Diaphragm Dimensions of the Healthy Preterm Infant

Virender K. Rehan, MD*; JoAnn Laiprasert*; Michael Wallach, MD‡; Lewis P. Rubin, MD§; and F. Dennis McCool, MD∥

ABSTRACT. Background. The diaphragm is the major inspiratory muscle in the neonate; however, human neonatal diaphragm development has not been extensively studied. We hypothesized that diaphragm thickness (tdi) would be positively related to postmenstrual age (PMA), body weight, body length, head circumference, and nutritional intake.

Objectives. To evaluate the evolution of diaphragm growth and motion in the healthy, preterm infant.

Methods. We used ultrasound to measure tdi at the zone of apposition to the rib cage and diaphragm excursion (e-di) during inspiration. Thirty-four stable, preterm infants (16 males and 18 females) between 26 and 37 weeks' PMA were studied during quiet sleep at weekly intervals until the time of discharge or transfer from the neonatal intensive care unit. All infants were clinically stable and not receiving ventilatory support.

Results. We found that 1) tdi increased from 1.2 ± 0.1 to 1.7 ± 0.05 mm between 26 to 28 and 35 to 37 weeks' PMA; 2) tdi was positively correlated with PMA (r = 0.40), body weight (r = 0.52), body length (r = 0.53), and head circumference (0.49), but not with postnatal nutritional intake (r = 0.09); and 3) e-di decreased with increasing PMA.

Conclusions. Our findings suggest that diaphragm development in premature infants scales with body dimensions. We speculate that the increase in tdi with age is likely attributable to increased diaphragm muscle mass, and the reduced e-di with age may be resulting from a reduction in chest wall compliance. 

METHODS

Participants

We recruited 34 (16 males and 18 females) clinically stable, preterm infants between the gestational ages (GA) of 26 to 32 weeks (Table 1). Estimation of GA was based on the best obstetrical assessment and modified Ballard scoring.26 There was no evidence of any acute illness in the infants at the time of the study. Exclusion criteria included clinical instability, culture proven sepsis, current oxygen supplementation, continuous positive airway pressure or ventilatory support, congenital malformations, and ≥ grade II intraventricular hemorrhage. Written parental consent was obtained for each infant before the study. The Institutional Review Board of the Women and Infants’ Hospital of Rhode Island approved all studies.
The enrolled infants were followed longitudinally and measured using standard techniques. NI was assessed as daily kilocaloric intake. Furthermore, as in our previous study in term infants, we found an average edi for 5 consecutive tidal breaths. With tidal breathing, the %Δedi was not significantly different for all PMA categories studied. (23% at 26–28 weeks vs 25% at 35–37 weeks’ PMA; P > .05), but there was a significant decrease in edi with increasing maturation (5.5 mm at 26–28 weeks vs 4.4 mm at 35–37 weeks’ PMA; P < .05, Fig 4).

**DISCUSSION**

We longitudinally measured tdi and edi in 34 stable preterm infants, and described the relationship between tdi and PMA, BW, BL, HC, and NI. We found that tdi was positively associated with postmenstrual age. At 26 to 28 weeks’ PMA, the diaphragm was significantly thinner than at 35 to 37 weeks’ PMA. On average, tdi increased by 0.1 mm/week between 26 and 37 weeks’ PMA. We speculate that the progressive increase in tdi with increasing maturation results from a combination of an increase in the number of myofibers as well as to myofiber hypertrophy.

The increase in tdi with maturation most likely

### TABLE 1. Patient Characteristics

<table>
<thead>
<tr>
<th>PMA (Weeks)</th>
<th>26–28</th>
<th>29–31</th>
<th>32–34</th>
<th>35–37</th>
</tr>
</thead>
<tbody>
<tr>
<td>Participants (n)</td>
<td>6</td>
<td>11</td>
<td>11</td>
<td>6</td>
</tr>
<tr>
<td>BW (g)</td>
<td>1260 ± 120 1600 ± 80 1880 ± 70 2100 ± 150</td>
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<tr>
<td>BL (cm)</td>
<td>37 ± 1.5 42 ± 0.6 45 ± 0.6 47 ± 1.2</td>
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<tr>
<td>HC (cm)</td>
<td>27 ± 0.8 29 ± 0.5 31 ± 0.4 32 ± 0.5</td>
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</table>
| BW, BL, and HC values are means ± standard error of the mean.

### TABLE 2. Diaphragm Dimensions and NI in Different PMA Categories

<table>
<thead>
<tr>
<th>PMA (Weeks)</th>
<th>26–28</th>
<th>29–31</th>
<th>32–34</th>
<th>35–37</th>
</tr>
</thead>
<tbody>
<tr>
<td>tdi (mm)</td>
<td>1.09 ± 0.08* 1.25 ± 0.07 1.47 ± 0.06 1.74 ± 0.04</td>
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<tr>
<td>Δedi (mm)</td>
<td>0.28 ± 0.07* 0.33 ± 0.04 0.44 ± 0.04 0.44 ± 0.09</td>
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<tr>
<td>%Δedi</td>
<td>23 ± 25 27 ± 9 23 ± 14 25 ± 21</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>eedi (mm)</td>
<td>5.5 ± 0.2* 4.8 ± 0.2 4.6 ± 0.2 4.4 ± 0.3</td>
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<tr>
<td>NI (kcal/k/d)</td>
<td>120 ± 5 109 ± 5 93 ± 6 98 ± 0.9</td>
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Values are means ± standard error of the mean.
* P < .05 versus 35 to 37 weeks’ PMA.

**Measurements**

The infants were studied while sleeping quietly in the supine position and at least 1 hour postprandial. The diaphragm was visualized using a 7.5-MHz transducer placed in right midaxillary line at the level of the zone of apposition of the diaphragm to the rib cage. Ample prewarmed ultrasound gel was used to maintain acoustic coupling and to ensure good image quality throughout the imaging process. Using the B-mode, 2-dimensional coronal and parallelism for the 3 layers of diaphragm structure: the pleural reflection, muscular layer, and the peritoneal reflection.21 The infant’s breathing was recorded for 1 minute and replayed on the ultrasound screen to exactly time the beginning and end of each respiratory cycle. (The freeze frame control allowed us to determine precisely end-inspiration and end-expiration (FRC). Diaphragm thickness was measured as the perpendicular distance between the pleural and peritoneal reflections. Values reported for tdi were those obtained at FRC. The change in tdi during inspiration (Δtdi) was measured as the difference in tdi between end-expiration and end-inspiration during tidal volume and end-inspiratory volume. For each measurement of tdi and Δtdi, at least 5 breathing cycles were analyzed.

To assess diaphragm dome excursion (edi) during inspiration, the diaphragm was visualized in the sagittal plane by placing the transducer under the right costal margin in the mid-clavicular line. Motion of the dome was observed in real time and recorded on videotape for later review and analysis. Diaphragm excursion during inspiration was measured as the maximum caudal descent of the midpoint of the posterior third of the diaphragm between end-expiration and end-inspiration. An average eddi for 5 consecutive quiet breaths was obtained. A single investigator performed all ultrasound scans (J.L.).

Heart rate, respiratory rate, and arterial oxygen saturation were monitored continuously during the measurements of diaphragm dimensions. Sleep state was characterized by behavioral criteria as active or quiet, and all studies were conducted during quiet sleep.27 Body weight (BW), BL, and HC were measured using standard techniques. NI was assessed as daily kilocaloric intake. The enrolled infants were followed longitudinally and measurements of tdi, Δtdi, BW, BL, and HC were recorded once weekly until the infant was discharged or transferred out of the neonatal intensive care unit. To ensure that the same diaphragm segment was followed longitudinally, measurements of tdi were obtained at the same external chest wall locations (8th or 9th intercostal space in the right midaxillary line) for each infant at every recording.

Furthermore, as in our previous study in term infants, we found that in preterm infants, tdi is uniform over the 2 to 3 intercostal spaces scanned.

**Analysis**

The infants were separated into 4 groups according to PMA; 26 to 28, 29 to 31, 32 to 34, and 35 to 37 weeks. Analysis of variance for repeated measures was used to assess differences in tdi, Δtdi, eedi, and NI among different groups. If significant differences were found by analysis of variance, Newman-Keuls posthoc testing was used to detect differences among study periods. Linear regression and t tests were performed as appropriate. The influence of GA, various anthropometric parameters, and NI on tdi was assessed using mixed models regression to account for correlations within the participants.28 A P value of < .05 was considered significant.

**RESULTS**

A total of 190 observations were recorded for each parameter (tdi, Δtdi, %Δtdi, eedi, NI) in the 4 PMA categories: 22 between 26 and 28 weeks, 56 between 29 and 31 weeks, 70 between 32 and 34 weeks, and 42 between 35 and 37 weeks. Infants were grouped in PMA categories according to the completed week of PMA, eg, an infant at 28 3/7 weeks was placed into the 26 to 28 weeks’ PMA group and an infant at 34 2/7 into the 32 to 34 PMA group. The number of observations made for each infant ranged between 2 and 11 (median: 5). The coefficient of variation for measurements of tdi, was 9.8%. This degree of reproducibility of tdi was similar to what we have previously reported in adults and infants.17,22 Group mean values of tdi, BW, BL, and HC in Fig 1 and among tdi and BW, BL, and HC in Fig 2. tdi progressively increased with increasing PMA (1.2 mm at 26–28 weeks vs 1.7 mm at 35–37 weeks; P < .05, (r = 0.40). The increase in tdi with maturation was proportional to the increase in BW, BL, and HC with growth (r = 0.52, 0.53, and 0.49, respectively). tdi scaled with BW to the mean power of 0.61 (tdi ~ BW0.61). By contrast, there was no significant relationship between tdi and NI (Fig 3). Average daily caloric intake (NI) was higher at lower GAs.
increases diaphragm strength. However, a number of factors may affect the relationship between t_{di} and diaphragm strength, especially in the growing infant. First, maximal transdiaphragmatic force depends on the maximal specific force of the diaphragm myofibers. The specific force of neonatal diaphragm is less than the adult. With maturation, there is greater expression of the adult myosin heavy chain phenotype. This would increase specific force and therefore maximal transdiaphragmatic force for a given muscle cross-sectional area. Second, with maturation the myofibers become more closely packed as the interstitial water compartment decreases. This also increases maximal transdiaphragmatic force for a given t_{di}. Finally, changes in diaphragm configuration will affect the relationship between maximal transdiaphragmatic force and pressure. Devlieger’s work suggests that there are important configurational changes of the diaphragm between birth and adulthood. However, in contrast to his assertion that the zone of apposition is minimal or even absent in the neonate, we had no difficulty in visualizing the zone of apposition in even the most premature infant studied. The presence of a zone of apposition would improve the coupling of the diaphragm to the rib cage.

The increase in t_{di} with growth was significantly related to BW and length. In our previous cross-sectional study of children and adults of different sizes, we found that t_{di} scaled with BW to the 0.52 power and with height to the 1.82 power. In the absence of specific adverse influences on diaphragm development such as prolonged ventilatory support, asymmetric intrauterine growth restriction, and neurologic deficits, we may expect similar relationships in the growing newborn. In our current study, t_{di} scaled with BW to the 0.61 power. This closely approximates our previous findings of the relationship between t_{di} and BW in term infants as t_{di} ~ BW^{0.57} and in older children and adults as t_{di} ~ BW^{0.52}. Our finding that t_{di} scales with BW is consistent with previous observations that diaphragm mass is proportional to body mass in the growing animal as well as in normal adult men of different BWs and extends these observations to the healthy preterm infant. This proportionality between t_{di} and body size may account for the relative constancy of maximal transdiaphragmatic pressures among species of different sizes.

A number of studies suggest that preterm infants tolerate respiratory loads poorly and are at higher risk for respiratory failure when compared with older infants and children. This was thought to be because of the relative lack of highly oxidative, fatigue resistant type I fibers, in the neonatal diaphragm. In animal models and humans, diaphragm myofiber composition changes significantly during postnatal development and extends these observations to the healthy preterm infant. This proportionality between t_{di} and body size may account for the relative constancy of maximal transdiaphragmatic pressures among species of different sizes.

Fig 1. t_{di} is positively correlated (r = 0.40) with PMA.

Fig 2. t_{di} is positively correlated with BW (r = 0.52), BL (r = 0.53), and HC (0.49).
postnatal NI, the preterm infant’s inability to tolerate respiratory mechanics and other factors.

The effects of nutritional deprivation on diaphragm structure and function are age and gender specific. Acute nutritional deprivation (90 hours) has no effect on rat diaphragm contractility or morphology and only an inconsequential influence on diaphragm fatigue; whereas prolonged undernutrition can result in deleterious changes in diaphragm muscle structure and impair its ability to generate force despite preserving its mechanical efficiency.

We did not find a significant relationship between postnatal NI and tdi. However, our study was not designed to test specifically the effects of postnatal undernutrition on diaphragm development. In the present study, most of these infants received paren-
teral nutrition early in their clinical course. This may account for the greater daily caloric intake/kg of BW at lower PMA. At later PMA, caloric intake was provided solely by the enteral route. Reassuringly, the caloric intakes in these infants was sufficient to allow the diaphragm to grow to a similar thickness ex utero as compared with the $t_{di}$ observed in infants born at term.21

CONCLUSION

By using ultrasonography, we have established normative data for $t_{di}$ and excursion in healthy preterm infants. With increasing maturation, $t_{di}$ progressively increases and diaphragm excursion decreases. The significant correlations between $t_{di}$ and BW, BL, and HC extend the principles of scaling to premature infants. Ultrasonographic evaluation of diaphragm in premature infants, as described by us, may provide a noninvasive tool for assessment of diaphragm development and function under different pathologic situations.

REFERENCES


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*Pediatrics* 2001;108;e91
DOI: 10.1542/peds.108.5.e91

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