Swallowing dysfunction in very low birth weight infants with oral feeding desaturation

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Background: **We detected swallowing dysfunction by the modified barium swallow (MBS) test and determined risk factors for swallowing dysfunction in very low birth weight (VLBW) infants with oral feeding desaturation near discharge.**

Methods: **We retrospectively reviewed 41 VLBW infants referred for MBS test because of significant oral feeding desaturation at ≥35 weeks of postmenstrual age. Infants who showed impaired airway protection, including inadequate epiglottic closure, laryngeal penetration and/or tracheal aspiration by MBS test, were compared to those without impaired airway protection.**

Results: **Eleven infants (26.8%) showed impaired airway protection by MBS test. They had a significantly lower gestational age at birth but a similar postmenstrual age compared to those without impaired airway protection. All infants with impaired airway protection were born at ≤28 weeks of gestation.**

Conclusions: **Swallowing dysfunction resulting in aspiration should be considered as a cause of significant oral feeding desaturation in infants born at ≤28 weeks of gestation regardless of postmenstrual age.**

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Key words: **aspiration;**
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Original article

Introduction

Although advanced neonatal intensive care has markedly improved the survival rates of very low birth weight (VLBW) infants, oral feeding difficulties often delay the discharge from the neonatal intensive care unit (NICU). Safe oral feeding implies a minimal risk of aspiration and proper coordination of the suck-swallow-breath sequence.[1] This coordination occurs between 33 to 34 weeks[2,3] and matures significantly between 33 and 36 weeks of postmenstrual age in premature infants.[4] However, many VLBW infants continue to experience desaturation during oral feeding near the time of discharge from the NICU.[5] Immature suck-swallow rhythmic integration[6] and inappropriate swallow-respiration interfacing[7] may cause apneic swallow or aspiration and are regarded as major causes of oral feeding difficulties including oxygen desaturation. However, the frequency of aspiration is often underestimated from clinical evaluations in this population, as most infants aspirate silently without such typical symptoms as coughing or choking.[8] In addition, it is difficult to determine whether a desaturation episode is associated with true aspiration. Comrie et al[9] pointed out that the etiology of unacceptable feeding episodes for infants who are 35 weeks of postmenstrual age with oral feeding-associated desaturation, apnea, and bradycardia needs to be evaluated in order to implement proper management strategies or alternative options. However, there are few direct evidence-based data on swallowing dysfunction in VLBW infants with oral feeding desaturation near the time of discharge.

Modified barium swallow (MBS) test is safer than upper gastrointestinal examination or esophagogram because of its shorter testing time and the use of a small

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amount of barium even in premature babies. It is also the favored method for evaluation of the pharyngeal and cervical esophageal phases of deglutition[10-12] and is the only reliable means of identifying aspiration during swallowing.[13] Therefore, the MBS test is valuable to provide information about interventions for the improvement of feeding efficiency and safety.[9]

This study was undertaken to detect swallowing dysfunction resulting in aspiration during oral feedings by MBS test and to determine risk factors in VLBW infants with significant oral feeding desaturation near the time of discharge.

Methods

Subjects

This study was approved by the Institutional Review Board of the Samsung Medical Center, and a waiver of consent was granted for chart review without patient contact. Of 196 VLBW infants admitted within 30 days of birth who survived until discharge from the NICU of the Samsung Medical Center between January 2003 and December 2004, 44 were referred for videofluoroscopic MBS test because of significant oral feeding desaturation at ≥35 weeks of postmenstrual age by attending neonatologists. As a general unit policy, oral feedings were initiated when infants were stable and showed oromotor cues. Significant oral feeding desaturation was defined as the presence of one or more episodes of SpO_2 below 80% for 15 seconds with bradycardia during regular oral feedings by the nursing staff of the NICU. Infants who experienced these episodes with more than half of feeds per day (more than 4 out of oral feeds per day)[14-16] were enrolled. Infants with multiple congenital anomalies or other conditions interfering with oral feeding, such as cleft palate and cardiac disease, were excluded. Three of the 44 infants were excluded after analysis due to congenital abnormalities (one with Beckwith-Wiedemann syndrome, one with a chromosome 1p deletion, and one with tracheoesophageal fistula). Before referral for MBS test, all infants were observed by attending physicians, nurses, and oral pathologists, who determined that clinical modifications were not effective for reducing these episodes. At the time of MBS test, all infants were on full enteral bolus feeds; more than half of the milk was fed by oral bottle feeds. Ten (24.3%) of 41 infants were given combined gavage feeding by an orogastric tube, 15 (36.6%) required oxygen supplementation (FiO_2 <0.3 by blender) via nasal prong or side nasal administration continuously or intermittently, and 7 (17.0%) required oxygen administration only at the time of oral bottle feeding. The median number of significant oral feeding desaturation events was 10 (4-12) day and the average lowest oxygen saturation level by pulse oximeter (SpO_2) was 70%±9% (40%-79%) on the day before referral to MBS. The 41 enrolled VLBW infants were born between 23.4 and 30.6 weeks of postmenstrual age (mean: 27.3±1.8 weeks). They were grouped into 3 subgroups by gestational age at birth: (a) 25 weeks and below (*n*=10), (b) 26 to 28 weeks (*n*=22), and (c) 29 weeks and above (*n*=9). Birth weight ranged from 439 to 1490 g (mean: 972±284 g). At the time of initial MBS test, corrected gestational age ranged from 35.1 to 47.4 weeks (median: 37.0 weeks) and body weight ranged from 1725 to 3800 g (mean: 2561±504 g) (Table 1).

MBS test

Videofluoroscopic MBS test was performed to investigate the oral, pharyngeal, and upper esophageal stages of swallowing by experienced rehabilitation pathologists, who used a fluoroscope (Shimavision HG320, Shimadzu Co., Tokyo, Japan) and recorded the test on a videocassette recorder (Winner SV-2200, Samsung Electronics Co., Suwon, Korea).

For the test, 30 mL liquid barium suspension was added to a 70 mL formula in a bottle. The infant was placed at approximately 45° upright on a fluoroscopic unit table. If no aspiration was observed on initial swallowing, the infant was allowed to suck. In order to minimize radiation exposure, the fluoroscopy unit was run only during the initial 5 to 10 serial swallows and when swallowing dysfunction was suspected. The frame capture rate was 30 frames/second. The maximum duration of radiation exposure was limited to 1 to 2 minutes. If there were serious symptoms such as significant desaturation with persistent bradycardia and/or definite tracheal aspiration on fluoroscopy, the test was ceased.

Recorded studies were reviewed and interpreted by the rehabilitation pathologists. The videotape was

Table 1. Demographic data of enrolled patients (*n*=41)

Average gestational age, wk (mean ± SD)	27.3±1.8
Average birth weight, g (mean ± SD)	972±284
Outborn (%)	3 (7.3)
Male (%)	21 (51.2)
Enteral feeding start day (mean ± SD)	4±5
Full enteral feeding day (mean ± SD)	26±14
BPD (%)	21 (51.2)
NEC (stage ≥2) (%)	6 (14.6)
Grade III/IV IVH (%)	3 (7.3)
Cystic PVL (%)	0 (0.0)
Hospital duration, d (mean ± SD)	92±27

BPD: bronchopulmonary dysplasia; NEC: necrotizing enterocolitis; IVH: intraventricular hemorrhage; PVL: periventricular leukomalacia.

played with a videocassette recorder and a monitor, which allowed for slow-motion and frame-by-frame analysis. For interpretation of the oral phase, frequency and power of sucking and tongue movement were assessed subjectively as weak/poor or strong. In the pharyngeal phase, the adequacy of vocal cord closure and movement and the presence or absence of vallecular or pyriform sinus pooling and nasopharyngeal reflux were assessed, as were the adequacy of epiglottic closure movement during swallowing and the presence or absence of laryngeal penetration and tracheal aspiration. Nasopharyngeal reflux was identified by barium reflux from the oropharynx to the nasopharynx. Inadequate epiglottic closure and movement (IECM) was defined as delay or lag in epiglottic closure when swallowing of oral bolus was initiated. Laryngeal penetration was identified by the detection of barium underneath the epiglottis and within the vocal cords. Tracheal aspiration was identified by barium below the level of the true vocal cords. Among the abnormal findings of the pharyngeal stage, IECM, laryngeal penetration, and tracheal aspiration were classified as impaired airway protection during swallowing, which resulted in true aspiration.[17] Finally, the presence or absence of gastroesophageal reflux was also evaluated during the esophageal phase.

Data collection and analysis

The medical records of the enrolled infants were retrospectively reviewed. Data related to the timing of enteral (tube) or oral feeding and full enteral or oral feeds were collected. Full enteral feeds were considered for achieving an adequate feeding volume without the need of total parenteral nutrition to achieve proper weight gain. Full oral feeding implied that the infant fed well without the need of gavage supplementation to maintain growth. Data on the number of events of significant oral feeding desaturation (SpO_2 below 80% for 15 seconds and associated bradycardia) and the lowest SpO_2 level during oral feeding desaturation were also collected the day before the MBS test. Demographic and morbidity characteristics were collected. Bronchopulmonary dysplasia was defined as the need of supplemental oxygen support at 36 weeks of postmenstrual age[18] and necrotizing enterocolitis was defined as Bell's stage II or greater.[19] Information about stage III or IV intraventricular hemorrhage[20] and cystic periventricular leukomalacia on cranial ultrasonogram was also noted. Records of initial MBS test and follow-up clinical course were also collected. The results of the initial MBS test were summarized in the 3 GA-based subgroups. Based on the results of the MBS test, subgroup analyses were performed on enrolled infants who were divided into two groups: infants with impaired airway protection (presence of one or more components of impaired airway protection) and infants without impaired airway protection (normal or other abnormal findings). The demographic and clinical characteristics of the two groups were analyzed and compared.

For statistical analysis, discrete variables were compared using the Chi-square test, while unpaired *t* tests or Wilcoxon's rank-sum test was used to analyze subgroup differences within continuous variables. Stata software (ver. 11.0, Stata Corp LP, College Station, TX, USA) was used for analyses.

Results

MBS findings

Of the 41 VLBW infants, 13 (31.7%) did not show any abnormalities by MBS test and 28 (68.3%) showed abnormalities by the test. Eleven infants (26.8%) showed impaired airway protection and 17 (41.5%) showed other abnormalities at oral, pharyngeal, and esophageal stages (Table 2).

Those abnormalities in the oral phase included weak sucking power and poorly sustained sucking in 2 infants (4.9%). During the pharyngeal phase, one infant (2.4%) showed reduced pharyngeal peristalsis with stasis in the vallecula, and 9 infants (22.0%) showed NPR consistent with incompetent closure of the nasopharynx.

Concerning impaired airway protection during pharyngeal swallowing, IECM without aspiration or penetration was observed in 2 infants (4.9%). Silent laryngeal penetration without aspiration was observed in 2 infants (4.9%), one of whom was associated with IECM. Significant tracheal aspiration was observed in 7 infants (17.1%) who had IECM.

With regard to abnormalities at esophageal stage, 5

Table 2. Results of modified barium swallow test*

Normal	13 (31.7%)
Other abnormalities	17 (41.5%)
Weak and poor sustained sucking	2 (4.9%)
Reduced pharyngeal peristalsis and stasis in vallecula	1 (2.4%)
Nasopharyngeal reflux	9 (22.0%)
Gastroesophageal reflux	3 (7.3%)
Nasopharyngeal reflux + Gastroesophageal reflux	2 (4.9%)
Impaired airway protection	11 (26.8%)
Inadequate epiglottic closure & movement	2 (4.9%)
Silent laryngeal penetration	1 (2.4%)
Penetration + Inadequate epiglottic closure and movement	1 (2.4%)
Aspiration + Inadequate epiglottic closure and movement	7 (17.1%)
Total	41 (100%)

*: Expressed as number (percentage) of patients.

infants (12.2%) had gastroesophageal reflux; 3 of these infants had simultaneous gastroesophageal reflux and nasopharyngeal reflux.

Impaired airway protection assessed by MBS test

Impaired airway protection assessed by MBS test differed significantly in gestational age subgroups. Six (60%) of 10 infants with ≤25 weeks of gestational age showed impaired airway protection, while only 5 (23%) of 22 infants with gestational age ranging from 26 to 28 weeks showed impaired airway protection by MBS test. None of the 9 infants with ≥29 weeks of gestational age showed impaired airway protection by MBS test (P=0.04).

Comparison of infants with impaired airway protection with those without impaired airway protection (Table 3) showed that gestational age was significantly lower in infants with impaired airway protection than in those without impaired airway protection (P=0.02). However, no significant difference was observed between the 2 groups in body weight, postmenstrual age, postnatal day of life at MBS, number of feeding desaturation events, or lowest SpO_2 level during oral feeding desaturation. Postnatal age and days from oral feeding at MBS, postnatal age and postmenstrual age at the first oral feeding, postnatal time to attain oral feeding, and total hospital duration did not differ between the two groups. Also there were no significant differences in the incidence of morbidities, including bronchopulmonary dysplasia, necrotizing enterocolitis (stage ≥2), grade III/IV intraventricular hemorrhage, and periventricular leukomalacia.

Follow-up

For infants who showed abnormalities including impaired airway protection at MBS, strategies like pacing, position change, and/or modified sucking pattern or nipple flow rate to facilitate smaller bolus sizes[9] were implemented to facilitate feeding and safe swallowing. Most of these infants responded well and were able to maintain oral feeding (Table 4). However, 3 of 7 infants (Table 4; cases 9, 10, and 11) who had tracheal aspiration at MBS did not respond to modified oral feeding and continued to show oral feeding desaturation. Therefore, full gavage feedings by an orogastric tube and oral rehabilitation for oral feeding skills were prescribed to avoid obvious aspiration. Two of the 7 infants (Table 4; cases 10 and 11) attained safe oral feeding by about 42 weeks of postmenstrual age; however, one infant (Table 4; case 9) continued to have obvious aspiration until 60.9 weeks of postmenstrual age.

In 6 of 7 (Table 4; cases 6-11) infants with tracheal aspiration, follow-up MBS tests were performed. The

Table 3. Demographic and morbidity characteristics of patients with impaired airway protection at modified barium swallowing test*

Variables	Infants with IAP (n=11)	Infants without IAP (n=30)
Gestational age, wk	26.3±1.6 (23.7–28.1)*‡	27.6±1.7 (23.4–30.6)
Birth weight, g	901±194 (626 –1274)	997±309 (439–1490)
PMA at MBS, wk	37.1±1.7 (35.3–47.4)	38.1±2.7 (35.1–41.7)
Median value†	36.9	37.1
Weight at MBS, g	2444±451 (1725–3190)	2605±523 (1810–3800)
Oxygen supply at the time of MBS		
Above 8 hours/day (%)	4 (36)	11 (37)
Only for oral feeding (%)	2 (18)	3 (10)
Combined gavage feeding at the time of MBS (%)	3 (27)	7 (23)
Postnatal days at MBS	75±18 (49–112)	78±28 (42–145)
Postnatal days, start of enteral gavage feeding	3.2±2.7 (1–9)	4.7±5.5 (1–27)
Postnatal days, full enteral feeding	27±13 (6–49)	26±14 (9–56)
PMA at the start of oral feeding, wk	34.1±1.0 (33.1–35.1)	34.4±1.3 (32.3–36.9)
Days from initial oral feeding at the time of MBS	26±14 (13–59)	28±17 (2–81)
Days, full oral feeding from initial oral feeding	48±65 (5–238)	21±10 (5–47)
Outborn (%)	0 (0)	3 (10)
Male (%)	4 (36)	17 (57)
SGA (%)	2 (18)	6 (20)
BPD (%)	7 (64)	14 (47)
NEC (stage ≥2) (%)	4 (36)	2 (7)
IVH (grade ≥3) (%)	1 (9)	2 (7)
Hospital duration, d	91±21 (53–125)	92±29 (54–178)

*: expressed as mean ± SD (minimum-maximum value) unless otherwise indicated; †: expressed as median; ‡: statistically significant between the two groups (P<0.05). PMA: postmenstrual age; IAP: impaired airway protection; MBS: modified barium swallow; SGA: small for gestational age; BPD: bronchopulmonary dysplasia; NEC: necrotizing enterocolitis; IVH: intraventricular hemorrhage; PVL: periventricular leukomalacia.

Table 4. Follow-up results of patients with impaired airway protection at modified barium swallow test

Case No.	GA (wk)	BW (g)	PMA(wk)/wt(g) at 1st MBS	O_2/G-tube at 1st MBS	1st MBS finding	Recommend	f/u MBS No.	PMA (wk) at final MBS	PMA (wk) at full oral feed
	No F/U								
1	23.7	665	40.6/3180	+/-	IECM, NPR, penetration	Careful OF			40.4
2	25.1	839	36.3/2385	-/+	IECM, aspiration	Careful OF			36.7
3	25.7	972	41.9/3190	-/-	IECM	Keep OF			38.7
4	25.9	834	36.3/2705	+/-	Silent penetration	Careful OF			35.1
5	28.7	811	36.6/1725	-/-	IECM	Keep OF			35.3
	F/U								
6	26.4	906	37.4/2430	+/+	IECM, aspiration	Keep OF	1	41.0	35.4
7	27.0	960	37.0/2310	+/-	IECM, aspiration, GER	Keep OF	1	39.1	35.9
8	28.1	1179	35.1/2150	-/-	Silent aspiration	Monitoring	1	39.1	35.0
9	24.7	626	38.1/2200	+/+	IECM, aspiration	G-F	5	60.9	67.9
10	25.9	850	36.4/2035	+/+	IECM, aspiration	G-F	2	43.4	42.3
11	28.0	1274	36.6/2570	+/-	IECM, aspiration, NRP	G-F	2	41.9	42.1

GA: gestational age; BW: birth weight; PMA: postmenstrual age; O_2: oxygen supply; G-tube: gavage tube; MBS: modified barium swallow; IECM: inadequate epiglottic closure and movement; NPR: nasopharyngeal reflux; GER: gastroesphageal reflux; OF: oral feeding; G-F: gavage feeding by orogastric tube; F/U: follow up MBS test.

average postmenstrual age and time between initial and final MBS tests were 44.1 (39.1-60.9) weeks and 8.0 (2.1-22.7) weeks, respectively. At the final MBS, 4 of 6 infants exhibited complete improvement, while 2 infants (Table 4; cases 9 and 11) had partial improvement with residual laryngeal penetration and tracheal aspiration.

Discussion

In our study, 70% of 41 VLBW infants who were referred for MBS for significant oral feeding desaturation at postmenstrual age ≥35 weeks exhibited various swallowing abnormalities, and 30% exhibited impaired airway protection resulting in potential or obvious aspiration. The most important factor associated with impaired airway protection during swallowing was low gestational age at birth. Bronchopulmonary dysplasia and grade III/IV intraventricular hemorrhage were not significant risk factors for impaired airway protection in this cohort. Safe transition from tube to independent oral feeding in preterm infants indicates a minimal risk of aspiration.[1] However, safe oral feeding requires not only maturation of swallowing function but also adequate coordination of sucking, swallowing, and respiration.[21] Moreover, swallowing must occur during a safe phase of the respiratory cycle.[7]

Sequential or rhythmic sucking, swallowing, and respiration are controlled by central pattern generators[22-24] and components of these three functions and their coordinated activities mature at different times and rates.[1] Swallowing rhythm is established as early as 32 weeks of postmenstrual age; however, the stability of the sucking rhythm increases steadily throughout the period between 32 and 40 weeks of postmenstrual age.[25,26] Gewolb et al[26] reported that the maturation of sucking and swallowing in preterm infants was better correlated with postmenstrual age than with postnatal age. Amaizu et al[1] demonstrated that maturation levels of sucking, swallowing, and respiration and their coordinated activity depend on gestational age rather than postmenstrual age, which indicates that gestational age influences the ex utero development of oral feeding skills. The present study demonstrated that gestational age at birth was significantly lower in infants with impaired airway protection compared to those without impaired airway protection although infants in the two groups had similar postmenstrual age at the time of MBS. In addition, none of the VLBW infants born later than 28 weeks of gestational age presented with impaired airway protection in our infants. These findings suggest that infants with lower gestational age have a higher rate of impaired airway protection at a comparable postmenstrual age compared to those with higher gastational age when they experience significant oral feeding desaturation.

Bronchopulmonary dysplasia is the major factor responsible for the development of desaturation during oral feedings.[16] Mizuno et al[27] found that deglutition apnea or apneic swallow lasted longer in infants with bronchopulmonary dysplasia. In the present study bronchopulmonary dysplasia was not a risk factor for impaired airway protection, which suggests that aspiration during swallowing might not be a major cause of increased oral feeding desaturation in infants with bronchopulmonary dysplasia.

In the present study, grade III/IV intraventricular hemorrhage was not a risk factor for impaired airway

protection. Since poor feeding ability is known to be a marker of delayed brain development,[28] further studies are required to investigate the relationship between abnormal MBS and neurodevelopmental outcomes.

Nasopharyngeal reflux may stimulate the nasopharynx and account for the apneic responses seen during feeding in premature infants.[29] It is associated not only with apnea, but also with choking and history of pneumonia in infants.[30-32] Although none of the 7 infants with nasopharyngeal reflux in our study showed laryngeal penetration or aspiration, the potential for aspiration might be underestimated.

Stasis was observed in the vallecula in one infant without findings of impaired airway protection at MBS in our study. Newman et al[29] demonstrated that pooled feeding material in the pyriform sinus tended to penetrate or be aspirated only at the later stages of MBS studies. They suggested that a routine swallowing evaluation by MBS (which lasts for only a few swallows) might miss laryngeal penetration or aspiration.

The role of isolated gastroesophageal reflux in causing such swallowing difficulties as dysphagia and feeding desaturation remains unclear. In the present study, no infants who exhibited gastroesophageal reflux at MBS exhibited concurrent impaired airway protection. Because significant gastroesophageal reflux in infants can result in a variety of respiratory signs and symptoms,[33,34] there is a possibility that feeding desaturation in such cases could be attributed to gastroesophageal reflux.

Our study has several limitations. As a retrospective study, a direct and clear causal relationship between desaturation and impaired airway protection at MBS during swallowing could not be delineated. We defined impaired airway protection as incomplete laryngeal closure or entry of milk into the airway at MBS only. As mentioned above, other abnormal findings such as nasopharyngeal reflux and stasis of the vallecula may be associated with potential aspiration in clinical situations; this may lead to possible underestimation of the frequency of impaired airway protection. Furthermore, the short period of observation in MBS can also lead to underestimation of the frequency of penetration or aspiration. However, even with the underestimation of the presence and frequency of impaired airway protection, our results strongly suggest that a number of VLBW infants with oral feeding desaturation near discharge have swallowing dysfunction that leads to potential and/or true aspiration. In spite of the fact that laryngeal penetration and aspiration may lead to pulmonary inflammation and secondary infection,[35] newborn infants have poorly developed cough reflexes.[8]

In the present study, 7 infants who showed tracheal aspiration on MBS and IECM, exhibited no significant clinical symptoms like coughing and choking. Furthermore, the degree of oxygen desaturation (such as the number of episodes and lowest SpO_2 level during oral feeding desaturation) was not different between infants with impaired airway protection and those without impaired airway protection. Clinically, these problems can be detected only when they are of clinical significance. Therefore, diagnostic evaluations for excluding the possibility of impaired airway protection should be performed in VLBW infants with significant oral feeding desaturation as a lung protection strategy. Three of the 7 infants with tracheal aspiration in our study were given gavage feedings to avoid tracheal aspiration until they were capable of safe swallowing. Finally, the wide range of postmenstrual age at MBS might be a limitation of the retrospective study. However, the postmenstrual age at the start of oral feeding of these infants was not different statistically.

In conclusion, 30% of the VLBW infants at MBS at ≥35 weeks of postmenstrual age due to significant oral feeding desaturation demonstrated swallowing dysfunction resulting in silent or obvious aspiration. These infants were born at ≤28 weeks of gestation. Infants who were born at <26 weeks of gestation experienced an increased probability of aspiration (60%) regardless of the presence of bronchopulmonary dysplasia or high-grade intraventricular hemorrhage. This finding suggests that swallowing dysfunction depends on gestational age rather than postmenstrual age. Therefore, possible aspiration and implementation of appropriate and alternative feeding options should be considered cautiously in VLBW infants with low gestational age (≤28 weeks) at birth who present with significant oral feeding desaturation near the time of discharge.

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Ethical approval: The Institutional Review Board of the Samsung Medical Center approved this retrospective study and a waiver of consent was granted for chart review without patient contact.

Competing interest: The authors declare no conflict of interest.

Contributors: Park WS proposed the study. Lee JH and Chang YS wrote and contributed to this paper equally. All authors contributed to the design and interpretation of the study and to further drafts.

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