.

2007 Dec;49(12):915-9.

52. Zarem C, Kidokoro H, Neil J, Wallendorf M, Inder T, Pineda R. Psychometrics of the neonatal oral motor assessment scale. Dev Med Child Neurol. 2013 Dec;55(12):1115-20.

53. Fucile S, Gisel E, Lau C. Oral stimulation accelerates the transition from tube to oral feeding in preterm infants. J Pediatr. 2002 Aug;141(2):230-6.

54. Dodrill P, McMahon S, Ward E, Weir K, Donovan T, Riddle B. Long-term oral sensitivity and feeding skills of low-risk pre-term infants. Early Hum Dev. 2004 Jan;76(1):23-37.

55. Lau C. Development of infant oral feeding skills: What do we know? Am J Clin Nutr. 2016 Feb;103(2):616S-21S.

56. Bazyk S. Factors associated with the transition to oral feeding in infants fed by nasogastric tubes. Am J Occup Ther. 1990 Dec;44(12):1070-8.

57. Capilouto GJ, Cunningham TJ, Mullineaux DR, Tamilia E, Papadelis C, Giannone PJ. Quantifying neonatal sucking performance: promise of new methods. Semin Speech Lang. 2017 Apr;38(2):147-158.

58. Wolthuis-Stigter MI, Luinge MR, Da Costa SP, Krijnen WP, van der Schans CP, Bos AF. The association between sucking behavior in preterm infants and neurodevelopmental outcomes at 2 years of age. J Pediatr. 2015 Jan;166(1):26-30.

59. Lau C, Alagugurusamy R, Schanler RJ, Smith EO, Shulman RJ. Characterization of the developmental stages of sucking in preterm infants during bottle feeding. Acta Paediatr. 2000 Jul;89(7):846-52.

60. Pickler RH. A model of feeding readiness for preterm infants Neonatal Intensive Care. 2004;17(4):31-36.

61. Ben XM. Nutritional management of newborn infants: practical guidelines. World J Gastroenterol. 2008 Oct 28;14(40):6133-9.

62. Erick M. Breast milk is conditionally perfect. Med Hypotheses. 2018 Feb;111:82-89.

63. Yi YG, Sung IY, Yuk JS. Comparison of second and third editions of the Bayley Scales in children with suspected developmental delay. Ann Rehabil Med. 2018 Apr;42(2):313-320.

64. Jadcherla SR. Advances with neonatal aerodigestive science in the pursuit of safe swallowing in infants: invited review. Dysphagia. 2017 Feb;32(1):15-26.

65. Jadcherla SR, Stoner E, Gupta A, Bates DG, Fernandez S, Di Lorenzo C, et al. Evaluation and management of neonatal dysphagia: impact of pharyngoesophageal motility studies and multidisciplinary feeding strategy. J Pediatr Gastroenterol Nutr. 2009 Feb;48(2):186-92.

66. Jadcherla SR, Hoffmann RG, Shaker R. Effect of maturation of the magnitude of mechanosensitive and chemosensitive reflexes in the premature human esophagus. J Pediatr. 2006 Jul;149(1):77-82.

67. Gryboski JD. Suck and swallow in the premature infant. Pediatrics. 1969 Jan;43(1):96-102.

68. Mizuno K, Ueda A. The maturation and coordination of sucking, swallowing, and respiration in preterm infants. J Pediatr. 2003 Jan;142(1):36-40.

69. Lau C, Smith EO, Schanler RJ. Coordination of suck-swallow and swallow respiration in preterm infants. Acta Paediatr. 2003 Jun;92(6):721-7.

70. Lau C, Sheena HR, Shulman RJ, Schanler RJ. Oral feeding in low birth weight infants. J Pediatr. 1997 Apr;130(4):561-9.

71. Lau C, Smith EO. A novel approach to assess oral feeding skills of preterm infants. Neonatology. 2011;100(1):64-70.

72. Glackin SJ, O'Sullivan A, George S, Semberova J, Miletin J. High flow nasal cannula versus NCPAP, duration to full oral feeds in preterm infants: a randomised controlled trial. Arch Dis Child Fetal Neonatal Ed. 2017 Jul;102(4):F329-F332.

73. Giannì ML, Sannino P, Bezze E, Comito C, Plevani L, Roggero P, et al. Does parental involvement affect the development of feeding skills in preterm infants? A prospective study. Early Hum Dev. 2016 Dec;103:123-128.

74. Bingham PM, Ashikaga T, Abbasi S. Relationship of Neonatal Oral Motor Assessment Scale to feeding performance of premature infants. J Neonatal Nurs. 2012 Feb 1;18(1):30-36.

75. Tsai SW, Chen CH, Lin MC. Prediction for developmental delay on Neonatal Oral Motor Assessment Scale in preterm infants without brain lesion. Pediatr Int. 2010 Feb;52(1):65-8.

76. Nieuwenhuis T, Da Costa SP, Bilderbeek E, Geven WB, van der Schans CP, Bos AF. Uncoordinated sucking patterns in preterm infants are associated with abnormal general movements. J Pediatr. 2012 Nov;161(5):792-8.

77. Bolisetty S, Dhawan A, Abdel-Latif M, Bajuk B, Stack J, Lui K. Intraventricular hemorrhage and neurodevelopmental outcomes in extreme preterm infants. Pediatrics. 2014 Jan;133(1):55-62.

78. Gewolb IH, Bosma JF, Reynolds EW, Vice FL. Integration of suck and swallow rhythms during feeding in preterm infants with and without bronchopulmonary dysplasia. Dev Med Child Neurol. 2003 May;45(5):344-8.

79. Mizuno K, Ueda A.. Neonatal feeding performance as a predictor of neurodevelopmental outcome at 18 months. Dev Med Child Neurol. 2005 May;47(5):299-

304.

80. Strychowsky JE, Dodrill P, Moritz E, Perez J, Rahbar R. Swallowing dysfunction among patients with laryngeal cleft: More than just aspiration? Int J Pediatr Otorhinolaryngol. 2016 Mar;82:38-42.

81. Palmer MM, Crawley K, Blanco IA. Neonatal Oral-Motor Assessment scale: a reliability study. J Perinatol. 1993 Jan-Feb;13(1):28-35.

82. Mizuno K, Nishida Y, Taki M, Hibino S, Murase M, Sakurai M, et al. Infants with bronchopulmonary dysplasia suckle with weak pressures to maintain breathing during feeding. Pediatrics. 2007 Oct;120(4):e1035-42.

83. Pridham KF. Feeding behavior of 6- to 12-month-old infants: assessment and sources of parental information. J Pediatr. 1990 Aug;117(2 Pt 2):S174-80.

84. Pérez Lizaur AB. Complementary feeding [Article in Spanish]. Gac Med Mex. 2011;147(Suppl 1):39-45.

85. Hansen TS, Engberg AW, Larsen K. Functional oral intake and time to reach unrestricted dieting for patients with traumatic brain injury. Arch Phys Med Rehabil. 2008 Aug;89(8):1556-62.

86. Hansen TS, Larsen K, Engberg AW. The association of functional oral intake and pneumonia in patients with severe traumatic brain injury. Arch Phys Med Rehabil. 2008 Nov;89(11):2114-20.

87. Kamal M, Barrow MP, Lewin JS, Estrella A, Gunn GB, Shi Q, et al. Modeling symptom drivers of oral intake in long-term head and neck cancer survivors. Support Care Cancer. 2019 Apr;27(4):1405-1415.

88. Fong R, Sun N, Ng YW, Rumbach AF, Ward EC, Tsang R. Office-based cricopharyngeus balloon dilation for post chemoirradiation dysphagia in nasopharyngeal carcinoma patients: a pilot study. Dysphagia. 2019 Aug;34(4):540-547.

89. Zuniga S, Ebersole B, Jamal N. Improved swallow outcomes after injection laryngoplasty in unilateral vocal fold immobility. Ear Nose Throat J. 2018 Aug;97(8):250-256.

90. Patel MA, Eytan DF, Bishop J, Califano JA. Favorable swallowing outcomes following vagus nerve sacrifice for vagal Schwannoma resection. Otolaryngol Head Neck Surg. 2017 Feb;156(2):329-333.

91. Yi YG, Oh BM, Seo HG, Shin HI, Bang MS. Dysphagia-related quality of life in adults with cerebral palsy on full oral diet without enteral nutrition. Dysphagia. 2019 Apr;34(2):201-209.

92. Ottaviani F, Schindler A, Klinger F, Scarponi L, Succo G, Mozzanica F. Functional fat injection under local anesthesia to treat severe postsurgical dysphagia, case

report. Head Neck. 2019 Jan;41(1):E17-E21.

93. Luchesi KF, Campos BM, Mituuti CT. Identification of swallowing disorders: the perception of patients with neurodegenerative diseases. Codas. 2018 Nov 29;30(6):e20180027.

94. Fraga BF, Almeida ST, Santana MG, Cassol M. Efficacy of myofunctional therapy associated with voice therapy in the rehabilitation of neurogenic oropharyngeal dysphagia: a pilot study. Int Arch Otorhinolaryngol. 2018 Jul;22(3):225-230.

95. Slattery J, Morgan A, Douglas J. Early sucking and swallowing problems as predictors of neurodevelopmental outcome in children with neonatal brain injury: a systematic review. Dev Med Child Neurol. 2012 Sep;54(9):796-806.

국문초록

뇌성 마비, 신경 근육 질환, 발달 장애 및 경관 수유 의존성과 같은 광범위한 질환에서 영유아의 삼킴 장애에 대하여 다양한 방법으로 치료가 적용되어 왔다. 따라서, 영아에서 식이 상태를 기술하고 삼킴 장애를 가진 영아의 치료 효과를 평가할 수 있는 검증된 평가도구가 필요하다. 여러가지 평가도구가 영아의 식이 상태를 평가하기 위해 개발되어 왔으나, 이러한 평가 도구의 대부분은 체크리스트 형식이며 검증되지 않았거나 주관적인 경우가 대부분이다.

신생아 구강 운동 평가 척도는 출생 후 48 미만의 월경 후 연령 (postmenstrual age) 에서 영아의 빨기 능력을 평가하는 데 사용되는 육안 관찰 방법이다. 신생아 구강 운동 평가 척도의 관찰 항목 중 비조직 (disorganization) 에 속하는 항목은 3개의 군집으로 나뉘게 되는데 군집 2는 불규칙한 (arrhythmical) 빨기를 보이는 경우이며, 군집 3 는 빨기를 지속하기 힘든 (unable to sustain) 경우이며, 군집 4는 부조화된 (incoordination) 빨기를 보이는 경우이다. 이 군집 시스템은 다양한 신생아 구강 운동 평가 척도 결과를 범주로 그룹화했지만 각 범주의 임상 적 유용성은 아직 입증되지 않았다. 기능적 구강섭취척도는 뇌졸중 환자의 기능성 구강 섭취 변화에 대한 기록을 위해 개발되었다. 성인의 연하 장애를 평가하기 위해 기능적

구강섭취척도를 광범위하게 사용하고 있음에도 불구하고, 영아에서는 사용되지 못하고 있다. 영아는 월 령에 따라 섭취하는 음식이 변화하기 때문에, 성인의 기능적 구강섭취척도를 그대로 적용하기 힘들다.

본 학위연구에서는 세 가지의 연구를 수행하였다. 첫째, 신생아 구강 운동 평가 척도 중 비조직 (disorganization) 빨기 패턴을 가지는 조산아를 대상으로, 특정 군집의 빨기 패턴이 완전 경구 수유까지 도달하는 데 걸리는 시간을 예측할 수 있는지 조사했다. 둘째, 신생아 구강 운동 평가 척도 중 부조화된 (incoordination) 빨기 패턴이 미숙아의 인지발달에 영향을 미치는지 조사하였다. 마지막으로 영아를 대상으로 한 기능성 구강 섭취 척도의 검사자 간 신뢰성과 타당성을 밝히고자 하였다.

첫 번째 연구는 월경 후 연령 (postmenstrual age) 50 주 이전에 신생아 구강 운동 평가 척도에서 비조직 (disorganization) 빨기 패턴을 보이는 조산아를 포함하였다. 비조직 (disorganization) 빨기 패턴 (n = 109)을 보이는 조산아는 3 개의 군집 (군집 2-4)으로 분류되었고, 부조화 (incoordination) 빨기 양성 (군집 4) 및 부조화 (incoordination) 빨기 음성 그룹 (군집 2 및 3)으로 나누어 완전 경구 수유에 도달하는 시간에 차이가 있는지 분석하였다. 8-12 개월, 18-24 개월 령의 발달과 부조화 (incoordination) 빨기 패턴의 연관성을 평가하는 연구에서는 71 명의 조산아의 신생아 구강 운동 평가 척도를 포함하였다. 부조화 (incoordination) 빨기 양성 및 부조화 (incoordination) 빨기 음성

그룹에 대한 Bayley-III 인지 점수를 독립 t- 검정으로 비교하였다. 영아에 대한 기능적 구강섭취척도의 신뢰성과 타당성을 평가하는 연구에서 비디오 연하 조영 검사를 시행한 영아가 분석에 포함되었다. 비디오 연하 조영 검사 당시의 영양 기록은 영아를 위한 5 점 기능적 구강섭취척도를 사용하여 두 명의 평가자가 별도로 평가하였다. 비디오 연하 조영 검사를 통해 객관적인 삼킴 장애 점수 및 흡인 점수를 얻었다.

첫 번째 연구에서, 부조화 (incoordination) 빨기 양성의 조산아는 완전 경구 수유에 도달하는 데 걸린 시간이 중앙값 22 일 (범위: 4-121 일)로 부조화 음성 그룹 (중앙값 6일, 범위: 1–25 일)보다 더 길었다. 다변량 선형 회귀 분석에서, 전이 시간과 관련이 있는 것으로 밝혀진 변수는 종합 비경구 수액 지속기간, 재태령에 비해 작은 태아 및 부조화 (incoordination) 빨기 패턴의 존재였다. 두 번째 연구에서 67 명의 비조직 (disorganization) 빨기 패턴을 보인 조산아는 중에서, 부조화 (incoordination) 빨기 양성군은 18-24개월 Bayley-III 인지 점수 중앙값 90.0 점으로 부조화 빨기 음성군 (중앙값 100.7점) 보다 낮았다 (독립 t-검정, $p = 0.005$). 다중 선형 회귀 분석 결과, 부조화 (incoordination) 빨기 패턴 양성, 등급 3 또는 4 의 뇌실내 출혈 및 중등도/중증의 기관지폐이형성증이 18-24 개월 령에 인지 발달을 예측하는 것으로 나타났다. 세 번째 연구에서 영아에 대한 기능적 구강섭취척도의 평가자 간 신뢰도는 201 명의 평가 된 영아들 사이에서 95.5 % 의 절대 동의로 높았으며, 이 척도는 비디오

연하조영검사에서의 흡인 점수와 연관성이 존재하였다. 평가 당시 부분 경구 식이 중이었던 33 명의 영아들이 평가 후 1 년 이내에 완전 경구 수유를 달성했는지 여부를 조사한 결과, 26 명의 영아가 1 년 후 완전 경구 식이에 도달하였으며, 1년 후 완전 경구 식이에 도달한 아이들이 평가 당시에 튜브 대신 입으로 영양을 섭취하는 비율이 높았다.

요약하면, 치료가 필요한 조산아를 선별할 때, 신생아 구강 운동 평가 척도에서 부조화 (incoordination) 빨기 패턴을 보이는 경우 더 주의를 기울여야 하며, 발달을 주기적으로 모니터링해야 한다. 또한 영아의 5 점 기능적 구강섭취척도는 충분한 신뢰성과 타당성을 가지고 있어, 신생아 구강 운동 평가 척도와 기능적 구강섭취척도를 영아의 삼킴 장애 평가에 유용하게 사용할 수 있다.

색인 : 신생아 구강 운동 평가 척도, 기능적 구강섭취척도, 평가 도구, 영아, 삼킴, 연하, 연하장애, 경구 식이, 발달

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감사의 글

전임의를 시작하던 3월 초, 신생아의 삼킴 장애에 대해서 어떻게 평가하고 치료해야 할지 고민해보자고 하셨던 말씀에 이런저런 논문을 찾아보던 기억이 납니다. 당시에 둘째가 태어난 지 1년이 채 안 되어 수유 중이던 터라, 아기의 빠는 모습이 생소하지 않았고, 180 여 개의 조산아의 수유하는 비디오를 관심을 가지고 보았던 기억이 납니다. 그 때 고민하기 시작한 주제가 어느덧 이렇게 현실이 되어 박사학위 논문까지 마무리하게 되었습니다. 그때 수유 중이던 아이는 이제 유치원에 입학하기 위해 입학 원서를 내러 다니고 있습니다. 감사한 분들의 얼굴이 한 분 한 분 머리 속에 스쳐 지나갑니다.

우선 부족한 제자를 변함없는 믿음으로 지지해주시고, 글의 한 문장 한 문장 손수 가르쳐주신 신형익 지도교수님께 큰 감사를 올립니다. 연구 초창기 시절, 신생아 삼킴 기능 평가에 대해서 손수 가르쳐주신 오병모 교수님께도 특별한 감사 올립니다. 그리고 지난 연구기간 동안 관심을 표해주신 방문석 교수님, 학위 연구를 지속할 수 있도록 지지해주신 정선근 주임교수님을 비롯한 서울대병원 재활의학과 모든 의국 선생님들께도 이 자리를 빌어 감사를 드립니다. 그리고 이 논문의 아이디어를 제공해주신 김이경 교수님께도 감사의 인사 올립니다.

저의 아버지, 어머니 제가 이룬 것이 있다면 그 모든 것이 두 분으로부터 비롯된 것입니다. 항상 힘을 보태주시는 시아버님,

시어머님께도 진심으로 감사를 올립니다.

이 모든 과정에 학생 때부터 지켜봐 준 저의 남편의 지지가 없었다면 불가능했을 것입니다. 작은 호기심으로 시작한 연구가 논문이 되고, 학문을 발전시키듯이 저의 두 아들 딸 현호와 현서도 세상에 보람 있고 의미 있는 일을 하는 어른으로 성장하길 이 글을 통해 기원해 봅니다.