

# Prevalence and Risk Factors for Feeding and Swallowing Difficulties in Spinal Muscular Atrophy Types II and III

Yen-Shan Chen, MD, Hsiang-Hung Shih, MD, Tai-Heng Chen, MD, Chang-Hung Kuo, MD, and Yuh-Jyh Jong, MD, DMSci

**Objective** To identify the prevalence and risk factors of feeding and swallowing problems in patients with type II and type III spinal muscular atrophy (SMA).

**Study design** Cross-sectional data from 108 genetically confirmed patients with SMA (age range, 3-45 years; 60 with type II and 48 with type III) were analyzed. The questionnaire survey included demographic data, current motor function and respiratory status, feeding and swallowing difficulties, and consequences. The risk factors were analyzed via logistic regression.

**Results** The 3 most common feeding and swallowing difficulties in patients with type II and III SMA were choking (30.6%), difficulty conveying food to the mouth (20.4%), and difficulty chewing (20.4%). Current motor function status was an independent risk factor for feeding and swallowing difficulties (sitters vs walkers: OR, 7.59; 95% CI, 1.22-47.46). All 4 nonsitters (ie, patients with type II SMA who had lost their sitting ability) had feeding and swallowing difficulties. Patients with feeding and swallowing difficulties had significantly higher rates of underweight and aspiration pneumonia than those without these problems.

**Conclusion** Patients with type II and III SMA have a high prevalence of risk factors for feeding and swallowing difficulties, suggesting that an individualized treatment plan should depend on current motor function status. (*J Pediatr* 2011; ■: ■-■).

Spinal muscular atrophy (SMA) is an autosomal recessive neurodegenerative disease caused by mutations of the survival motor neuron 1 gene (*SMN1*).<sup>1,2</sup> The survival motor neuron 2 (*SMN2*) copy number on a group level has been correlated with clinical severity in patients with SMA<sup>3</sup> and in SMA-like mice.<sup>4</sup> Classification of SMA types I, II, III, and IV is based on the age at onset and the highest function achieved.<sup>1</sup>

A previous study found a 36% prevalence of at least one feeding problem in patients with SMA.<sup>5</sup> Limited mouth opening, difficulty conveying food into the mouth, chewing difficulties, choking, and dysphagia have been reported in patients with SMA.<sup>5</sup> The prevalence of feeding difficulties is fairly high in patients with type II SMA aged >20 years.<sup>6</sup> Choking may be associated with aspiration and can lead to pneumonia and life-threatening events in SMA.<sup>7</sup> Compensatory head posture is a major determinant for dysphagia in type II SMA.<sup>8</sup> Feeding difficulties in SMA leading to malnutrition have been reported.<sup>6</sup> Various feeding and swallowing difficulties are observed in patients with type II and III SMA, whereas feeding difficulties are inevitable outcomes of type I SMA.<sup>9</sup>

The risk factors for feeding and swallowing difficulties have not been identified in type II and III SMA. Identifying these risk factors is important because of the high prevalence and serious consequences of SMA. Treatment plans may be dependent on the risk factors rather than on the type of SMA.

## Methods

Between September 2008 and November 2009, 108 patients with type II or III SMA were enrolled in this study. The inclusion criteria were genetically confirmed *SMN1* homozygous deletion, clinical diagnosis of SMA type II or III, and age >3 years. Patients with type I SMA were excluded, because prophylactic interventions are routinely performed for feeding difficulties in this group of patients.<sup>9</sup> A questionnaire survey was conducted at the Kaohsiung Medical University Hospital, Kaohsiung, Taiwan. The study protocol was approved by the hospital's Institutional Review Board, and written informed consent was obtained from all participants aged ≥18 years or from the parents of younger subjects before participation.

From the Department of Pediatrics (Y-S.C., H-H.S., T-H.C., C-H.K., Y-J.J.), Division of Pediatric Emergency, Department of Emergency (T-H.C.), Department of Laboratory Medicine (Y-J.J.), Kaohsiung Medical University Hospital, Kaohsiung Medical University; Department of Pediatrics, Kaohsiung Municipal Ta-Tung Hospital (Y-S.C.); Department of Pediatrics, Kaohsiung Municipal Hsiao-Kang Hospital (H-H.S.); and Graduate Institute of Medicine, College of Medicine, Kaohsiung Medical University (C-H.K., Y-J.J.), Kaohsiung, Taiwan. Supported in part by the Kaohsiung Medical University-Spinal Muscular Atrophy Fund, Kaohsiung Medical University. Y-J.J. holds patents for hydroxyurea treatment for spinal muscular atrophy and the method for diagnosing spinal muscular atrophy; he also serves as editor-in-chief of *Pediatrics and Neonatology*. The other authors declare no conflicts of interest.

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SMA	Spinal muscular atrophy
SMN1	Survival motor neuron 1
SMN2	Survival motor neuron 2
W/A	Weight-for-age

The interview was performed using a semistructured questionnaire, answered by the patients or the main caregivers of the children aged <8 years. This questionnaire was based on previous research on SMA<sup>6</sup> and Duchenne muscular dystrophy<sup>10</sup> and was modified by a group comprising pediatric neurologists, pediatric gastroenterologists, general pediatricians, and an occupational therapist. The questionnaire included specific questions on feeding and swallowing ability, time needed to complete a meal, current motor function status, and current respiratory status (**Appendix**; available at [www.jpeds.com](http://www.jpeds.com)). Also assessed were mouth opening ability, ability to convey food to the mouth, solid/semisolid food chewing difficulties, drooling, oral hypersensitivity, choking from solid food/semisolid food/liquid, sensation of food getting stuck after swallowing or pain after swallowing, and regurgitation of solid food/semisolid food/liquid. All questionnaires were reviewed by doctors, who confirmed the problems. Poor head control while eating or being fed was recorded. Prolonged mealtime was defined as lasting more than 30 minutes.<sup>11</sup>

The frequency of aspiration pneumonia was documented by chart review. All episodes were recorded, regardless of whether the aspiration pneumonia with hospitalization was due to choking or regurgitation. Nutritional interventions included dietary modification, nasogastric tube feeding, and gastrostomy placement in combination with fundoplication. Respiratory dysfunction was classified according to the need for respiratory support, such as airway secretion mobilization and clearance technique using a CoughAssist machine (Philips, Eindhoven, The Netherlands), oral suctioning, and manual or mechanical chest physiotherapy.<sup>12</sup> Respiratory support options included noninvasive ventilation, mechanical ventilation, and ventilation with tracheostomy.<sup>12</sup>

Current motor function status was classified as walker, sitter, and nonsitter. A walker could walk independently, with or without the assistance of long leg braces; a sitter could not walk, but could sit independently; and a nonsitter could not sit independently.<sup>7</sup> Body weight was recorded and converted into a z score calculated according to World Health Organization 2006 child weight-for-age (W/A) and sex-specific growth charts for patients aged 0-5 years,<sup>13,14</sup> World Health Organization 2007 child W/A and sex-specific growth charts for those aged 5-10 years,<sup>15</sup> and Centers for Disease Control and Prevention 2000 W/A and sex-specific growth charts for those aged >10 years.<sup>16</sup>

### Statistical Analysis

Data are expressed as mean  $\pm$  SD unless indicated otherwise. Continuous variables (ie, age, body weight z score, and SMN2 gene copy number) were compared using the Mann-Whitney U test; categorical variables (ie, SMA type, sex, and head posture control when feeding) were compared using the  $\chi^2$  test. The Fisher exact test was used for comparing current motor function status and current respiratory status due to small cell sizes. ORs were calculated by multiple logistic regression with independent variables of age, sex, body weight z score, SMA type, SMN2 gene copy number, current motor function

status, current respiratory status, and head posture control when feeding. SPSS version 14.0 (SPSS Inc, Chicago, Illinois) was used for statistical analyses. A P value <.01 was considered significant.

## Results

We analyzed the questionnaires of 108 patients with SMA (50 females) who met the inclusion criteria; this included 60 patients with type II and 48 patients with type III. They ranged in age from 3 to 45 years (mean, 16.3  $\pm$  10.6 years) (**Table I**).

### Feeding and Swallowing Difficulties in SMA Types II and III

The prevalence and classifications of feeding and swallowing issues in type II and III SMA are shown in **Table II**. Nearly one-half of our patients (48 of 108; 44.4%) had at least one feeding or swallowing problem. The 3 most common kinds of feeding and swallowing difficulties in patients with type II and III SMA were choking (33 of 108; 30.6%), difficulty conveying food to the mouth (22 of 108; 20.4%), and chewing difficulties (22 of 108; 20.4%). Nearly one-third of patients (35 of 108; 32.4%) had prolonged mealtimes.

### Risk Factors for Feeding and Swallowing Difficulties

We compared clinical characteristics between patients without any feeding or swallowing problems (group 1) and patients with such difficulties (group 2). Type II SMA, sitter and nonsitter status, respiratory management needs, and poor head control were significantly more common among those with feeding and swallowing difficulties than in those without these problems. Patients with feeding and swallowing difficulties had significantly lower body weight (**Table III**). Interestingly, current motor function status

**Table I.** Demographic data and clinical characteristics (n = 108)

Age, years, mean $\pm$ SD (range)	16.3 $\pm$ 10.6 (3~45)
Body weight z score, mean $\pm$ SD (range)	-1.1 $\pm$ 1.7 (-4.5~3.1)
SMN2 copy number, mean $\pm$ SD (range)	3 $\pm$ 0.7 (2~5)
SMA type, n (%)	
Type II	60 (55.6)
Type III	48 (44.4)
Sex, n (%)	
Male	58 (53.7)
Female	50 (46.3)
Current motor function status, n (%)	
Walker	28 (25.9)
Sitter	76 (70.4)
Nonsitter	4 (3.7)
Current respiratory status, n (%)	
Not needing respiratory management	91 (84.3)
CoughAssist machine + suction	6 (5.6)
Noninvasive ventilation/invasive ventilation + CoughAssist machine + suction	11 (10.2)
Head posture control when feeding	
Normal head posture control	95 (88.0)
Poor head control	13 (12.0)

**Table II.** Prevalence and classifications of feeding and swallowing difficulties in patients with types II and III SMA (n = 108), n (%)

No feeding or swallowing problems	60 (55.6)
At least 1 feeding or swallowing problem	48 (44.4)
Limited mouth opening	12 (11.1)
Difficulty conveying food to the mouth	22 (20.4)*
Chewing difficulties	22 (20.4)*
Solid food chewing difficulty	22 (20.4)
Semisolid food chewing difficulty	6 (5.6)
Oral hypersensitivity	15 (13.9)
Drooling	9 (8.3)
Choking	33 (30.6)*
Solid food choking	23 (21.3)
Semisolid food choking	13 (12.0)
Liquid choking	18 (16.7)
Dysphagia	18 (16.7)
Solid food dysphagia	18 (16.7)
Semisolid food dysphagia	6 (5.6)
Liquid dysphagia	3 (2.8)
Prolonged mealtimes (longer than 30 minutes)	35 (32.4)

\*The 3 most common feeding or swallowing difficulties in patients with type II and III SMA.

was an independent risk factor for feeding and swallowing difficulties in patients with type II and III SMA (sitters vs walkers; OR, 7.59; 95% CI, 1.22-47.46). The 4 nonsitters were all type II SMA (aged 5, 6, 13, and 16 years at enrollment). All 4 nonsitters and all 13 patients with poor head control had feeding and swallowing difficulties; the OR for this could not be calculated due to zero cells (Table III). *SMN2* copy number did not contribute to the risk of feeding disorders in our patients with type II and III SMA. Age was not an independent risk factor for feeding and swallowing difficulties.

In the 4 nonsitters, the age of onset of SMA symptoms was 10 months, 1 year, 1 year, and 1 year and 2 months. In these 4 patients, the duration of ability to maintain independent sitting was 9 years and 2 months, 3 years, 7 years and 5 months, and 4 years and 10 months, respectively; thus, these patients became nonsitters at age 10 years, 4 years, 8 years and 5 months, and 6 years, respectively.

### Consequences of Feeding and Swallowing Difficulties

Aspiration pneumonia was reported in 10 patients (9.3%). Episodes of aspiration pneumonia involving hospitalization were increased significantly in patients with at least one feeding or swallowing difficulty. Thirty-six patients (33.3%) were underweight (W/A below 2 SD of the reference median; *z* score  $\leq -2$ ). Patients with feeding and swallowing difficulties had significantly higher rates of underweight than those without these problems (Table IV).

## Discussion

In our study cohort of patients with type II and III SMA, choking was the most common feeding problem, with a prevalence of 30.6%. A previous study reported that difficulty conveying food to the mouth and chewing difficulties were the most common problems in patients with type II SMA.<sup>6</sup> Another study reported that choking (45%) was more common than chewing problems (38%) in patients with type I and II SMA.<sup>17</sup>

We found a correlation between current motor function status and feeding and swallowing difficulties. Current

**Table III.** Comparison of clinical characteristics in patients without feeding or swallowing problems (group 1) and those with feeding and/or swallowing difficulties (group 2)

Variables	Group 1 (n = 60)	Group 2 (n = 48)	P value*	OR (95% CI)
Age, years, mean $\pm$ SD	15.5 $\pm$ 9.0	17.1 $\pm$ 11.8	.391	0.97 (0.92-1.03)
Body weight <i>z</i> score, mean $\pm$ SD	-1.0 $\pm$ 1.6	-2.0 $\pm$ 1.7	<.01	0.83 (0.61-1.13)
<i>SMN2</i> copy number, mean $\pm$ SD	2 $\pm$ 0.7	2 $\pm$ 0.8	1.000	1.25 (0.61-2.58)
SMA type, n (%)				
Type II	23 (38.3)	37 (77.1)	<.001	Reference
Type III	37 (61.7)	11 (22.9)		0.99 (0.25-3.96)
Sex, n (%)				
Male	30 (50.0)	28 (58.3)	.440	Reference
Female	30 (50.0)	20 (41.7)		1.12 (0.40-3.12)
Current motor function status, n (%)				
Walker	25 (41.7)	3 (6.3)	<.001	Reference
Sitter	35 (58.3)	41 (85.4)		7.59 (1.22-47.46)
Nonsitter	0 (0)	4 (8.3)		NC
Current respiratory status, n (%)				
Not needing respiratory management	58 (96.7)	33 (68.8)	<.001	Reference
CoughAssist machine + suction	1 (1.7)	5 (10.4)		2.42 (0.18-33.21)
Noninvasive ventilation/invasive ventilation + CoughAssist machine + suction	1 (1.7)	10 (20.8)		1.51 (0.12-19.01)
Head posture control when feeding				
Normal head posture control	60 (100.0)	35 (72.9)	<.001	Reference
Poor head control	0 (0)	13 (27.1)		NC

NC, not calculated (because of zero cells).

ORs were computed by multiple logistic regression with all variables in this table as independent variables.

\*P values were computed using the Mann-Whitney *U* test (for age, body weight *z* score, and *SMN2* gene copy number), the  $\chi^2$  test (for SMA type, sex, and head posture control when feeding), and the Fisher exact test (for current motor function status and current respiratory status).

**Table IV.** Comparison of consequences in patients without feeding or swallowing problems (group 1) and those with feeding and/or swallowing difficulties (group 2)

Consequences	Group 1 (n = 60)	Group 2 (n = 48)	P value
Aspiration pneumonia with hospitalization, n (%)	1 (1.7)	9 (18.8)	.005
Underweight, n (%)	12 (20.0)	24 (50.0)	.002

motor function status was an independent risk factor for feeding and swallowing difficulties in type II and III SMA. All 4 nonsitters in our study, all of whom had type II SMA, had feeding and swallowing difficulties. It appears that the need for intervention for feeding and swallowing difficulties is highly correlated with current motor function status.

Although we could not calculate the OR by logarithmic regression because all 13 patients with poor head control had feeding and swallowing difficulties, we found a clear relationship between poor head control and feeding and swallowing difficulties. A previous study found that dysphagia in patients with type II SMA was due to lower motor neuron problems, causing muscle weakness and decreased efficiency of movements of the tongue and submental muscle group, with decreased compensatory head posture.<sup>8</sup>

Our patients who required respiratory management had significantly more feeding and swallowing difficulties than those who did not. A possible explanation for this finding is that bulbar dysfunction leads to progressive respiratory dysfunction and feeding and swallowing difficulties. This finding has been reported previously only in patients with type I SMA.<sup>18</sup> Bulbar dysfunction also has been reported in type II SMA, but rarely in type III.<sup>5</sup>

Age was not an independent risk factor for feeding and swallowing difficulties in the present study, although a previous study found more frequent difficulties in conveying food to the mouth, choking, and dysphagia in patients with type II SMA aged >20 years.<sup>6</sup> These discrepant results are related to the fact that there were 10 patients aged <20 years who had feeding and swallowing difficulties (age range, 3-19 years; all type II SMA), all of who required respiratory management. Four of these patients became nonsitters, and 7 of them had poor head control. These findings suggest that besides age, respiratory support, current motor function status, and head posture control during feeding may play important roles in feeding and swallowing difficulties.

The present study is a cross-sectional observational study. Although we found several potential risk factors, demonstrating causative associations between these risk factors and chronic feeding difficulties is difficult in a cross-sectional study. A large, long-term prospective cohort study in this population may help establish the causative relationship between risk factors and the onset of feeding or swallowing difficulties. This would provide guidance on how

early to begin monitoring and managing these feeding problems.

In conclusion, the 3 most frequent feeding and swallowing difficulties in our patients with type II and III SMA were choking, difficulty conveying food to the mouth, and chewing difficulties. Current motor function status was an independent risk factor for feeding and swallowing difficulties. These results suggest that management of feeding and swallowing difficulties in patients with type II and III SMA should be based on current motor function status rather than on SMA subtype. Early detection, monitoring, and management of feeding and swallowing difficulties may avoid further unfavorable consequences in these patients. ■

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Reprint requests: Yuh-Jyh Jong, MD, Department of Pediatrics, Kaohsiung Medical University Hospital, 100, Shih-Chuan 1st Road, Kaohsiung 80708, Taiwan. E-mail: yjjong2@gap.kmu.edu.tw

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## Appendix

### Questionnaire for Feeding and Swallowing Difficulties in Spinal Muscular Atrophy

Questionnaire for feeding and swallowing difficulties in spinal muscular atrophy

(Please answer the questions and mark with an X in , )

Patient's name: \_\_\_\_\_

Date: \_\_\_\_\_

Completed by :  Patient,  Mother,  Father,  Other \_\_\_\_\_ (main caregiver)

Chart No. in KMUH \_\_\_\_\_

Birthday: \_\_\_\_\_

Body weight: \_\_\_\_\_ kg; Sex:  male,  female

Diagnosis: \_\_\_\_\_ (For doctor)

SMN gene copy number: \_\_\_\_\_ (For doctor)

#### PART A: Feeding and swallowing difficulties

1. Limited mouth opening:  Yes,  No.
2. Difficulties in getting food into the mouth:  Yes,  No.
3. Solid food (e.g., meats, apples) chewing difficulty:  Yes,  No.
4. Semisolid food (e.g., mashed potatoes or vegetables) chewing difficulty:  
 Yes,  No.
5. Distinct patterns of food textural preference:  Yes,  No.
6. Drooling or incomplete lip closure:  Yes,  No.
7. Choking when eating solid food (e.g., meats, apples):  Yes,  No.
8. Choking when eating semi-solid food (e.g., mashed potatoes or vegetables):  
 Yes,  No.
9. Choking when drinking liquid (e.g., water, milk):  Yes,  No.
10. Sensation of food sticking in the chest/throat or regurgitation or repeated attempts to swallow after eating solid food (e.g., meats, apples):  Yes,  No.
11. Sensation of food sticking in the chest/throat or regurgitation or repeated attempts to swallow after eating semi-solid food (e.g., mashed potatoes or vegetables):  
 Yes,  No.
12. Sensation of food sticking in the chest/throat or regurgitation or repeated attempts to swallow after drinking liquid (e.g., water, milk):  Yes,  No.
13. Prolonged mealtimes of more than 30 minutes:  Yes,  No.
14. Poor head control:  Yes,  No. (For doctor)
15. Aspiration pneumonia with hospitalization:  Yes,  No.
16. Change the consistency and/ or quantity of administered food:  Yes,  No.
17. Nutritional intervention:  No nutritional intervention,  Nasogastric tube feeding,  Gastrostomy feeding,  Others \_\_\_\_\_

#### PART B: Respiratory function and current motor function status

1. Current respiratory status:
  - Not needing respiratory management
  - Needing CoughAssist machine and non-invasive ventilation
  - Tracheostomy with/without ventilation
2. Current motor function status:
  - Walks independently or walks with support (eg, long leg braces)
  - Cannot walk but can sit alone
  - Unable to sit independently