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Relationship between lung-to-head ratio and lung volume in normal fetuses and fetuses with diaphragmatic hernia

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KEYWORDS: 3D ultrasound; congenital diaphragmatic hernia; fetal lung volume; lung-to-head ratio; VOCAL

ABSTRACT

Objective *To examine the relationship between the fetal lung area and lung area to head circumference ratio (LHR) and lung volume by three-dimensional (3D) ultrasonography in normal fetuses and in fetuses with unilateral congenital diaphragmatic hernia (CDH).*

Methods *In 64 fetuses with CDH at median 26 (range, 20–32) weeks of gestation the contralateral lung volume, lung area and LHR were measured and the values were compared to those of 650 normal fetuses at 12–32 weeks. In the normal fetuses both lungs were assessed but in the 64 fetuses with CDH only the contralateral lung was measured because the ipsilateral lung could be visualized adequately in only 40 (62.5%) of the cases. Regression analysis was used to assess the significance of the association between lung volume and lung area or LHR. In the fetuses with CDH, the observed to expected ratios for lung area and LHR were calculated. The expected lung area and LHR were the normal median for a given lung volume. The significance of the differences between the observed to expected lung area and LHR in fetuses with CDH and normal fetuses was determined. In the 64 fetuses with CDH and in 64 normal fetuses, matched for gestational age, the lung length between the apex and the superior aspect of the diaphragm dome was also recorded.*

Results *In normal fetuses the median lung area and LHR in both the left and right lungs increased significantly with lung volume. In the fetuses with CDH, the lung area and lung volume for gestation were substantially lower than in normal fetuses and the ratios of observed to expected lung area and LHR for a given lung volume were significantly lower than the respective values in normal fetuses. Additionally, the mean lung length was 13% greater and the mean lung area was 44% smaller than the respective values in the normal controls matched for gestational age.*

Conclusions *The finding of a significant association between LHR and lung volume has validated the use of LHR in the assessment of lung growth. However, the study has also demonstrated that in fetuses with CDH, LHR underestimates the actual lung volume, because the herniated viscera cause a greater lateral, rather than vertical, compression of the contralateral lung. Copyright © 2006 ISUOG. Published by John Wiley & Sons, Ltd.*

INTRODUCTION

In congenital diaphragmatic hernia (CDH), chronic intrathoracic pulmonary compression, by the herniated abdominal viscera, interferes with normal development of the lungs. Consequently CDH is associated with a high postnatal mortality, owing to pulmonary hypoplasia and/or pulmonary hypertension[1,2]. Sonographic measurement of the fetal lung area to head circumference ratio (LHR) is currently the most widely used method for the antenatal prediction of outcome[3–9]. The rationale for the use of LHR is that it provides an indirect assessment of the contralateral lung volume and therefore the likelihood of pulmonary hypoplasia.

Recent studies have established that firstly, in normal fetuses the lung area and LHR, as well as the lung volumes, measured by three-dimensional (3D) ultrasonography, increase with gestation, and secondly, in fetuses with CDH the LHR is decreased and both lungs are substantially smaller than normal[10–13].

In this study we examine the relationship between LHR and lung volume in normal fetuses and in fetuses with CDH. The aim was to determine whether in CDH the

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lung area or LHR for a given lung volume is smaller, greater or the same as in normal fetuses.

METHODS

This was a cross-sectional study in which the lung volume, lung area and LHR were measured in 64 fetuses with unilateral CDH at median 26 (range, 20–32) weeks of gestation and the values were compared to those of 650 normal fetuses at 12–32 weeks[10,11]. In the normal fetuses both lungs were measured but in the fetuses with CDH only the contralateral lung was assessed because the ipsilateral lung could be visualized adequately in only 40 (62.5%) of the cases.

All examinations were performed transabdominally, with a Voluson 730 Expert scanner, equipped with an RAB 4-8L probe (GE Medical Systems, Milwaukee, WI, USA). For measurement of the lung area, a transverse section of the fetal chest, containing the four-chamber view of the heart, was obtained and the areas of each lung were measured in this sonographic plane by first, manual tracing of the limits of the lungs; second, by multiplication of the longest diameter of the lung by its longest perpendicular diameter; and third, by multiplication of the anteroposterior diameter of the lung at the mid-clavicular line by the perpendicular diameter at the midpoint of the anteroposterior diameter[3–10,12]. In addition, the head circumference was measured at the standard biparietal diameter view, showing the midline echo dividing the brain into two equal hemispheres, the cavum septi pellucidi one third of the way from the front to the back and the posterior horns of the lateral ventricles. The LHR was then calculated by dividing the area of each lung (mm^2) by the head circumference (mm).

For the measurement of lung volume, several 3D volumes of the fetal chest were acquired and those with the best image quality were chosen for analysis. During the acquisition we tried to ensure that the fetus was not moving and that it was preferably facing towards the transducer. The sweep angle was set from 40° to 85°, depending on the gestational age. The virtual organ computer-aided analysis (VOCAL) technique was used to obtain a sequence of six sections of each lung around a fixed axis, from the apex to the highest point of the superior aspect of the diaphragm dome, each after a 30° rotation from the previous one (Voluson 730 Expert Operation Manual, GE Medical Systems, Milwaukee, WI, USA). The contour of each lung was drawn manually in the six different rotation planes to obtain the 3D volume measurement. The starting plane of rotation for each lung included their largest anteroposterior diameters. In the 64 fetuses with CDH and in 64 normal fetuses, matched for gestational age, the lung length between the apex and the superior aspect of the diaphragm dome was also recorded. Every measurement was done off-line after the scan.

Statistical analysis

Regression analysis was used to assess the significance of the association between lung volume and LHR, as well as lung area, in the normal fetuses for both the left and right lungs and in the fetuses with CDH for the contralateral lung. The Kolmogorov–Smirnov test demonstrated that the data were normally distributed. In the fetuses with CDH, the observed to expected LHR ratio and observed to expected lung area ratio were calculated. The expected LHR and lung area were the respective normal median for a given lung volume. The Mann–Whitney *U*-test was used to determine the significance of differences between the observed to expected LHR and lung area in fetuses with CDH and normal fetuses. In each fetus with CDH the lung length and lung area were expressed as a percentage of the respective value from the gestation-matched normal control, and paired–samples *t*-test was used to determine whether there was a significant difference between mean values in the CDH group and controls. The data were analyzed using the statistical software SPSS 13.0 (Chicago, Illinois, USA) and Excel for Windows 2000 (Microsoft Corp., Redmond, WA, USA). A *P* of less than 0.05 was considered statistically significant.

Table 1 Relationship between lung area and lung area to head circumference ratio (LHR) with lung volume in normal fetuses. The lung area was measured by manual tracing of the limits of the lungs, by multiplication of the longest diameter of the lung by its longest perpendicular diameter, and by multiplication of the anteroposterior diameter of the lung at the mid-clavicular line by the perpendicular diameter at the midpoint of the anteroposterior diameter

Parameter	*Relationship between area (mm^2) and LHR with volume (mL)*	r	*SD*	P
Lung area (tracing the limits)	Left area = 41.127 + (42.357 × volume) − (0.802 × volume^2)	0.938	66.196	< 0.001
	Right area = 49.179 + (48.275 × volume) − (0.7 × volume^2)	0.947	92.222	< 0.001
Lung area (longest diameter)	Left area = 60.446 + (63.863 × volume) − (1.301 × volume^2)	0.928	103.36	< 0.001
	Right area = 66.655 + (70.019 × volume) − (1.036 × volume^2)	0.949	129.13	< 0.001
Lung area (anteroposterior diameter)	Left area = 42.508 + (40.475 × volume) − (0.704 × volume^2)	0.938	66.465	< 0.001
	Right area = 60.114 + (67.153 × volume) − (0.984 × volume^2)	0.950	123.63	< 0.001
LHR (tracing the limits)	Left LHR = 0.603 + (0.135 × volume) − (0.003 × volume^2)	0.885	0.257	< 0.001
	Right LHR = 0.832 + (0.159 × volume) − (0.003 × volume^2)	0.832	0.375	< 0.001
LHR (longest diameter)	Left LHR = 0.894 + (0.204 × volume) − (0.005 × volume^2)	0.857	0.420	< 0.001
	Right LHR = 1.173 + (0.231 × volume) − (0.004 × volume^2)	0.902	0.519	< 0.001
LHR (anteroposterior diameter)	Left LHR = 0.615 + (0.126 × volume) − (0.003 × volume^2)	0.885	0.255	< 0.001
	Right LHR = 1.094 + (0.223 × volume) − (0.004 × volume^2)	0.908	0.485	< 0.001

Table 2 Prediction of lung volume (median and 95% confidence interval) from the lung area to head circumference ratio (LHR). The lung area was measured by manual tracing, by multiplication of the longest diameter by its longest perpendicular diameter, and by multiplication of the anteroposterior diameter by the perpendicular diameter at the midpoint of the anteroposterior (A-P) diameter

	Left lung			*Right lung*		
LHR	*Tracing the limits*	*Longest diameter*	*A-P diameter*	*Tracing the limits*	*Longest diameter*	*A-P diameter*
< 0.6	0.5 (0.2–1.3)	0.3 (0.2–0.8)	0.5 (0.2–2.0)	0.4 (0.2–0.9)	0.4 (0.2–0.6)	0.3 (0.2–0.6)
0.60–0.79	1.2 (0.5–2.1)	0.5 (0.3–1.6)	0.9 (0.4–3.4)	0.8 (0.3–3.0)	0.4 (0.3–2.0)	0.5 (0.3–2.0)
0.80–0.99	2.2 (0.8–6.4)	0.8 (0.4–1.7)	2.2 (0.9–8.9)	1.1 (0.6–3.7)	0.7 (0.3–1.2)	0.8 (0.3–1.4)
1.00–1.19	3.5 (1.6–9.8)	1.6 (0.7–6.8)	3.5 (1.3–12.4)	2.0 (0.7–4.7)	0.8 (0.4–2.0)	0.8 (0.4–3.0)
1.20–1.39	5.5 (2.5–20.9)	2.0 (1.0–8.8)	6.5 (2.6–20.6)	2.5 (1.5–10.0)	1.3 (0.6–3.0)	1.6 (0.6–3.1)
1.40–1.59	9.7 (3.3–22.6)	3.0 (0.8–9.6)	9.7 (3.3–22.4)	4.6 (1.4–13.2)	1.9 (0.6–3.2)	1.6 (0.7–3.7)
1.60–1.79	12.2 (4.9–27.5)	3.8 (2.0–16.4)	12.4 (5.0–23.6)	5.7 (2.6–18.1)	2.0 (0.7–8.7)	2.5 (1.0–10.9)
1.80–1.99	15.0 (6.5–28.8)	4.9 (2.0–20.9)	14.8 (7.5–27.3)	8.7 (3.6–26.9)	2.9 (1.1–14.0)	3.4 (1.5–13.8)
2.00–2.49	16.1 (7.6–29.8)	10.6 (3.4–22.6)	16.2 (8.9–29.7)	11.5 (4.8–31.8)	5.0 (1.9–15.4)	5.2 (2.2–15.4)
2.50–2.99	20.6 (17.8–31.9)	13.9 (5.0–29.1)	22.1 (16.0–31.9)	19.0 (8.3–36.2)	7.6 (3.4–23.2)	8.5 (4.1–22.5)
≥ 3.00		15.6 (7.7–29.1)		22.8 (11.2–39.4)	19.0 (6.4–36.7)	19.6 (7.8–37.1)

RESULTS

There were 52 fetuses with left-sided CDH and 12 with right-sided CDH. In 10 cases the pregnancies were terminated at the request of the parents, in 27 they were managed expectantly and in 27 they were treated by fetoscopic tracheal occlusion (FETO) by means of an inflatable balloon[14].

In the normal fetuses the median lung area (measured by three methods) and the LHR, in both the left and right lungs, increased significantly with lung volume (Table 1; Figures 1 and 2). The median and 95% confidence intervals (CI) of lung volumes for a given LHR are shown in Table 2. In the fetuses with CDH, compared to normal fetuses matched for gestational age, the contralateral lung area was below the 2.5th centile in all cases (Figure 3)[10] and the lung volume was below the 2.5th centile in 94% (60 of 64) of cases (Figure 4)[11]. In the fetuses with CDH the ratios of observed to expected lung area and LHR for a given lung volume were significantly lower than the respective values in normal fetuses (Table 3). In the fetuses with CDH the mean lung length was 13% longer and the mean lung area was 44% smaller than the respective value in the gestation-matched normal controls ($P < 0.001$ for both; Figure 5).

DISCUSSION

The data of this study demonstrate that first, in normal fetuses the lung area and LHR increase with lung volume, and second, in the fetuses with CDH the lung area and lung volume for gestation are lower than in normal fetuses and the ratio of observed to expected lung area and LHR for a given lung volume are significantly lower than in normal fetuses.

In the calculation of LHR, the lung area can be measured by manual tracing of the limits of the lungs, by multiplying the longest diameter of the lungs by their longest perpendicular diameter, or by multiplying the anteroposterior diameter of the lung by the perpendicular diameter at the midpoint of the anteroposterior diameter.

Table 3 Mean difference (95% confidence interval) between the ratios of observed to expected lung area and lung area to head circumference ratio (LHR) in fetuses with congenital diaphragmatic hernia and the ratios of the observed to expected lung area and LHR in normal fetuses

Lung area or LHR	*Mean difference (95% CI) with normal fetuses**
Lung area (tracing the limits)	
Total	−0.24 (−0.29 to −0.19)
Right lung	−0.26 (−0.32 to −0.21)
Left lung	−0.12 (−0.21 to −0.03)
Lung area (longest diameter)	
Total	−0.29 (−0.33 to −0.24)
Right lung	−0.30 (−0.35 to −0.25)
Left lung	−0.22 (−0.30 to −0.14)
Lung area (anteroposterior diameter)	
Total	−0.40 (−0.45 to −0.35)
Right lung	−0.46 (−0.51 to −0.42)
Left lung	−0.16 (−0.28 to −0.04)
LHR (tracing the limits)	
Total	−0.42 (−0.45 to −0.38)
Right lung	−0.45 (−0.49 to −0.41)
Left lung	−0.32 (−0.39 to −0.25)
LHR (longest diameter)	
Total	−0.45 (−0.48 to −0.41)
Right lung	−0.46 (−0.50 to −0.42)
Left lung	−0.39 (−0.49 to −0.34)
LHR (anteroposterior diameter)	
Total	−0.55 (−0.59 to −0.51)
Right lung	−0.59 (−0.63 to −0.56)
Left lung	−0.38 (−0.45 to −0.30)

*Mann–Whitney U-test for all comparisons. $P < 0.001$

In a previous study we found that the tracing method is the most reproducible one[10]. Furthermore, the method employing the longest diameter, compared to the tracing method, overestimated both the left and the right lung area by about 45%, and the method employing the anteroposterior diameter overestimated the area of the right lung by about 35%, but did not affect that of the left lung[10]; this is because on the right side the anteroposterior and the longest diameters are often similar, whereas on

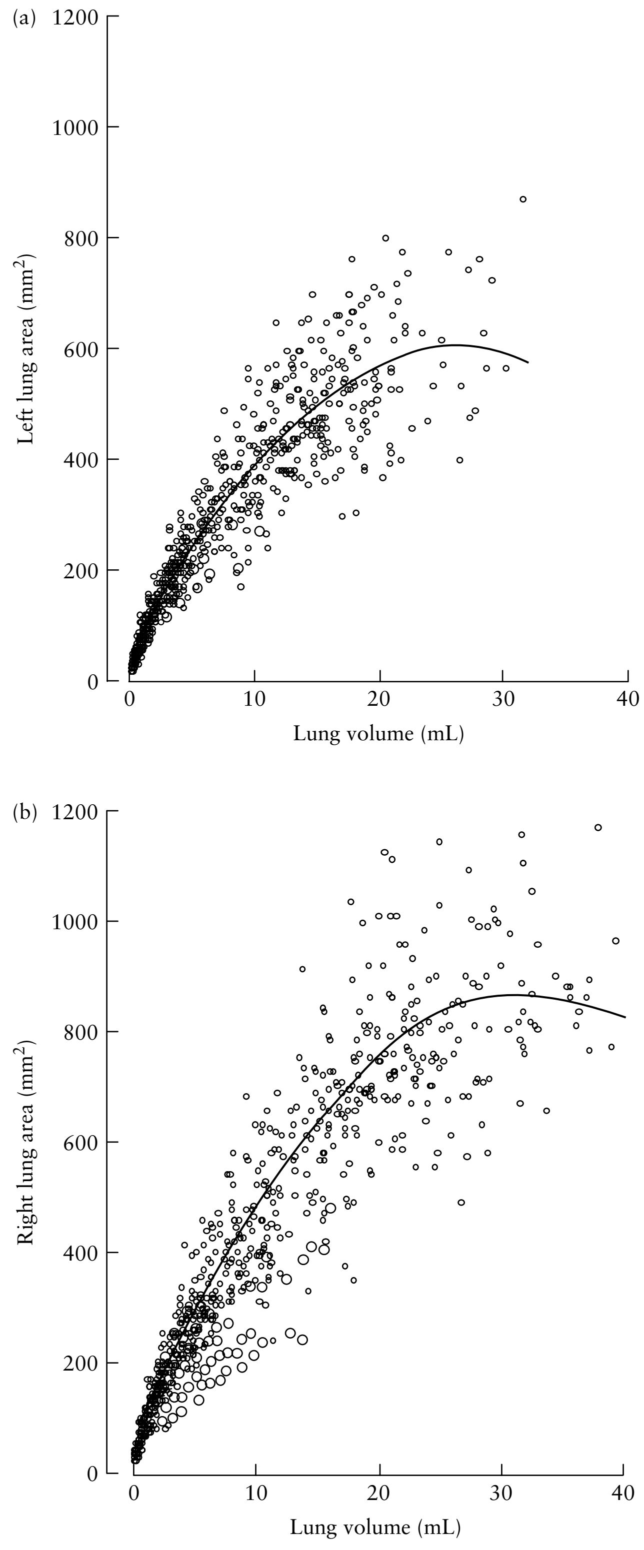

Figure 1 Relationship between left (a) and right (b) lung area with lung volume in normal fetuses (small circles and solid line). Measurements from the contralateral lungs of fetuses with either left- or right-sided diaphragmatic hernia are the larger circles.

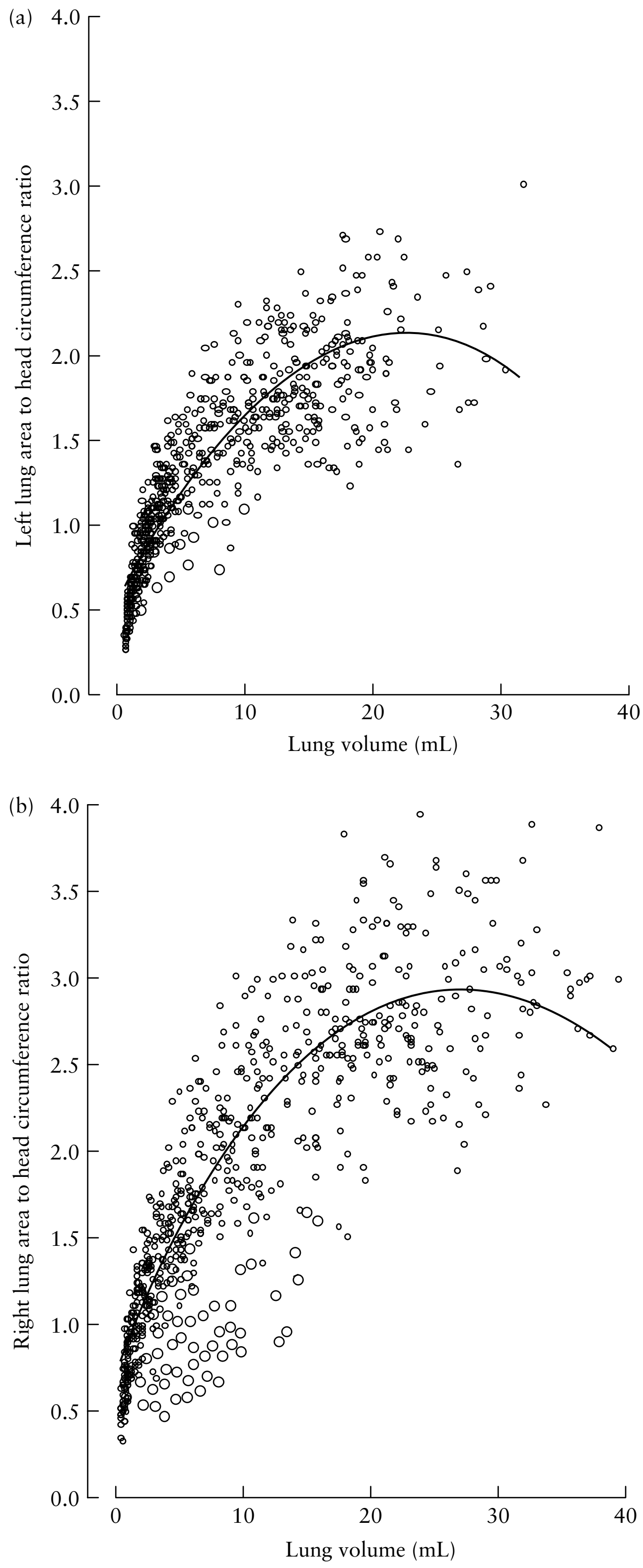

Figure 2 Relationship between left (a) and right (b) lung area to head circumference ratio with lung volume in normal fetuses (small circles and solid line). Measurements from the contralateral lungs of fetuses with either left- or right-sided diaphragmatic hernia are the larger circles.

the left side the anteroposterior diameter is substantially lower.

In the normal fetuses the increase in lung area and LHR with lung volume was not linear and the pattern of the association suggests that in early pregnancy, when the lung volumes are small, the lateral and vertical growth of the lungs is similar, whereas with advancing gestation there is a greater increase in the vertical than the lateral

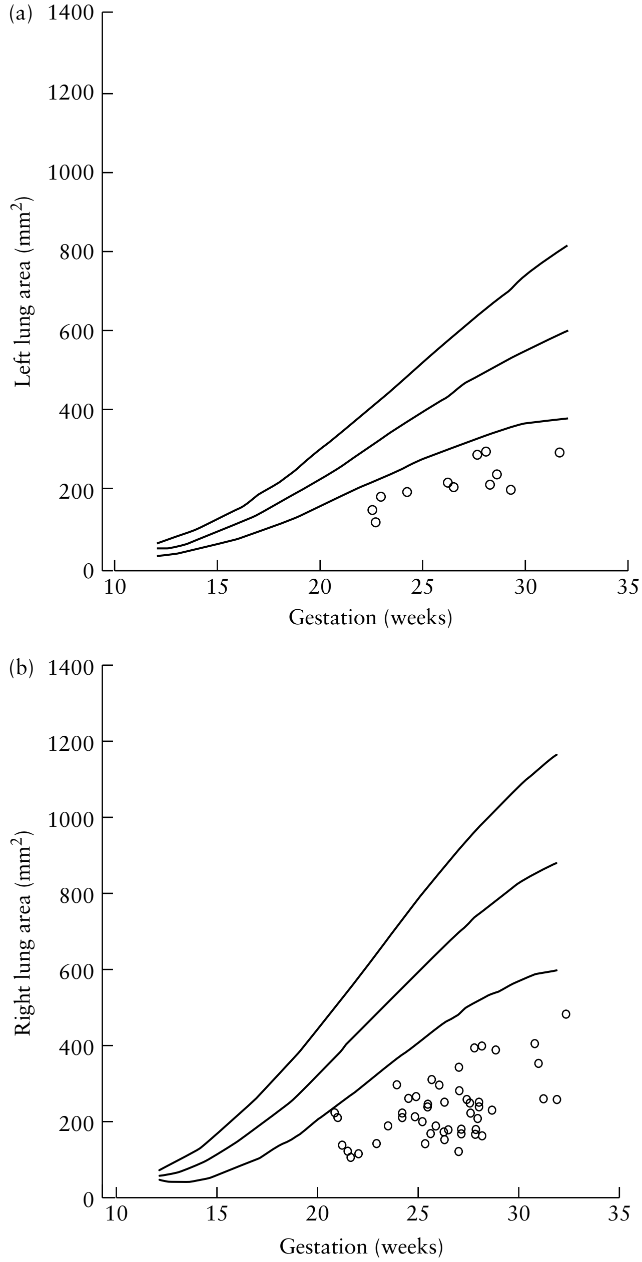

Figure 3 Contralateral left (a) and right (b) lung area in fetuses with diaphragmatic hernia (open circles) plotted on the normal range for gestation (mean, 2.5th and 97.5th centile)[10].

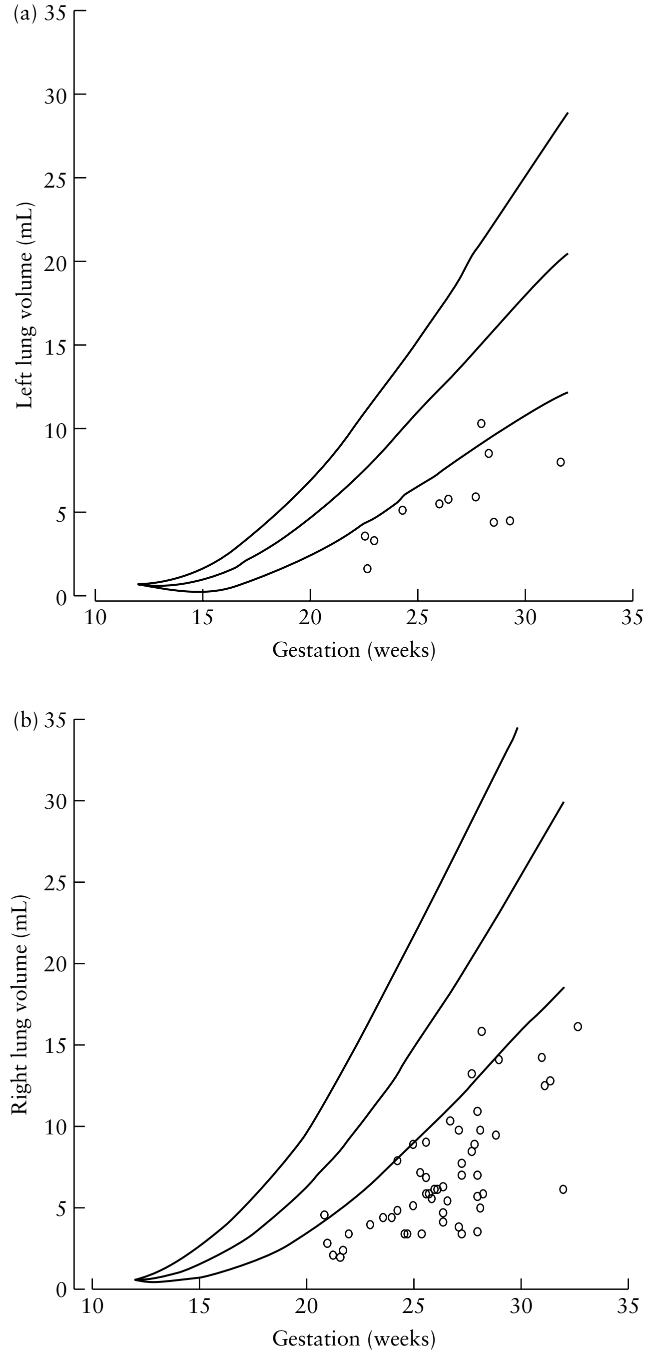

Figure 4 Contralateral left (a) and right (b) lung volume in fetuses with diaphragmatic hernia plotted on the normal range for gestation (mean, 2.5th and 97.5th centile)[11].

growth. An additional factor, which primarily applies to the left lung, is that the lung area, which is measured at the level of the four-chamber view of the heart, is affected by the gestation-related expansion in heart volume. Consequently, it is only in the low range of LHR that this index provides an accurate assessment of lung volume. When the lung area was measured by the tracing method, for LHR greater than 1.2 on the left side and 1.4 on the right side there was a very wide range of possible lung volumes (Table 2). In the case of the lung area being measured by the method employing the longest diameter of the lungs, useful prediction of lung volume was provided by LHR of up to 1.6 on the left side and 1.8 on the right side. The apparently better performance of LHR derived from the longest diameter is likely to be the beneficial consequence of the fact that this method overestimates the true lung area.

The inaccuracy of LHR in predicting lung volume may not in itself constitute a major limitation in the use of this index in the assessment of fetuses with CDH, because in these fetuses lung volume is invariably small. Several studies have documented that the prognosis of fetuses with CDH is poor if the LHR, measured by the method employing the longest diameter of the lungs, is below 1.0[3–9]. In a multicenter study of 184 fetuses with isolated left-sided

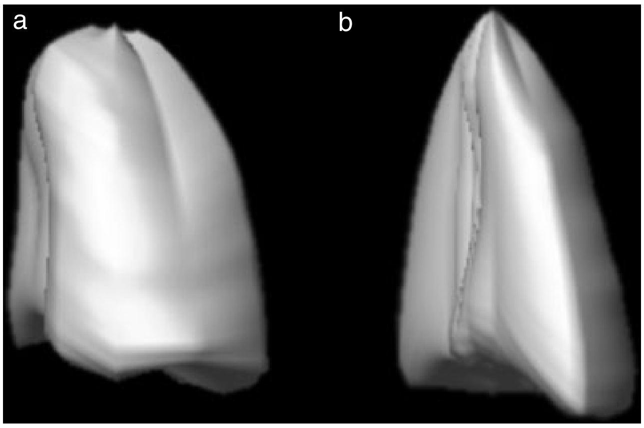

Figure 5 Right lung in a normal fetus (a) and in one with left-sided diaphragmatic hernia (b), both at 25 weeks of gestation, demonstrating that in diaphragmatic hernia the contralateral lung is thinner and longer.

CDH, which were managed expectantly and were live-born after 30 weeks of gestation, significant predictors of survival were the presence or absence of intrathoracic herniation of the liver and the LHR in the right lung[12]. Essentially, in the group with liver herniation the survival rate increased from 0% for those with LHR of 0.4–0.7 to about 15% for LHR of 0.8–0.9, 65% for LHR of 1.0–1.5 and 85% for LHR of 1.6 or more. Consequently, in the clinical management of fetuses with CDH, in terms of distinguishing between the poor from the good outcome group, the critical value of LHR is 1.0, where this value does provide accurate prediction of lung volume.

In fetuses with CDH, the findings that the observed to expected LHR and lung area, for a given lung volume, are significantly lower than in normal fetuses, suggest that the herniated viscera cause a greater lateral, rather than vertical, compression of the contralateral lung. Indeed, we found that in the fetuses with CDH the mean lung length was about 15% longer than in the gestation-matched normal controls, whereas the mean lung area was about half.

CONCLUSIONS

This study has demonstrated an association between LHR and lung volume and in this respect it has validated the use of LHR in the assessment of lung growth, especially in cases of CDH where the lung volume is small. However, the study has also demonstrated that in fetuses with CDH, LHR underestimates the true lung volume. The extent to which the 3D ultrasound measurement of lung volume is better than LHR in predicting the outcome of fetuses with CDH remains to be determined.

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