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Left and right lung volumes in fetuses with diaphragmatic hernia

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ABSTRACT

Objective *To compare the volume of the ipsilateral and contralateral lungs in fetuses with congenital diaphragmatic hernia (CDH).*

Methods *Left and right lung volumes were measured using three-dimensional (3D) ultrasonography in 42 fetuses with CDH at median 26 (range, 20–32) weeks of gestation. Each value was then expressed as a difference, in standard deviations, from the normal mean for gestation, previously established from the study of 650 normal fetuses at 12–32 weeks (Z-score). The Mann–Whitney* U*-test was used to determine the significance of the differences between the measurements in fetuses with CDH and normal fetuses and between the ipsilateral and contralateral lungs in fetuses with left- and right-sided CDH.*

Results *There were 34 fetuses with left-sided CDH and eight with right-sided CDH. In CDH both the ipsilateral and contralateral lung volumes were substantially lower than in normal fetuses. In left CDH the left lung volume was 4.03 (median; range, 3.11–4.78) SDs below the normal mean for gestation, and the respective values for the right lung were 3.04 (median; range, 1.78–4.31) SDs ($P < 0.001$ for both). In right CDH, the left lung volume was 2.91 (median; range, 1.62–4.07) SDs below the normal mean for gestation and the respective values for the right lung were 4.35 (median; range, 3.07–4.99) SDs ($P < 0.001$ for both). In both left and right diaphragmatic hernia the deficit in the volume of the ipsilateral lung was significantly greater than the deficit in the contralateral lung.*

Conclusions *In fetuses with CDH both the ipsilateral and contralateral lung volumes are substantially lower than in normal fetuses.* Copyright © 2006 ISUOG. Published by John Wiley & Sons, Ltd.

INTRODUCTION

Three-dimensional (3D) ultrasonography has made it possible to measure fetal lung volume in both normal and pathological pregnancies[1–7]. In a study of 650 normal fetuses we established that both the left and right lung volumes increase exponentially with gestation from respective mean values of about 0.6 mL and 0.6 mL at 12 weeks to 4.6 mL and 6.3 mL at 20 weeks and 20.5 mL and 30.0 mL at 32 weeks[7].

In congenital diaphragmatic hernia (CDH), chronic intrathoracic pulmonary compression, by the herniated abdominal viscera, prevents normal development of the lungs. Consequently, CDH is associated with a high postnatal mortality, due to pulmonary hypoplasia and/or pulmonary hypertension[8,9]. The potential value of fetal lung volume measurement by 3D ultrasonography in the prediction of outcome in fetuses with CDH, which requires the examination of a large number of patients, remains to be established.

The aim of this study was to examine the effect of CDH on the volume of the ipsilateral and contralateral lungs to define the extent to which both lungs are affected in this condition.

METHODS

A total of 65 fetuses with CDH at median 26 (range, 20–32) weeks of gestation were evaluated. In 42 (65%) of these cases it was possible to measure both the left and the right lung volumes using 3D ultrasonography, and these measurements were compared with those of 650 normal fetuses at 12–32 weeks, reported in a previous study[7]. In 23 of the 65 cases the ipsilateral lung could not be adequately visualized, and these were excluded from the final analysis.

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Several 3D volumes of the fetal chest were acquired by transabdominal sonography (RAB 4-8L probe, Voluson 730 Expert, GE Medical Systems, Milwaukee, WI, USA) and the volumes with the best image quality were chosen for analysis. During the acquisition of the volumes we tried to ensure that the fetus was not moving and 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 base, 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 greatest antero-posterior diameters. Every measurement was done off-line after the scan had been completed.

Statistical analysis

Each lung volume measurement was expressed as a difference, in standard deviations, from the appropriate normal mean for gestation, previously established from the study of 650 normal fetuses at 12–32 weeks' gestation (*Z*-score)[7]. The Mann–Whitney *U*-test was used to determine the significance of differences between the measurements in fetuses with CDH and normal fetuses and between the left and right lung in fetuses with left- and right-sided CDH.

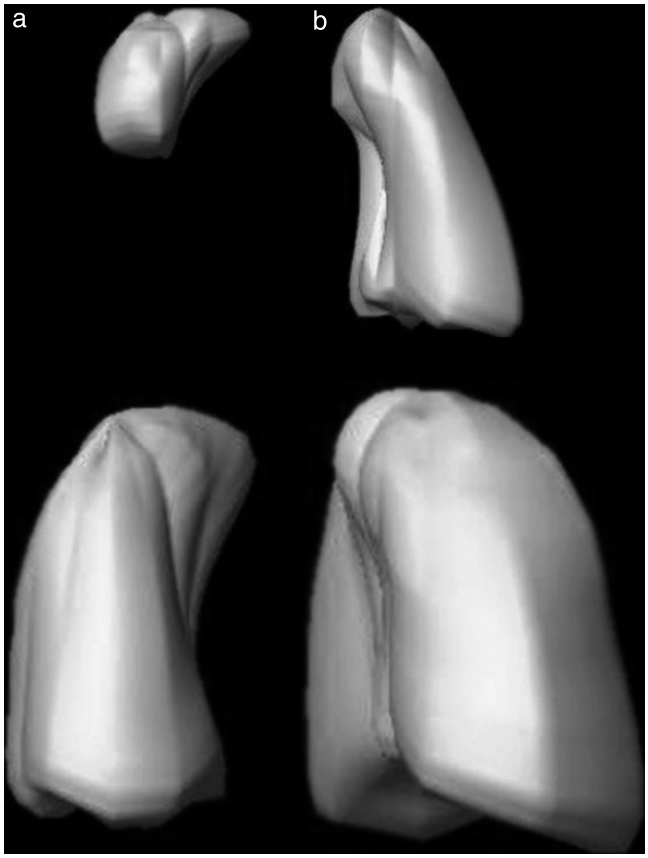

Figure 1 Left (a) and right (b) lungs in a fetus at 23 weeks' gestation with left-sided congenital diaphragmatic hernia (CDH) (above) and a normal fetus at 23 weeks' gestation (below).

RESULTS

In 34 of the 42 cases the CDH was left-sided and in eight it was right-sided. The patients were managed expectantly or by fetoscopic tracheal occlusion (FETO) by means of

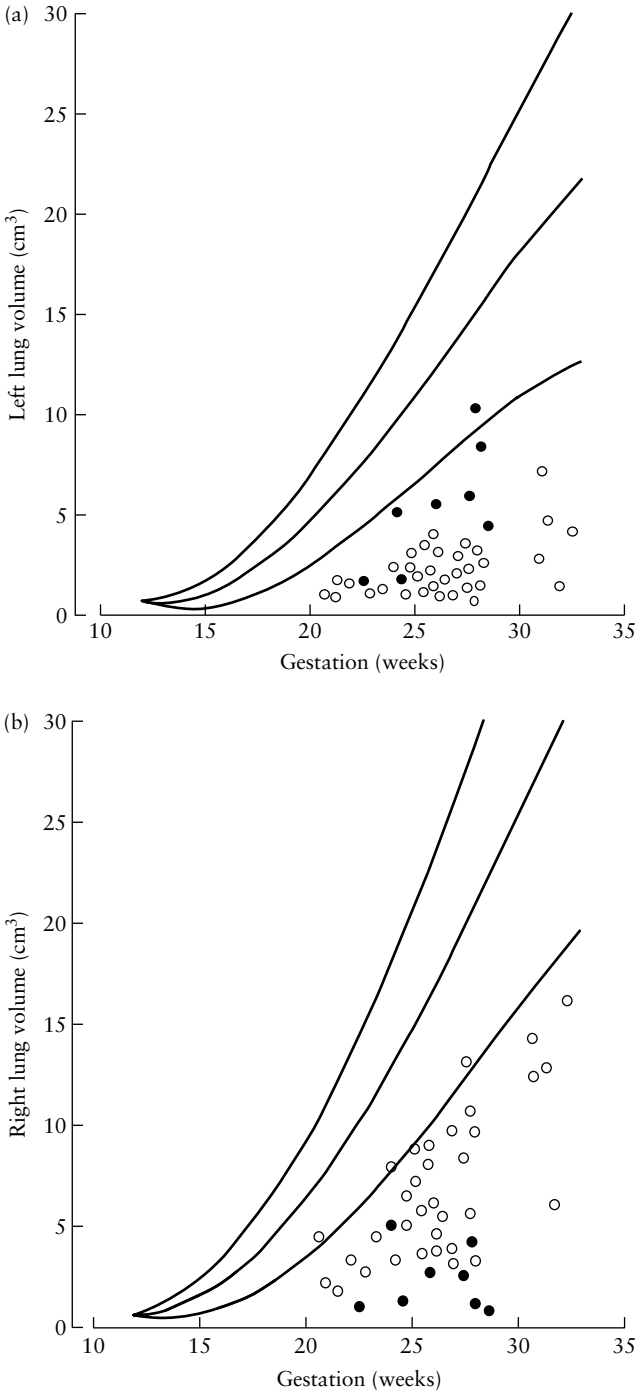

Figure 2 Left (a) and right (b) lung volumes in left-sided (open circles) and right-sided (filled circles) diaphragmatic hernia plotted on the reference range for gestation (mean, 5th and 95th centiles)[1].

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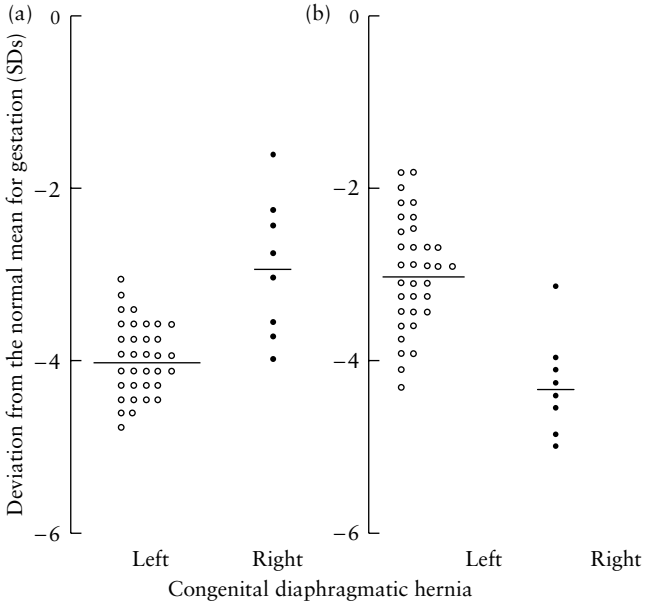

Figure 3 Deviation of left (a) and right (b) lung volumes in left-sided (open circles) and right-sided (filled circles) diaphragmatic hernia, expressed as a difference, in standard deviations, from the appropriate normal mean for gestation[1].

an inflatable balloon[10], or pregnancy termination at the request of the parents. The value of fetal lung volume measurement by 3D ultrasonography in the prediction of outcome is the subject of our ongoing research.

In CDH both the ipsilateral and contralateral lung volumes were substantially lower than in normal fetuses (Figures 1–3). In left CDH, the left lung volume was 4.03 (median; range, 3.11–4.78) SDs below the normal mean for gestation and the respective values for the right lung were 3.04 (range, 1.78–4.31) SDs ($P < 0.001$ for both). In right CDH, the left lung volume was 2.91 (median; range, 1.62–4.07) SDs below the normal mean for gestation and the respective values for the right lung were 4.35 (range, 3.07–4.99) ($P < 0.001$ for both). At 26 weeks, which was the median gestational age of our patients, the normal mean left and right volumes were 12.3 mL and 16.7 mL, respectively. The equivalent mean lung volumes in left-sided CDH were 2.0 mL and 6.3 mL for the left and right lungs respectively, and in right-sided CDH the volumes were 5.1 mL and 2.30 mL for the left and right lungs, respectively.

In both left and right CDH the deficit in the volume of the ipsilateral lung was significantly greater than the deficit in the contralateral lung ($P < 0.001$). In left CDH the median ratio of left to right lung *Z*-score was 1.24 (range, 0.98–2.49), and in right CDH the median ratio of right to left lung *Z*-score was 1.42 (range, 1.11–2.56).

DISCUSSION

The data of this study demonstrate that in fetuses with CDH both the ipsilateral and contralateral lung volumes are substantially lower than in normal fetuses, but the ipsilateral lung is more severely affected. On average, in fetuses with CDH at 26 weeks' gestation the ipsilateral lung volume was about 15% of the normal mean for gestation and the contralateral lung volume was 40% of the normal.

In this study we used the VOCAL technique to measure each lung separately. Previous studies have demonstrated that the results obtained by the multiplanar and VOCAL techniques are similar[11,12]. The main difficulty in measuring the fetal lung volume in cases of CDH is the identification of the inferior limit of the ipsilateral lung, because the diaphragm is one of the main landmarks used during lung volumetry. In addition, in fetuses with CDH the lungs are distorted and their limits can be obscured by the surrounding structures. The main advantages of using the VOCAL technique in CDH cases are that the lowermost and irregular parts of the ipsilateral lung can be included in the measurement and, after the initial calculation of the lung volume has been carried out, it is possible to modify the contour in each plane so that a more accurate final measurement can be obtained. In the multiplanar technique, once the contour has been drawn it cannot be subsequently modified. As described in our previous study of 650 normal fetuses, the reason for choosing the VOCAL 30° rotation step and the greatest anteroposterior diameter of each lung as a starting plane of rotation is because this guarantees the inclusion of the whole organ in the final volume measurement[7]. Other authors have described different techniques[1,2,11,12], but our approach minimizes the need for further correction of the initial volume calculation, which makes the process less time consuming.

Our findings that in CDH the development of both lungs is impaired, but more so the ipsilateral than the contralateral lung, are compatible with the results of previous postnatal studies. In CDH there is lung parenchymal hypoplasia and excessive muscularization of the peripheral pulmonary arteries, leading to pulmonary hypertension. Quantitative analysis of the bronchi, arteries and alveoli, in infants dying after repair of CDH, have confirmed that all are reduced in both lungs, but the ipsilateral lung is more severely affected[13,14]. Similarly, a magnetic resonance imaging study of infants after the repair of left-sided CDH reported that the right lung was more than twice as large as the left[15]. Another study examined the lungs of 21 children dying after CDH repair at 1 to 391 days of postnatal life, and reported that significant lung growth does occur postnatally, with an increase in the radial alveolar number and vascular remodeling resulting in larger and less muscularized arteries[16]. These changes were most marked in the contralateral lung.

CONCLUSIONS

This study has documented the ability to measure fetal lung volume prenatally and has demonstrated that in CDH the volume of both lungs is affected. Further studies are necessary to examine the prognostic significance of these findings from the investigation of a large cohort of

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fetuses with CDH managed expectantly, and to determine the differential effect on the antenatal growth of the ipsilateral and contralateral lung following intrauterine therapy with FETO[10].

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