previously [1-4], the assessment of the residual lung size seems to be one of the most reasonable and realistic methods. It has previously been reported that the LHR, which was first described in 1996 [5], was increased according to the gestational age in normal fetuses [21] and also in the fetuses with CDH [11, 19]. The reason for this increase in the LHR with the gestational age is due to the difference in the rate of the increase of the lung area and head circumference. Peralta et al. reported that there was a four-fold increase in the LHR between 12 and 32 weeks of gestation in normal fetuses because of these differences [21]. Approaches to standardize the LHR by using the normal mean value of the LHR have been proposed to provide a constant value throughout the gestational period [11]. The LHR was originally defined as the contralateral lung area determined using a two-dimensional perpendicular linear measurement, divided by the head circumference [5]. However, two other methods to determine the lung area were subsequently proposed [9, 21], and the tracing method was finally found to be the most reproducible method to measure the lung area [21, 23].

The L/T ratio has been widely used in Japan, because it was first described in 1990 for the assessment of pulmonary hypoplasia in CDH [6], and was has been applied for the assessment of pulmonary hypoplasia in CDH neonates since then [15, 16, 26]. The L/T ratio was originally reported to be constant throughout the gestational period in normal fetuses [6]. This parameter was redefined as the contralateral lung area, to make it more consistent with the LHR, divided by the area of the thorax as measured by the tracing method [19], although the original definition was determined by using the area of both lungs. Thus, there are several similarities between these two parameters. First, both parameters exhibit constant values throughout the gestational period, and the other is that only the contralateral lung area is measured by using the tracing method. However, the relationship between these two parameters has not been studied, despite their similarities.

A strong positive correlation between the L/T ratio and the O/E LHR was found, and a linear regression equation between the L/T ratio and the O/E LHR was obtained. According to this linear regression equation, several important cut-off values of both parameters can be interchanged. Interestingly, a 25% O/E LHR, the cut-off value for the most severe cases as used in the TOAL trial for fetal CDH, was found to be equivalent to a L/T ratio of 0.08, a commonly accepted cut-off value for identifying the most severe cases of fetal CDH in Japan. These results suggested that the patients considered to be the most severe cases in Japan also met the criteria for fetal intervention for left CDH patients with severe pulmonary hypoplasia in the TOTAL trial protocol, which was the first international prospective randomized controlled trial for fetoscopic tracheal occlusion [12, 13]. In the nationwide Japanese survey for fetal CDH, 57.7% of the patients were measured for the L/T ratio, and only 42.3% of the patients were measured for the O/E LHR. However, owing to this conversion equation, both of the parameters can be generated for the evaluation of the patient CDH severity if either of the parameters was measured.

To verify the accuracy and the universal applicability of the prenatal risk-stratified classification, which was proposed by Usui et al., and was defined as the combination of the L/T ratio and the presence of liver herniation [16], we applied the classification to this cohort as a different population from the original cohort using the conversion equation. Although the patient demographics except for the side of the hernia, were similar between the three groups classified using this system, the prenatal and postnatal profiles, including the stomach position, parameters indicating the respiratory status, circulatory status, surgical findings and outcome were significantly different between the three groups, suggesting that the prenatal risk-stratified classification is also valid in other cohorts, such as that in the nationwide Japanese questionnaire survey. The indication for a fetal intervention of the patients proposed by Deprest et al. [25] can be estimated by using the conversion equation in the patients whom the L/T ratio was solely measured without measurement of LHR. The rate of survival to discharge was 93% in the mild group, 80% in the moderate group, 52% in the severe group and 43% in the extreme group (**Figure 2**). Compared to this four-step stratification used in the TOTAL trial, our prenatal risk-stratified classification therefore seems to have better discrimination of disease severity. It is possible to describe the prenatal risk-stratified classification as shown in Table 4 using the O/E LHR instead of the L/T ratio according to the linear regression equation (**Table 4**).

Table 4

When the characteristics of both parameters were compared, the gestational variation and the procedure of the lung area measurements were similar. However, there were concerns that the individual fetal growth variation is not considered when determining the O/E LHR. There may be a possibility for an overestimation in a small-for-date fetus, as the O/E LHR of these fetuses, which should have a lower LHR compared to an appropriate-for-date fetus, would be evaluated based on the normal mean value. The L/T ratio includes, by nature, individual fetal growth variation, and it can be determined with standard values for gestational age or with for a relevant population. More importantly, calculating the L/T ratio is a simple task to perform.

A major limitation of this study is that it was conducted in a retrospective manner using a questionnaire. Many of the institutions had a small number of cases, and the treatment strategies, including the indication criteria for surgery, were determined by each institution. There may have been inaccurate measurement of both parameters due to the limited experience of the physicians with such infants. More accurate prospective studies and an analysis of the correlation based on the timing of the measurement are therefore needed to confirm the present findings. Despite these limitations, an excellent positive correlation was observed between the L/T ratio and O/E LHR in the present study, and these two parameters proved to be compatible according to a linear regression equation. These results suggested that the linear regression equation may become a useful tool for all populations.

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Figure legends

Figure 1:

The relationship between the O/E LHR and the L/T ratio. There was a linear positive correlation between the L/T ratio and the O/E LHR. The linear regression line was: L/T ratio = 0.0223 + (0.00222 x O/E LHR), where the regression coefficient was 0.00222, the correlation coefficient was 0.847 and the coefficient of determination was 0.717 ($p<0.0001$). The open triangles represent the survivors and the closed triangles represent the non-survivors. The 25% O/E LHR was equivalent to a L/T ratio of 0.08 according to this equation, as indicated by broken lines.

Figure 2:

The survival rates depending on the O/E LHR measurements and presence of liver herniation.

*: Liver-up, liver occupying more than one-third of the thoracic space

Figure 3:

The survival curves for patients with isolated CDH, compared using the prenatal risk-stratified classification [16]. *, $P < .001$; **, $P < .001$; †, $P < .001$

Table 1:

The patient demographics

Table 2:

The patient demographics and prenatal findings according to the prenatal risk-stratified classification [16]

Table 3:

The respiratory status, circulatory status, intraoperative findings and outcomes according to the prenatal risk-stratified classification [16]

Table 4:

The prenatal risk-stratified classification described using the O/E LHR instead of the L/T ratio

Table 1: The patient demographics

Number of patients	242
Gestational age (days) †	264.3 ± 8.6
Birth weight (g) †	2746 ± 386
Apgar score at 1min §	4, (2 - 6)
Liver-up *	68/239 (28.5%)
Contralateral stomach herniation **	35/236 (14.8%)
Caesarean section delivery	177 (73.1%)
Gender (male)	138 (57.0%)
Side of hernia (left)	229 (94.6%)
Surgery performed for diaphragmatic hernia	224 (92.6%)
Time of surgery after birth (hours) §	56, (30 - 95)
Patch closure	81/224 (36.2%)
Use of HFOV	212/233 (91.0%)
Use of iNO	166/241 (68.9%)
Use of ECMO	19 (7.9%)
Survival to discharge	200 (82.6%)
Intact discharge	177 (73.1%)

†: mean ± standard deviation, §: median, (interquartile range), *: Liver-up, liver occupying more than one-third of the thoracic space; **: Contralateral stomach herniation, more than half of the stomach was herniating into the contralateral thoracic cavity; HFOV: high-frequency oscillatory ventilation, iNO: inhaled nitric oxide, ECMO: extracorporeal membrane oxygenation

Table 2. The patient demographics and prenatal findings according to the prenatal risk-stratified classification [16]

	Group A	Group B	Group C	*P*
Definition of the group [16]	L/T ratio ≥ 0.08 with liver-down	L/T ratio ≥ 0.08 with liver-up * or L/T ratio < 0.08 with liver-down	L/T ratio < 0.08 with liver-up *	
Number of patients	151	71	17	
Gender (male)	89 (58.9%)	36 (50.7%)	12 (70.6%)	0.265
Side of hernia (left)	149 (98.7%)	64 (90.1%)	13 (76.5%)	< 0.001
Gestational age at birth (days)	265 ± 7.7	263± 10.6	264 ± 6.9	0.313
Birth weight (kg)	2.76 ± 0.37	2.68 ± 0.45	2.87 ± 0.26	0.141
Caesarian section delivery	109 (72.2%)	53 (74.7%)	12 (70.6%)	0.908
Liver-up *	0 (0.0%)	51 (71.8%)	17 (100%)	< 0.001
Contralateral stomach herniation	5/148 (3.4%)	20/71 (28.2%)	10/17 (58.8%)	< 0.001
L/T ratio	0.148 ± 0.053**	0.106 ± 0.039†	0. 059 ± 0.020‡	< 0.001

*: Liver-up, liver occupying more than one-third of the thoracic space; Contralateral stomach herniation, more than half of the stomach was herniating into the contralateral thoracic cavity; L/T ratio, contralateral lung to thorax transverse area ratio; **, *P* < .05 A vs B; †, *P* < .05 B vs C; ‡, *P* < .05 C vs A;

Table 3. The respiratory status, circulatory status, intraoperative findings and outcomes according to the prenatal risk-stratified classification [16]

	Group A	Group B	Group C	*P*
Definition of the group [16]	L/T ratio ≥ 0.08 with liver-down	L/T ratio ≥ 0.08 with liver-up * or L/T ratio < 0.08 with liver-down	L/T ratio < 0.08 with liver-up *	
Number of patients	151	71	17	
Apgar score at 1 min	5 (3-7) (n=143)	4 (2-5) (n=66)	2.5 (1.25-4) (n=16)	< 0.001
Highest preductal PaO_2 (Torr) §	257 ± 134** (n=145)	199 ± 135† (n= 69)	75 ± 70‡ (n=17)	< 0.001
Best oxygenation index §	5.7 ± 5.9** (n=143)	14.3 ± 17.5† (n=68)	32.0 ± 24.5‡ (n=17)	< 0.001
Right to left shunting at ductus §	55/143 (38.5%)	40/68 (58.8%)	13/17 (76.5%)	0.001
Use of HFOV	130/145 (89.7%)	64/69 (92.8%)	16/17 (94.1%)	0.680
Use of iNO	85/151 (56.3%)	63/71 (88.7%)	15/16 (93.8%)	< 0.001
Use of prostaglandin E_1	45/149 (30.2%)	35/71 (49.3%)	14/17 (82.4%)	< 0.001
Use of ECMO	4 (2.7%)	9 (12.7)	5 (29.4%)	< 0.001
Inoperable cases	2 (1.3%)	10 (14.1%)	6 (35.3%)	< 0.001
Diaphragmatic defects ≥ 75% ††	27/149 (18.1%)	38/61 (62.3%)	8/11(72.7%)	< 0.001
Patch closure	31/149 (20.8%)	40/61 (65.6%)	8/11 (72.7%)	< 0.001
Survival to discharge	141 (93.4%)	51 (71.8%)	6 (35.3%)	< 0.001
Intact discharge	131 (86.8%)	41 (57.8%)	3 (17.7%)	< 0.001

*, Liver-up, liver occupying more than one-third of the thoracic space; §, The highest pre PaO_2, best oxygenation index and the right to left shunting at ductus were determined within 24 hours after birth; ††, The size of the diaphragmatic defect was rated by a surgeon according to the surgical record. **, $P < .05$ A vs B; †, $P < .05$ B vs C; ‡, $P < .05$ C vs A HFOV, high-frequency oscillatory ventilation, iNO, nitric oxide inhalation; ECMO, extracorporeal membrane oxygenation

Table 4. The prenatal risk-stratified classification described using the O/E LHR instead of the L/T ratio

Group A	O/E LHR ≥ 25% with liver-down
Group B	O/E LHR ≥ 25% with liver-up *, or O/E LHR < 25% with liver-down
Group C	O/E LHR < 25% with liver-up *

*, Liver-up, liver occupying more than one-third of the thoracic space

Figure 1

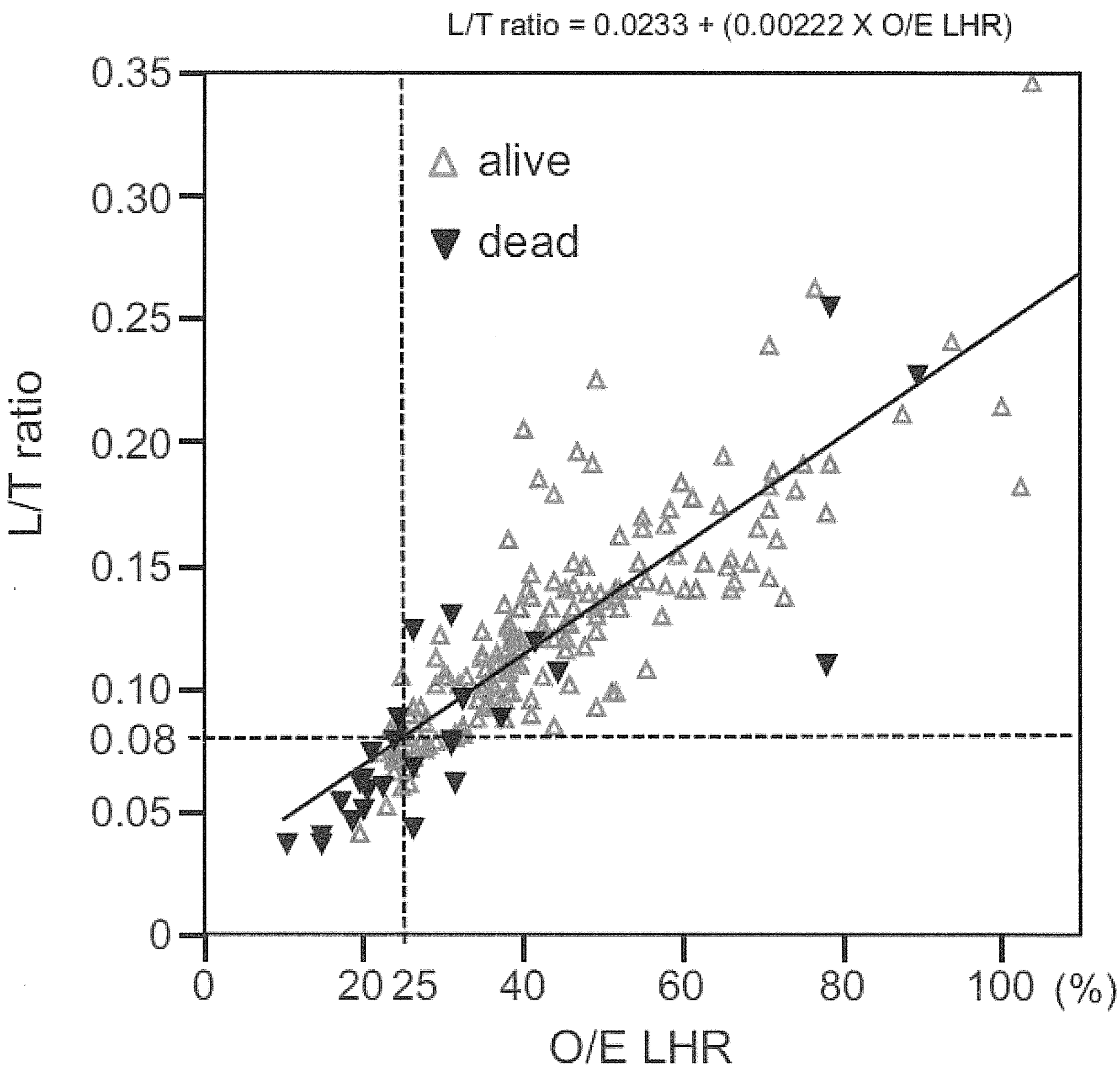
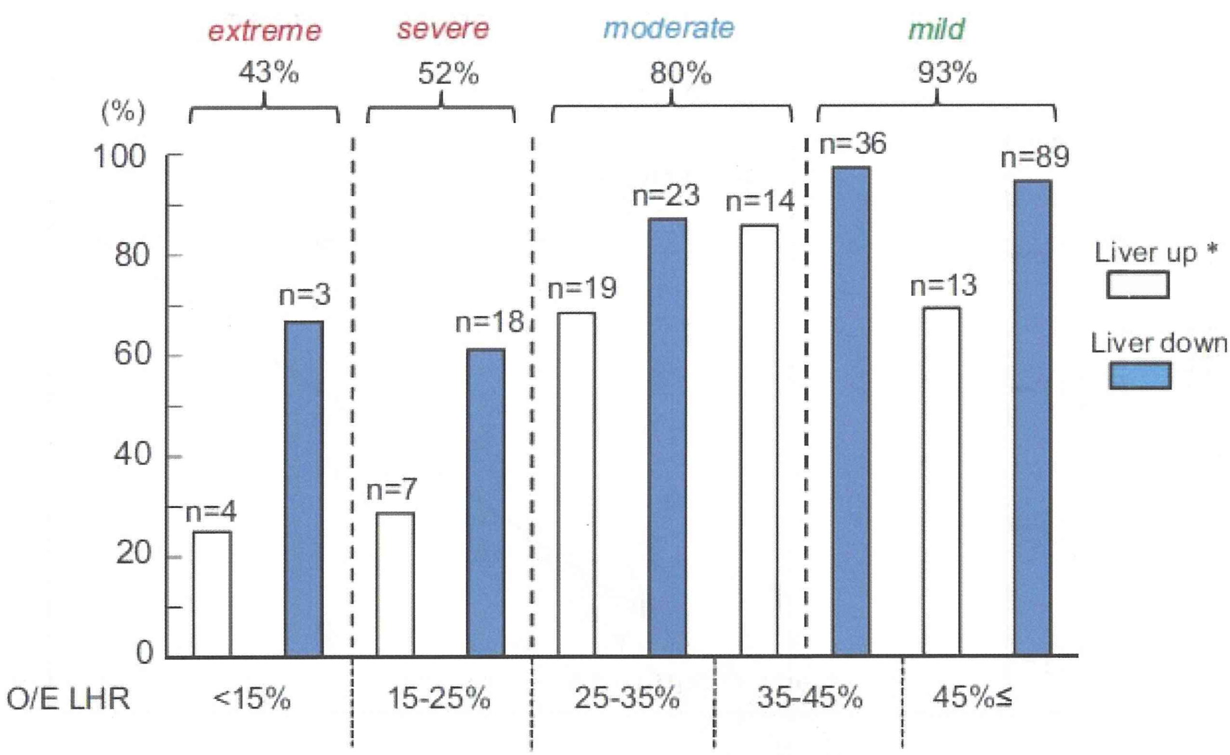
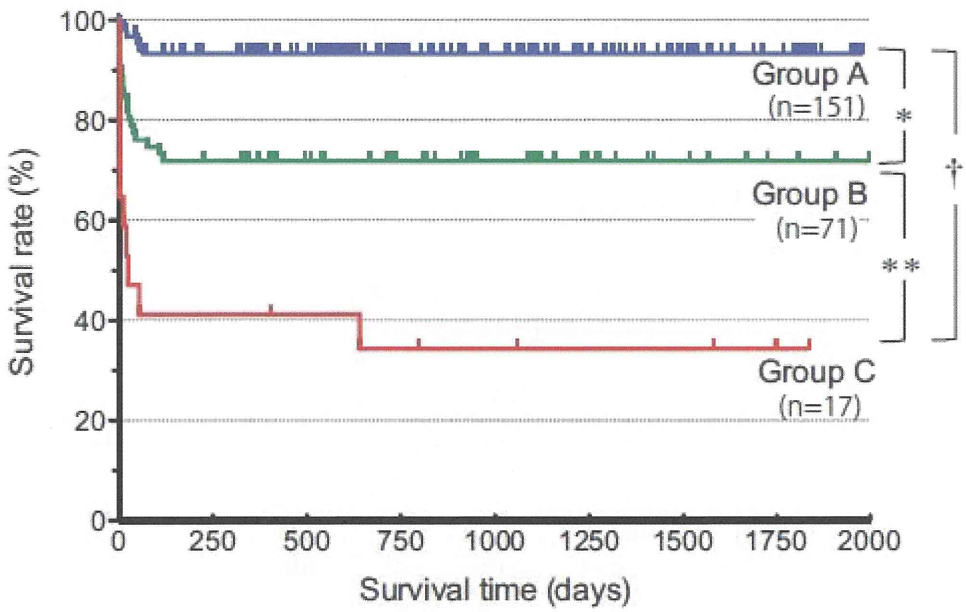

L/T ratio = 0.0233 + (0.00222 X O/E LHR)
alive
dead
L/T ratio
0.35
0.30
0.25
0.20
0.15
0.10
0.08
0.05
0
0
20
25
40
60
80
100
(%)
O/E LHR

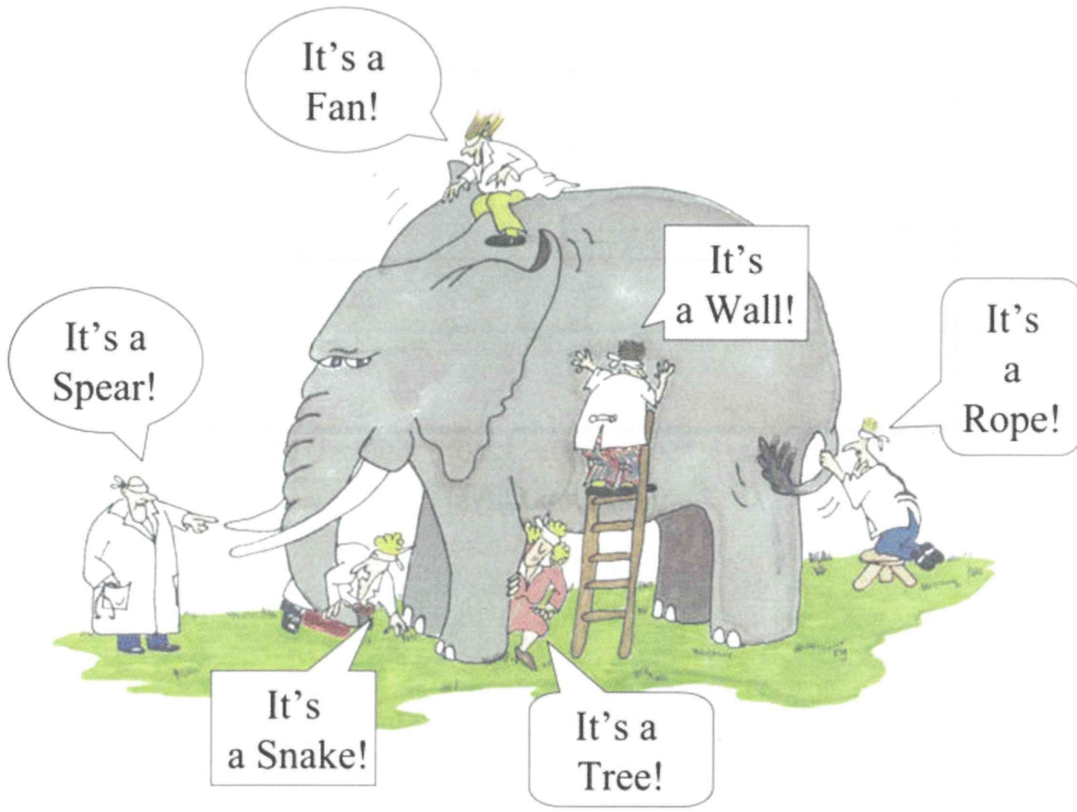
Figure 2



extreme
43%
severe
52%
moderate
80%
mild
93%
(%)
100
80
60
40
20
0
n=4
n=3
n=7
n=18
n=19
n=23
n=14
n=36
n=13
n=89
Liver up *
Liver down
O/E LHR
<15%
15-25%
25-35%
35-45%
45%≤

Figure 3


100
80
60
40
20
0
Survival rate (%)
0
250
500
750
1000
1250
1500
1750
2000
Survival time (days)
Group A
(n=151)
Group B
(n=71)
Group C
(n=17)
*
**
†


It's a
Fan!
It's
a Wall!
It's a
Spear!
It's
a
Rope!
It's
a Snake!
It's a
Tree!