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Effect of Postnatal Maturation on the Mechanisms of Esophageal Propulsion in Preterm Human Neonates: Primary and Secondary Peristalsis

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Abstract

OBJECTIVES—The changes in esophageal propulsive characteristics during maturation are not known. Our aim was to define the effects of postnatal maturation on esophageal peristaltic characteristics in preterm human neonates. We tested the hypotheses that: (i) maturation modifies esophageal bolus propulsion characteristics, and (ii) the mechanistic characteristics differ between primary and secondary peristalsis.

METHODS—Esophageal motility in 10 premature neonates (mean 27.5 weeks gestational age) was evaluated twice at 33.8 weeks (time 1, earlier study) and 39.2 weeks (time 2, later study) mean postmenstrual age. Esophageal manometry waveform characteristics (amplitude and duration, peristaltic velocity, and intrabolar pressure domains) were analyzed during spontaneous primary peristalsis and infusion-induced secondary peristalsis. Repeated-measures and

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CONFLICT OF INTEREST

Guarantor of the article: Sudarshan R. Jadcherla, MD, FRCPI, DCH.

Specific author contributions: Alankar Gupta, MD was involved with the conduct of study protocol, data acquisition, data analysis, and paper writing. Parul Gulati, MS was involved with statistical analysis and interpretation of data. Walter Kim, MPH was involved with data analysis and assistance with the study protocol. Soledad Fernandez, PhD was involved with development of the statistical design, analysis of data, and writing of paper. Reza Shaker, MD was involved with research consultation, data interpretation, and writing of this paper. Sudarshan R. Jadcherla, MD as the principal investigator of the current study protocol was involved with the development of methods, concept, study design, IRB process and conduct, performance of study protocol, data analysis, interpretation of data, and writing of this paper.

Potential competing interests: None.

unstructured variance–covariance or compound symmetry matrixes were used for statistical comparison. Values stated as least squares means $\pm$ s.e.m. or percent.

RESULTS—A total of 200 primary peristalsis and 227 secondary peristalsis events were evaluated. Between time 1 and time 2: (i) proximal esophageal waveform amplitude increased ($P < 0.02$), with primary peristalsis (38 ± 6 vs. 48 ± 7 mm Hg) and with secondary peristalsis (34 ± 6 vs. 46 ± 5 mm Hg); (ii) distal esophageal waveform amplitude was similar ($P = \text{NS}$), with primary peristalsis (42 ± 4 vs. 43 ± 4 mm Hg) and secondary peristalsis (29 ± 3 vs. 32 ± 4 mm Hg); (iii) proximal esophageal waveform onset to peak duration decreased ($P = 0.02$) with primary (2.6 ± 0.3 vs. 1.9 ± 0.1 s, $P < 0.003$) and with secondary peristalsis (2.2 ± 0.2 vs. 1.8 ± 0.1 s); (iv) distal esophageal waveform onset to peak duration decreased ($P = 0.01$) with primary (2.4 ± 0.3 vs. 1.8 ± 0.1 s) and with secondary peristalsis (1.9 ± 0.2 vs. 1.5 ± 0.1 s); (v) effects of identical stimulus volume on intrabolar pressure were similar ($P = \text{NS}$); however, greater infusion volumes (2 vs. 1 ml) generated higher intrabolar pressure at both time 1 and time 2 (both P s < 0.05). Between primary and secondary peristalsis (mechanistic variable): (i) no differences were noted at either period, with proximal esophageal waveform amplitudes ($P = \text{NS}$); (ii) differences were noted with distal esophageal waveform amplitudes at each time period ($P = 0.0002$); (iii) no differences were noted with both esophageal waveforms duration at either period ($P = \text{NS}$); (iv) peristaltic velocity was faster with secondary peristalsis than with primary peristalsis at either period (at earlier study, 7.9 ± 1.4 vs. 2.5 ± 1.4 cm/s and at later study 6.2 ± 1.6 vs. 1.2 ± 1.5 cm/s, both P s < 0.01).

CONCLUSIONS—In preterm neonates, longitudinal maturation modulates the characteristics of primary and secondary peristalsis. Differences in proximal striated muscle and distal smooth muscle activity during peristalsis are evident. Peristaltic velocity is faster with secondary peristalsis. These findings may represent maturation of central and peripheral neuromotor properties of esophageal bolus propulsion in healthy preterm human neonates.

INTRODUCTION

Two types of peristaltic mechanisms have been described in human neonates: primary peristalsis and secondary peristalsis (1,2). Primary peristalsis is initiated by the act of swallowing under basal conditions, and represents the classic coordinated motor sequences within the esophagus. A rapid progression of pharyngeal pressure waveform transfers the bolus through a relaxed upper esophageal sphincter (UES) into the esophageal segments. An orderly contraction requires coordination and integration of activity from skeletal muscle to mixed muscle through smooth muscle portion of the esophagus. Previous studies in animal model suggest that the primary peristalsis in the skeletal muscle portion is controlled by the central pattern generator, and that the smooth muscle part requires interaction of central and peripheral neuromotor mechanisms (3–5). The presence of primary peristalsis has been characterized in the fetus, and also as early as 32 weeks of post-menstrual age (PMA) (1,6–8).

On the other hand, secondary peristalsis is defined as an adaptive reflex response to esophageal distention (2,9–11), and has been described as early as 32-week PMA (2,11). Studies in the animal model suggest that this reflex is governed by visceral afferent and efferent innervation through the vagus (12,13).

Prematurely born human neonates commonly suffer from problems related to aerodigestive tract and gastroesophageal reflux, and these concerns improve during maturation in healthy neonates. Swallowing-mediated primary peristalsis and esophageal provocation-mediated secondary peristalsis facilitate aerodigestive clearance. This study was undertaken to elucidate the postnatal maturational changes in primary and secondary peristalsis in preterm human neonates. Specifically, we tested the hypotheses that (i) maturation modifies esophageal bolus propulsion characteristics, and (ii) the motility characteristics differ

between the types of esophageal peristaltic mechanisms, i.e., primary vs. secondary peristalsis. We accomplished these goals by evaluating swallow-integrated esophageal motility in healthy premature neonates studied during longitudinal maturation.

METHODS

Patients

Ten neonates with an average gestational age of 27.5 ± 0.6 weeks (mean $\pm$ s.e.m.) were evaluated twice at a PMA of 33.8 ± 1.1 (time 1, early study) and again at 39.2 ± 1.6 weeks (time 2, later study). Gestational age was determined by maternal history and obstetric data, and PMA was calculated by adding chronological ages to gestational age. Neonates with structural, chromosomal, neurological, and/or perinatal asphyxia were excluded. Patients were not receiving prokinetic or acid-suppressive therapies at evaluation. The study protocol was approved by institutional review board at The Research Institute at Nationwide Children's Hospital. Informed consents and Health Insurance Portability and Accountability Act of 1996 authorization were obtained from parents before the study.

Manometric methods

The use of esophageal manometry methods in neonates was described by us before (1,2,11,14). Briefly, the catheter assembly (Dentsleeve International, Mui Scientific, Ontario, Canada) was connected to the pneumohydraulic micromanometric water perfusion system by the resistors, pressure transducers (TNF-R disposable pressure transducers) and amplifiers (Solar modules, Solar 2; MMS Medical Instruments, Dover, NH). The esophageal manometry catheter assembly with dual sleeves and four side ports recording from pharynx, proximal, middle and distal esophageal loci, and a terminal gastric recording port was used. The water perfusion rate was 0.02 ml / min per port for esophageal ports, 0.01 ml/min per port for the pharyngeal port, and 0.04 ml/min per port for the sleeves. The catheter was passed nasally in the supine lying neonate without the aid of sedation. All studies were carried out in the same manner, with the transducers at the level of the patients' esophagus (mid axillary line). Respiratory inductance plethysmography (Respirace), heart rate, and pulse oximetry were recorded concurrent with manometry to document subject safety.

Manometric study design and experimental protocol

Continuous data acquisition and analysis were performed during manometric study based on waveform characteristics, as defined before (1,2,11,14). During manometric pull through, the high-pressure zones of the lower and UES were identified by the presence of a consistent increase in pressure greater than 5.0 mm Hg above the baseline for at least 15 s, in addition to the changes in pressure with respiration (14). Neonates were allowed to adapt to catheter placement for about 15 min and spontaneous swallowing-mediated primary peristalsis sequences were evaluated. Infusions of air and liquids (sterile water and apple juice) of 1 and 2 ml volumes were given through the mid esophageal infusion port to characterize the secondary peristalsis. These volume variables were chosen based on threshold volume in evoking secondary peristalsis (2,11). An example (line plot and contour plot) of primary and secondary peristalsis is shown in Figure 1a and b.

Data analysis

All measurements were taken at end expiration. Because the focus of the study is on the esophageal peristaltic propulsion characteristics, data points were evaluated for temporal changes in sequences at proximal (striated muscle) and at distal (smooth muscle) segments of esophagus during primary and secondary peristalsis, as shown in Figure 1a and b. The following variables that were defined *a priori* were analyzed.

Proximal and distal esophageal waveform amplitudes (mm Hg)—Proximal and distal esophageal waveform amplitudes (mm Hg) were measured as the maximum contractile pressure generated during a peristaltic sequence at these locations. These measurements signify the points of complete esophageal lumen occlusion at the recording sites during esophageal peristalsis (15).

Duration of peristaltic waveform onset to waveform peak (s)—Duration of peristaltic waveform onset to waveform peak (s) was measured at proximal and distal esophageal segments. This measurement signifies the period of initiation of bolus clearance at the recording site (15).

Peristaltic velocity (cm/s)—Peristaltic velocity (cm/s) was measured as time taken for waveform to traverse between proximal to distal esophageal segments. Peristaltic velocity was calculated by dividing the length between proximal and distal esophageal segments by the amount of time taken for waveform progression between the segments. It signifies the speed of esophageal bolus clearance between the segments.

Intrabolus pressure (mm Hg)—Intrabolus pressure (mmHg) was measured as the maximum pressure before the onset of peristaltic contraction wave, at each locus. The duration of intrabolus pressure (s) was also measured as the amount of time this pressure was exerted at each locus.

Statistical analysis

Pairwise comparisons between the two types of peristalsis (primary vs. secondary peristalsis) and between two levels of time (time 1 vs. time 2) were performed. Data were adjusted for multiple testing by applying the Tukey – Kramer method. The data are considered repeated because multiple responses were measured from the same neonate. Repeated-measures and unstructured variance–covariance or compound symmetry matrix were used to analyze the repeated-measures data. STATA (version 9, Stata Corp, College Station, TX) and SAS (version 9.1, SAS Institute, Cary, NC) were used to perform the analyses. Least squares means $\pm$ s.e.m. are reported, unless stated otherwise. Adjusted *P* values <0.05 were considered statistically significant.

RESULTS

Patient characteristics

Ten patients (six men) of 27.5 weeks (0.6) gestation, birth weight 1.1 kg (0.01), length 38.4 cm (2.0), head circumference 27.1 cm (1.3) were evaluated at time 1 and time 2 (Table 1). Patients were of appropriate growth for gestational age at birth and also were appropriate for PMA at evaluation. The median Apgar scores were 4 at 1 min and 5 at 5 min. Because of prematurity and respiratory distress syndrome, patient received intratracheal surfactant and respiratory therapy (ventilator and continuous positive airway pressure); however none had chronic lung disease. At time 1, 90 % ($n=9$) patients received feeds by nasogastric route; whereas one patient (10 %) was transitioning to oral feeds. At time 2 all patients had oral feeding ability (100 %, $n=10$). Majority of neonates ($n=7$) were fed formula milk and the rest ($n=3$) were fed breast milk at early and later studies.

A total of 200 primary peristalsis sequences (average 10 events per patient at each time) and 227 secondary peristaltic events (average 11 events per patient at each time) were evaluated.

Changes in proximal esophageal waveform amplitude with maturation and with type of peristalsis

The increases in proximal esophageal waveform amplitude with maturation during primary peristalsis and also during secondary peristalsis are shown in Figure 2a. We further analyzed the effect of the variables (time and type of peristalsis) on the repeated measures (proximal esophageal waveform amplitude). Time variable alone had significant effect on maximum amplitude at proximal esophagus ($P<0.02$). There were no differences between the mechanism of peristalsis (primary vs. secondary peristalsis, $P=NS$), or the interaction of time and mechanisms on proximal esophageal amplitude ($P=NS$).

Changes in distal esophageal waveform amplitude with maturation and with type of peristalsis

The average distal esophageal waveform amplitude with maturation during primary peristalsis and secondary peristalsis is shown in Figure 2b. We further analyzed the repeated-measures data to test the effects of maturation and peristaltic types on the maximal distal esophageal waveform amplitude. Significance was noted with the effect of the mechanism of peristalsis on amplitude alone ($P=0.0002$), but not with the time variables ($P=NS$) or with the interaction of time and the type of reflex on the amplitude ($P=NS$).

Comparison of onset to peak waveform duration at proximal esophagus

Mean waveform duration decreased at the later study with primary peristalsis but remained similar with secondary peristalsis (Figure 3a). Statistical models were applied to analyze the repeated-measures data, and the time variable alone was significant ($P=0.02$). However, the durations were not different between the two mechanisms, as well as between the interaction of peristaltic mechanism and maturation (both $P=NS$).

Comparison of onset to peak waveform duration at distal esophagus

Comparison was performed across primary vs. secondary peristalsis and between time 1 vs. time 2 (Figure 3b). Maturation time variable was significant ($P=0.01$). However, no differences were noted between the mechanisms ($P=NS$), or the interaction of maturation and mechanism on the waveform onset to peak duration ($P=NS$).

Effect of maturation and type of peristaltic reflex on peristaltic velocity from proximal to distal esophagus

Comparison was performed across primary vs. secondary peristalsis, and between time 1 vs. time 2 (Figure 4). The peristaltic velocity was faster with secondary peristalsis compared to primary peristalsis at both time periods (both $P<0.01$). The time factor alone, and also the combined interaction of time factor and type of peristalsis on the peristaltic velocity were not significant (both $P=NS$).

Relationship of intrabolus pressure on peristaltic mechanisms

We tested if the esophageal intrabolus pressure was different between the maturational periods and between the mechanisms by comparing primary peristalsis at time 1 vs. time 2, and between secondary peristalsis at time 1 vs. time 2 at the locus of proximal, middle, and distal esophagus (Table 2). The time variable was not significant for all three esophageal locations. However, the intrabolus pressure that resulted in secondary peristalsis was significantly higher for all three esophageal locations in comparison to primary peristalsis (Table 2, mechanistic variable, all $P<0.05$).

We tested if the intrabolus pressure generated was related to the mid esophageal infusion during secondary peristalsis only at time 1 and time 2. The 2.0 ml volume generated more

intra-bolus pressure at both times than 1.0 ml infusions ($P<0.05$; Figure 5a). Effect of maturation on identical dose volume vs. intrabolus pressure was similar.

We tested the relationship between the duration of intrabolus pressure and the volumes of infusion during secondary peristalsis across time 1 and time 2 (Figure 5b). The duration of intrabolus pressure was different ($P<0.05$) than 2.0ml during secondary peristalsis only.

DISCUSSION

Esophageal peristalsis is of fundamental importance in facilitating esophageal emptying or clearance of its contents, be it during swallowing or after gastroesophageal reflux events. In human premature neonates, we examined longitudinal maturational changes in the esophageal propulsion mechanisms, primary and secondary peristalsis. The main findings of this study (Figure 6) are that (i) the amplitude at proximal esophagus increases regardless of the type of peristaltic mechanism at later study, (ii) the onset to peak duration of proximal esophageal waveform is shorter with primary peristalsis at later study; similar findings were not noted with secondary peristalsis, (iii) the onset to peak duration of distal esophageal waveform is shorter for primary and secondary peristalsis at later study, (iv) the amplitude at distal esophagus remains similar between the time periods, and significant differences are noted between primary vs. secondary peristalsis, (v) the propagating velocity is faster with secondary peristalsis than with primary peristalsis at both time periods. Clearly all of these findings, summarized in Figure 6, describe that peristaltic mechanisms are developed at a younger postmenstrual age and these mechanisms advance with growth and development.

The discrepancy in amplitudes or durations between primary peristalsis and secondary peristalsis can be explained by the bolus size or of its origin in evoking the peristaltic sequence. For example, primary peristalsis was spontaneous, and the nature of bolus may have been air or saliva of unknown volume. This primary peristalsis reflex originated in the pharynx and propagated distally in a sequential organized manner, and can be a measure of the central pattern generator function. On the contrary, secondary peristalsis occurs without pharyngeal or UES phase of swallow, and was induced by esophageal fluid infusions of known volumes, which has resulted in defined common cavity pressure change or intra-bolus pressure for a period of time. Thus secondary peristalsis can be considered a peripheral mechanism activated by a sensory stimulus. Collectively, the presence of these reflexes facilitates clearance and prevents stasis.

A significant increase in the peristaltic waveform amplitude was noted with primary or secondary peristalsis with maturation. These findings suggest that the force of contraction increases in the proximal esophagus that consisted of primarily striated muscles. In contrast, the distal esophageal amplitude remained similar during maturation with both primary and secondary peristalsis. However, amplitude with secondary peristalsis was significantly lower than with primary peristalsis. These findings may simply be the result of differences in myogenic properties of the muscles involved, neuromotor afferent inputs, and efferent outputs or the characteristics of the stimulus. Similar relationship with segmental waveforms during primary or secondary peristalsis was also seen in adults (16). In a previous study, using similar methodologies in neonates and adults, we compared frequency and propagation of primary peristalsis across the age range (1). The propagation velocity and frequency of propagation advance with maturation; however, the age at which an infant develops the characteristics of primary peristalsis seen in adults is not yet known. Similar comparison on secondary peristalsis between neonates and adults is difficult unless the experimental protocol is the same, including catheter design, infusion protocols, and locus of provocation. Furthermore, in adult studies (9,10), volition can influence the deglutition response. Reflexes in neonates are different in that these are truly reflexive, and that the

development of the volitional aspects of reflexes is not well understood, and may not develop until later life.

The esophageal clearance at proximal and distal esophageal loci becomes significantly faster with maturation. This is evident from the decrease in duration of onset to peak waveform. This finding combined with the contraction amplitude described above suggests that with growth, preterm healthy neonates are capable of quickly clearing the bolus at the proximal and distal segments of esophagus. Similarly, the peristaltic waveform onset velocity from proximal to distal esophagus was significantly faster with secondary peristalsis than with primary peristalsis at either period. Collectively, these findings suggest that the response to local esophageal sensory stimulation (mechano-, osmo-, or chemostimulation) becomes faster with maturation. Thus, the reproducible evaluation of secondary peristalsis will provide information regarding sensory and motor aspects of the peristalsis; and this response can be readily incorporated in diagnostic clinical manometry paradigms. This study was performed in preterm healthy neonates, and therefore can be a reference for further studies to evaluate disease-specific pathophysiology. Both primary peristalsis and secondary peristalsis are important defense mechanisms for the clearance of refluxate (17,18). Conversely, defective secondary or primary peristalsis characteristics might be mechanisms for swallowing disorders and gastroesophageal reflux disease in premature neonates, and further studies are needed to clarify the peristaltic dysfunction.

This study demonstrates that esophageal body propulsion characteristics during swallowing (primary peristalsis) and on distention (secondary peristalsis) responses are not identical. The amplitude, duration of waveforms, and the propagating velocities are distinct between the mechanisms. These findings further support the presence of distention-induced proximal excitation that is mediated by vagal pathways and cholinergic neurons, whereas the distal response is mediated by intrinsic and largely noncholinergic neural mechanisms including vasoactive intestinal peptide release or nitric-oxide-mediated pathways (19). In this paper we focused our investigation on esophageal body peristaltic mechanisms only, and the role of UES and lower esophageal sphincters has not been investigated. It is likely, that because of differences in neuromuscular characteristics of these sphincters, their functions are different. Further studies are needed to clarify sphincteric roles in health or neonatal dysphagia.

The intrabolus pressure domains, in relation to primary and secondary peristalsis, were studied at different loci and also across maturation. Interestingly, the intrabolus pressure at different esophageal loci associated with primary peristalsis was significantly lower, contrasting with secondary peristalsis. The relationship between the dose volume and the response time interval to evoke secondary peristalsis was also studied. On infusion, the intrabolus pressure or the duration of pressure that evoked secondary peristalsis was significant for a higher-order stimulus (2.0 ml) across the maturation. This finding suggests that larger volumes result in secondary peristalsis sooner with maturation. These findings also point to the distensibility of the esophagus involving tension or stretch receptors, or volume sensitivity in evoking secondary peristalsis (20).

The clinical implications of this study are that in preterm healthy neonates, maturation of proximal and distal esophageal function improves bolus propulsion mechanics and transit velocity. These reflex events contribute to esophageal defense mechanisms, by facilitating esophageal emptying, salivary clearance, and refluxate clearance. Thus, the esophageal contents are steered away from the proximal aerodigestive tract. Both central sequential patterns and peripheral mechanisms contribute to aerodigestive safety in healthy premature neonates. This study can be a reference for comparison among neonates with evolving

diseases such as dysphagia, gastroesophageal reflux disease, or chronic lung disease, particularly when aerodigestive concerns persist despite increase in maturational age.

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Study Highlights

WHAT IS CURRENT KNOWLEDGE

- Esophageal peristalsis mediated by primary or secondary peristalsis is well known in the adult human and animal model.
- The characteristics of neonatal esophageal peristaltic mechanisms during maturation are not known.
- Comparison of esophageal bolus propulsion characteristics mediated by primary or secondary peristalsis in human premature neonates is not known.

WHAT IS NEW HERE

- Definition of the changes in the mechanisms of peristalsis in human neonates during maturation is illustrated.
- Esophageal bolus propulsion characteristics mediated by primary or secondary peristalsis in human premature neonates is characterized.
- Application of the described models permits evaluation across maturation. Understanding the normality of human neonatal esophageal motility can provide a reference for investigating abnormality.

Figure 1.

Mechanisms of esophageal propulsion. **(a)** Waveform and contour plots of a primary peristalsis sequence. Note pharyngeal waveform, upper esophageal sphincter (UES) relaxation, and progression of primary peristalsis, and LES relaxation. Proximal (PE), middle (ME), and distal (DE) esophageal waveforms and contour plots are shown. Peak waveform amplitude, onset to peak duration, and peristaltic velocity were evaluated. The contour plot provides a two-dimensional color-coded visual representation of the same primary peristalsis sequence. **(b)** Waveform and contour plots of a secondary peristalsis sequence. Note the response to mid esophageal infusion (evidenced by common cavity and infusion signal) resulting in secondary peristalsis associated with LES relaxation. PE, ME, and DE esophageal waveforms and contour plots are shown. Note the absence of pharyngeal waveform and absence of UES relaxation that distinguishes secondary peristalsis. Peak waveform amplitude, onset to peak duration, and peristaltic velocity were evaluated. The

contour plot provides a two-dimensional color-coded visual representation of the same secondary peristalsis sequence.

Figure 2.

Maximum peristaltic waveform amplitude. In (a), the maturational changes in proximal esophageal segment showed significant increase with primary and secondary peristalsis ($P < 0.02$). In (b), the distal esophageal amplitude remained similar between time 1 and time 2 with both primary and secondary peristalsis. However, significant differences are noted between the mechanisms at both periods ($P = 0.0002$).

Figure 3.

Duration of peristaltic waveform onset to peak. In proximal esophagus (**a**), decreasing trends with maturation during primary ($P=0.02$) and during secondary peristalsis were visible. At either time points, there were no differences between the mechanisms. In distal esophagus (**b**), similar trends were noted with both primary and secondary peristalsis (both $P=0.01$).

Figure 4. Peristaltic velocity between proximal to distal esophagus. Differences between the mechanisms (primary vs. secondary peristalsis) are evident at both the time points (both $P < 0.01$).

Figure 5.

Intrabolar pressure. In (a), the relationship between infusion volume and intrabolar pressure is shown; higher volumes generated more intrabolar pressure at both periods (both P s < 0.05). In (b), the relationship between infusion volume and the duration of exposure is shown. The duration of intrabolar pressure resulting in secondary peristalsis at time 2 was shorter ($P < 0.05$).

Figure 6.
Overview of maturational and mechanistic effects on primary and secondary peristalsis.

Table 1

Subject characteristics during maturation, time 1 vs. time 2

Subject characteristics	Time 1	Time 2	<i>P</i> value
Gestational age at birth (weeks)	27.5±0.6 (25.0–30.0)	NA	NA
Post menstrual age at study (weeks)	33.8±1.1 (31.4–43.0)	39.1±1.6 (34.6–52.0)	0.01
Weight at study (kg)	1.8±0.3 (1.1–4.0)	2.8±0.3 (1.9–5.8)	0.03
Length at study (cm)	41.4±1.2 (36.0–50.0)	46.5±2.0 (40.0–62.0)	0.04
Head circumference at study (cm)	29.5±1.1 (26.0–38.0)	33.5±0.9 (31.0–37.0)	0.01
Oral feeding ability	10%	100%	0.05

NA, not applicable.

Mean±s.e.m. (range) are shown.

Table 2

Intrabolus pressure at proximal, middle, and distal esophagus during secondary and primary peristalsis at time 1 and time 2

Mechanism, Time	Intrabolus pressure (mm Hg)		
	Proximal esophagus	Middle esophagus	Distal esophagus
PP, time 1	5.6±0.8	5.9±1.1	6.1±0.7
PP, time 2	5.9±1.2	4.9±1.0	5.2±1.0
SP, time 1	9.4±1.2	8.2±1.0	9.1±0.5
SP, time 2	8.8±1.4	9.0±1.3	8.4±1.0
Time variable <i>P</i> values	NS	NS	NS
Mechanistic variable <i>P</i> values	< 0.0001	0.0007	0.0013

PP, primary peristalsis; SP, secondary peristalsis.

Mean±s.e.m. and significance are based on unstructured variance–covariance matrix.