The efficacy of the postnatal nasogastric tube position as a prognostic marker of left-sided isolated congenital diaphragmatic hernia

Jun Kono  
Kyushu University

Kouji Nagata (nagata.koji.318@m.kyushu-u.ac.jp)  
Kyushu University

Keita Terui  
Chiba University Graduate School of Medicine

Shoichiro Amari  
National Center for Child Health and Development

Katsuaki Toyoshima  
Kanagawa Children's Medical Center

Noboru Inamura  
Kinki University

Masaya Yamoto  
Shizuoka Children's Hospital

Tadaharu Okazaki  
Juntendo University Urayasu Hospital

Yuta Yazaki  
Juntendo University School of Medicine

Hiroomi Okuyama  
Osaka University Graduate School of Medicine

Masahiro Hayakawa  
Nagoya University Hospital

Taizo Furukawa  
Kyoto Prefectural University of Medicine

Kouji Masumoto  
University of Tsukuba

Akiko Yokoi  
Hyogo Children's Hospital

Noriaki Usui  
Osaka Women's and Children's Hospital

Tatsuro Tajiri
Keywords: congenital diaphragmatic hernia, stomach position, postnatal prognostic factor, nasogastric tube, mortality.

Posted Date: September 9th, 2022

DOI: https://doi.org/10.21203/rs.3.rs-2031610/v1

License: ☇️ ☂️ This work is licensed under a Creative Commons Attribution 4.0 International License. 
Read Full License
Abstract

**Purpose:** The prenatal diagnosis of the stomach position in congenital diaphragmatic hernia (CDH) has been a reliable prognostic factor, but few studies have focused on the postnatal position. We therefore evaluated the significance of the nasogastric (NG) tube position just after birth.

**Methods:** The Japanese CDH Study Group database enrolled 1037 CDH neonates over 15 years. In our multicenter retrospective study, 464 cases of left-sided isolated CDH with prenatal diagnoses were divided into 2 groups: NG tube below the diaphragm (BD; n=190) or above the diaphragm (AD; n=274). The primary outcome was the 90-day survival rate, and the secondary outcomes were mechanical ventilation duration, hospitalization duration, and recurrence rate.

**Results:** The BD group had a significantly higher 90-day survival rate (98.4% vs. 89.4%, p<0.001), shorter mechanical ventilation (11 vs. 19 days, p<0.001), shorter hospitalization (38 vs. 59 days, p<0.001), and lower recurrence rate (p=0.002) than the AD group. A multivariate analysis showed that BD (adjusted odds ratio, 3.68; 95% confidence interval, 1.02–13.30) was a favorable prognostic factor for the 90-day survival.

**Conclusion:** The assessment of the NG tube position revealed it to be a reliable prognostic factor of left-sided isolated CDH, therefore, it should be included as a routine assessment.

Introduction

Congenital diaphragmatic hernia (CDH) is a congenital defect in the diaphragm that allows the abdominal organs to migrate into the thoracic cavity, thus hampering the growth and development of the lung [1, 2]. Previous studies have shown that the frequency of CDH was approximately between 1 in 2500 and 1 in 4000 live births [1−3]. Although CDH has a wide variety of disease severities and associated anomalies, the mortality and morbidity rates mainly depend on lung hypoplasia and pulmonary hypertension [1, 2, 4, 5].

Prenatal prediction of the severity and prognosis enables doctors to deliver accurate information on a CDH fetus to the parents and allows sufficient time to prepare for adequate medical care [6, 7]. Previous reports have described reliable prenatal prognostic factors, such as the fetal lung volume, fetal stomach position, and fetal liver position [3, 8−14]. However, making a prenatal diagnosis requires a skillful technique and considerable experience. The accuracy of fetal sonography one of the most important modalities for making prenatal diagnoses, depends on the examiner, and its reproducibility is limited [14]. Conversely, magnetic resonance imaging (MRI), another modality for making fetal diagnoses, is an objective modality and enables all viewers to see the same view; however, MRI reading also requires substantial skill, and the MRI device itself is expensive. Therefore, a simpler, less expensive factor for predicting the outcome of such cases would be useful.
Many reports have found that the position of the fetal stomach was associated with the mortality and morbidity of CDH patients [10–11]; however, the postnatal position has been described in only few studies [15, 16], and most of these studies were performed in 1980’s and 1990’s except for one study that was carried out in 2012. Though these studies found that the stomach in the thorax was associated with mortality, the sample sizes were small, and in the 2012 study, the method used to identify the stomach position was not described in the paper. We therefore hypothesized that the postnatal position of the stomach soon after birth would also be a predictive factor for mortality.

In the present study, we focused on the position of the tip of the NG tube via X-ray, which was considered to accurately represent the position of stomach, because it is very simple to assess early after birth, to determine whether or not it was able to predict the prognosis of CDH patients.

**Materials And Methods**

**Patient selection**

We retrospectively reviewed the database from the Japanese CDH study group, which included CDH neonates admitted to 15 institutions between January 2006 and March 2021. Among the enrolled CDH neonates, left-sided isolated CDH neonates were included, while right-sided and bilateral CDH neonates as well as non-isolated CDH neonates were excluded. CDH patients without a prenatal diagnosis and radical operation were also excluded. In addition, cases with missing data regarding the prenatal stomach position and postnatal tube position were also excluded. Isolated CDH was defined as CDH without any associated life-threatening or chromosomal anomalies. Based on the position of the tip of the NG tube, patients were divided into two groups: the below diaphragm (BD) group and the above diaphragm (AD) group. The NG tube position was determined based on whether the tube was in the thoracic cavity (above) or the abdominal cavity (below) on X-ray obtained soon after birth.

**Outcomes**

The primary outcome was the 90-day survival rate. Secondary outcomes were the duration of mechanical ventilation and hospitalization and the recurrence rate. Both of the outcomes were compared between the BD and AD groups.

**Data collection**

The prenatal variables, including the presence of a prenatal diagnosis, location of the fetal stomach according to the Kitano category, presence of liver herniation, lung area-to-head circumference ratio (LHR), the observed/expected lung area-to-head circumference ratio (o/eLHR), and lung-to-thorax transverse ratio (LTR), were reviewed. The postnatal variables, including the sex, gestation week at delivery, birth weight, Apgar scores at 1 and 5 minutes, and lowest oxygenation index (OI) within 24 h after birth, were obtained. Data concerning the treatment were also examined. The diaphragmatic closure approach, defect size, presence of liver herniation, presence of stomach herniation, use of inhaled nitric oxide (iNO), and use of extracorporeal membrane oxygenation (ECMO) were reviewed. The defect size
was determined according to the CDH Study Group’s criteria during the operation [17]. The presences of liver and stomach herniation was defined in cases were the patient’s liver or stomach had herniated into the thoracic cavity during the operation.

**Statistical analyses**

The prenatal variables, postnatal variables, data on treatment, and outcomes were compared between the BD and AD groups. Frequencies were described as categorical data. Fisher’s exact test was used to analyze the categorical data. The median and range were used to describe the continuous data. Wilcoxon’s rank sum test was used to analyze the continuous data. The recurrence rate was calculated using Kaplan-Meier curves and compared between the BD and AD groups using a log-rank test. Variables related to mortality in previous reports were entered into a multiple logistic regression analysis. A value of p < 0.05 was considered to indicate a statistically significant difference.

**Results**

One thousand and thirty-seven CDH neonates were included over 16 years in the Japanese CDH study group database. Ninety-eight right-sided CDH neonates, 12 bilateral CDH neonates, and 142 left-sided non-isolated CDH neonates were excluded. Among the 785 left-sided isolated CDH neonates, 94 cases were excluded because the NG tube position was not noted. One hundred and three neonates without a prenatal diagnosis and 70 without radical operation were also excluded. In addition, 54 neonates who had been prenatally diagnosed but had a missing description concerning the fetal stomach position were also excluded. A total of 464 cases were ultimately included and divided into 2 groups according to the NG tube position. One hundred and ninety cases were included in the BD group, and 274 cases were included in the AD group (Fig. 1).

Table 1 shows the patients’ characteristics. The prenatal grading scale of the stomach position was significantly higher in the AD group than in the BD group, although the prenatal grading system was not perfectly consistent with the postnatal NG tube position (i.e., Grade 0 according to the Kitano classification was assigned to 63.7% in the BD group and 8.0% in the AD group). Other prenatal risk factors, such as the LHR, o/eLHR, and LTR, were lower in the AD group than in the BD group.
Table 1
The patients’ characteristics, operative findings and use of iNO and ECMO

<table>
<thead>
<tr>
<th>Variable</th>
<th>BD group (n = 190)</th>
<th>AD group (n = 274)</th>
<th>P values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Prenatal characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach position</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kitano Grade 0, no. (%)</td>
<td>121 (63.7)</td>
<td>22 (8.0)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Kitano Grade 1, no. (%)</td>
<td>40 (21.1)</td>
<td>118 (43.1)</td>
<td></td>
</tr>
<tr>
<td>Kitano Grade 2, no. (%)</td>
<td>24 (12.6)</td>
<td>79 (28.8)</td>
<td></td>
</tr>
<tr>
<td>Kitano Grade 3, no. (%)</td>
<td>5 (2.6)</td>
<td>55 (20.1)</td>
<td></td>
</tr>
<tr>
<td>Liver up, no. (%)</td>
<td>24 (12.6)</td>
<td>131 (47.8)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LHR median (range), total no.</td>
<td>1.67 (0.06–5.16)</td>
<td>1.25 (0.13–3.17)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>o/eLHR median (range), total no.</td>
<td>52.95 (3.05–166.98)</td>
<td>40.34 (10.00–95.28)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>LTR median (range), total no.</td>
<td>0.14 (0.05–0.35)</td>
<td>0.11 (0.03–0.28)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Postnatal characteristics</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sex (male:female)</td>
<td>95:95</td>
<td>145:129</td>
<td>0.571</td>
</tr>
<tr>
<td>Gestation age (weeks), median (range)</td>
<td>38.1 (32.3–41.6)</td>
<td>37.7 (29.7–40.7)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Birth weight (g), median (range)</td>
<td>2807 (1376–3994)</td>
<td>2707 (756–4150)</td>
<td>0.026</td>
</tr>
<tr>
<td>Apgar score at 1 minute, median (range), total no.</td>
<td>5 (1–9) n = 188</td>
<td>4 (1–9) n = 262</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Apgar score at 5 minutes, median (range), total no.</td>
<td>7 (1–10) n = 186</td>
<td>6 (1–10) n = 260</td>
<td>0.001</td>
</tr>
<tr>
<td>Lowest OI, median (range), total no.</td>
<td>3.45 (0.96–42.02)</td>
<td>4.69 (1.38–124.31)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Operative findings</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Simple closure, no. (%)</td>
<td>153 (80.5)</td>
<td>111 (40.5)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Defect size A, no. (%)</td>
<td>35 (18.4)</td>
<td>15 (5.5)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Abbreviations: BD, below diaphragm; AD, above diaphragm; LHR, lung area-to-head circumference ratio; o/e LHR, observed/expected lung area-to-head circumference ratio; LTR, lung-to-thorax transverse ratio; OI, oxygenation index; ECMO, extracorporeal membrane oxygenation; iNO, inhaled nitric oxide.
Variable | BD group (n = 190) | AD group (n = 274) | P values
--- | --- | --- | ---
Defect size B, no. (%) | 125 (65.8) | 113 (41.2) | 
Defect size C, no. (%) | 23 (12.1) | 99 (36.1) | 
Defect size D, no. (%) | 7 (3.7) | 47 (17.2) | 
Liver herniation, no. (%) | 24 (12.6) | 131 (47.8) | < 0.001
Stomach herniation, no. (%) | 76 (40.0) | 258 (94.2) | < 0.001
ECMO, no. (%) | 4 (2.1) | 25 (9.1) | 0.002
iNO, no. (%) | 120 (63.2) | 229 (83.6) | < 0.001

Abbreviations: BD, below diaphragm; AD, above diaphragm; LHR, lung area-to-head circumference ratio; o/e LHR, observed/expected lung area-to-head circumference ratio; LTR, lung-to-thorax transverse ratio; OI, oxygenation index; ECMO, extracorporeal membrane oxygenation; iNO, inhaled nitric oxide.

Regarding the postnatal characteristics, there was no significant difference in the sex between two groups. The gestational age at delivery was significantly younger and the birth weight significantly lower in the AD group than in the BD group. Apgar scores at 1 and 5 minutes were lower in the AD group than in the BD group, and the lowest OI within 24 h after birth was higher in the AD group than in the BD group. Table 1 also shows the operative findings and the rates of using iNO and ECMO. The defect size was larger and patch closure of diaphragmatic defects more often performed in the AD group than in the BD group. In addition, the rates of liver and stomach herniation at radical operation were higher in the AD group than in the BD group. The application rate of ECMO and iNO were higher in the AD group than in the BD group.

Regarding outcomes, the patients in the BD group showed significantly higher 90-day survival rates, shorter ventilation duration, and shorter hospitalization duration than those in the AD group (Table 2). The Kaplan-Meier analysis showed that the recurrence rate was significantly lower in the BD group than in the AD group (Fig. 2).
Table 2
Outcomes

<table>
<thead>
<tr>
<th>Variable</th>
<th>BD group</th>
<th>AD group</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>90-days-survival, no. (%)</td>
<td>187 (98.4)</td>
<td>245 (89.4)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Mechanical ventilation duration (days) median (IQR)</td>
<td>11 (7–18)</td>
<td>19 (11–31)</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Hospitalization (days) median (IQR)</td>
<td>38 (30–56)</td>
<td>59 (41–92)</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

Abbreviations: BD, below diaphragm; AD, above diaphragm; IQR, interquartile range.

Table 3 shows the odds ratios (ORs) in the univariate and multivariate analyses. These variables, including the lowest OI, Apgar score at 1 minute, defect size, and presence of liver herniation at surgery, had all been previously reported to predict mortality and were all postnatal factors. Our univariate analysis showed that BD (crude OR, 7.36; 95% confidence interval [CI], 2.23–38.28), lowest OI < 8 (crude OR, 10.23; 95% CI, 4.44–25.26), defect size A or B (crude OR, 5.51; 95% CI, 2.32–14.54), and non-liver herniation (crude OR, 4.23; 95% CI, 1.89–10.01) were the significant factors for the 90-day survival. A multiple logistic regression analysis showed that BD (adjusted OR, 3.68; 95% CI, 1.02–13.30) and lowest OI < 8 (adjusted OR, 6.73; 95% CI, 2.95–15.40) were significant factors for the 90-day survival.
Table 3
Odds ratio for 90-days-survival in univariate analysis and multiple logistic regression analysis

<table>
<thead>
<tr>
<th>Variables</th>
<th>Crude OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BD group</td>
<td>7.36</td>
<td>2.23–38.28</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Lowest OI &lt; 8</td>
<td>10.23</td>
<td>4.44–25.26</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Apgar score at 1 min &gt; 4</td>
<td>2.08</td>
<td>0.95–4.72</td>
<td>0.06</td>
</tr>
<tr>
<td>Defect size A, B</td>
<td>5.51</td>
<td>2.32–14.54</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Non-liver herniation</td>
<td>4.23</td>
<td>1.89–10.01</td>
<td>&lt; 0.001</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Variables</th>
<th>Adjusted OR</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>BD group</td>
<td>3.68</td>
<td>1.02–13.30</td>
<td>0.047</td>
</tr>
<tr>
<td>Lowest OI &lt; 8</td>
<td>6.73</td>
<td>2.95–15.40</td>
<td>&lt; 0.001</td>
</tr>
<tr>
<td>Defect size A, B</td>
<td>2.10</td>
<td>0.77–5.71</td>
<td>0.146</td>
</tr>
<tr>
<td>Non-liver herniation</td>
<td>1.25</td>
<td>0.49–3.18</td>
<td>0.633</td>
</tr>
</tbody>
</table>

Abbreviations: OR, odds ratio; CI, confidence interval; BD, below diaphragm; OI, oxygenation index.

To validate the differences observed between the prenatal and postnatal stomach position, the sensitivity, the specificity, and the area under the curve (AUC) of the correspondence rate of the stomach position at surgery were assessed. The sensitivity and the specificity of Kitano category Grade 0 associated with the intra-abdominal stomach at surgery were 78.5% and 87.7%, respectively. The AUC of the receiver operating characteristic (ROC) curve was 0.831. On the other hand, the sensitivity and the specificity of the BD group to no stomach herniation at surgery were 87.7% and 77.2%. The AUC of the ROC curve was 0.825. There was no significant difference between 2 AUCs (p = 0.777). Therefore, the NG tube position is considered to be a reliable prognostic factor for predicting the outcomes of left-sided isolated CDH neonates.

The correspondent rates for the prenatal and postnatal diagnoses in the BD and AD groups were 121/190 (63.6%) and 252/274 (92.0%), respectively. Furthermore, the survival rate of the BD group and grade 0 (BD-G0) was 100%, while that of the BD group and grade 1 (BD-G1) was 97.5%, that of the BD group and grade 2 (BD-G2) was 95.8%, that of the BD group and grade 3 (BD-G3) was 80.0%, that of the AD group and grade 0 (AD-G0) was 100%, that of the AD group and grade 1 (AD-G1) was 92.4%, that of the AD group and grade 2 (AD-G2) was 88.6%, and that of the AD group and grade 3 (AD-G3) was 80.0% (supplementary table 1).
To minimize the bias of stomach transition and technical failure, we performed a subgroup analysis. The BD group, whose fetal stomach did not herniate to the thoracic cavity, and the AD group, whose fetal stomach did herniate to the thoracic cavity, were included in this subgroup analysis, and the outcomes were compared between these groups (supplementary table 2). In this subgroup analysis, the 90-day survival rate in the BD group was 100%, while that in the AD group was 88.5% (p < 0.001). The mechanical ventilation duration was shorter in the BD group than in the AD group (11 vs. 19 days, p < 0.001). The hospitalization period was also shorter in the BD group than in the AD group (36 vs. 60 days, p < 0.001).

**Discussion**

CDH has an inherent wide variety in its severity and associated anomalies, and it is always important to assess the risks and determine a treatment strategy in both the prenatal and postnatal periods. A prenatal diagnosis is a powerful risk assessment modality, enabling us to plan the delivery mode, provide family counseling, and prepare for resource allocation. Since over 80% of CDH neonates in Japan are diagnosed prenatally, this treatment strategy can be presented to the patient's family in the last trimester, which may help in achieving consensus between medical staff and the family regarding the treatment strategy. In addition, the availability of alternative treatments according to risk stratification can improve the survival rate and reduce costs and complications [17]. However, in some countries, only around ≤ 50% of CDH neonates are diagnosed prenatally, making postnatal risk assessments more important in such locations [18].

Among the prenatal risk assessment parameters associated with the postnatal outcome, the fetal stomach position has reported to be significant, in addition to the fetal lung volume and liver herniation. Kitano et al. showed that their risk grading system, in combination with the fetal stomach position and presence of fetal liver herniation, was associated with intact discharge in their Japanese multicenter study [10]. Basta et al. also reported that the fetal stomach position was correlated with the survival rate, need for ECMO, non-primary repair, and long respiratory support [11]. Recently, the prenatal CDH risk grading system determined by evaluating the fetal stomach position was adopted by the European reference network on rare inherited and congenital anomalies (ERNICA) as a standardized prenatal prognostic factor [19].

However, there have been few reports on the CDH risk assessment using the postnatal stomach position. In the 1980s and 1990s, some studies found that the postnatal stomach position was correlated with the mortality [15]; however, since then, only one report has shown that the postnatal stomach position was correlated with the survival rate in left-sided CDH [16]. Although this report focused on the presence of the stomach in the thorax at birth increased the risk of a poor outcome, the definition of the stomach position was not clearly described, the sample size was quite small, therefore, determining the stomach position alone was insufficient to predict the outcomes in this study. As a result, it was necessary to determine both the stomach position and OI values in order to successfully predict the outcomes.
In the present study, the BD group was obviously correlated with a better 90-day survival, shorter ventilation period, shorter hospitalization, and lower recurrence rate than the AD group. A multivariate analysis also revealed that the postnatal stomach position below the diaphragm, which can be confirmed by the NG tube position via X-rays, and the lowest OI were favorable postnatal prognostic factors for CDH neonates who had not been diagnosed prenatally.

In this study, we did not aim to compare the prognostication ability for the outcome between the prenatal stomach position and the postnatal NG tube position. Our data showed that the corresponding rate between the Kitano classification and stomach position at surgery had a high specificity, while that between the NG tube position and the stomach position at surgery had a high sensitivity. This may have been because the stomach position can be a moving target after birth, based on the lung inflation due to ventilation, and the larger the defect size, the more easily the stomach can be pushed down into the abdomen. Because the 90-day survival rate of cases with Kitano grade 0 was 100%, the prenatal diagnosis may be a stronger prognostic parameter than the postnatal NG tube position, while the ability to predict actual stomach herniation at surgery did not differ markedly between these factors.

Advantages of this finding include the rapid collection of data on CDH without a prenatal diagnosis and support in making decisions concerning the operative strategy. The proportion of prenatally diagnosed CDH patients depends on the perinatal screening system and healthcare services provided by the health insurance system in a given country and the country's economic status. There is evidence that lower-income countries have lower rates of prenatal diagnoses and poorer outcomes of CDH neonates than wealthier countries [20]. NG tube insertion is routinely performed in CDH treatment, so this simple and fast evaluation of the NG tube position may be able to provide reliable information on the disease severity and prognosis of postnatally diagnosed CDH in lower-income countries.

When physicians must brief a family on a patients' prognosis even if a prenatal diagnosis is available, the faster the prognostic information can be obtained, the more effectively the physician will be able to build credibility between themselves and the family. The combination of prenatal diagnosis and postnatal factors is expected to provide us with more accurate information. Furthermore, the NG tube position in combination with other assessment variables, such as the prenatal stomach position, Kitano grade 0 and OI < 8, may indicate the suitability of thoracoscopic surgery, since an NG tube below the diaphragm may imply a small defect size, which suggests the ease of plicating the remnant of the diaphragm, and the NG tube below the diaphragm may imply high survival rates when the postnatal stomach below the diaphragm corresponds with the prenatal stomach position below the diaphragm.

Several limitations associated with the present study warrant mention. First, the NG tube position was not always consistent with the prenatal stomach position. This inconsistency may be due to the transition of the stomach or technical bias in the insertion of the NG tube. To reduce such inconsistency, we performed a subgroup analysis focusing on CDH patients in whom the prenatal and postnatal stomach position corresponded with each other precisely. Results showed that there were still significant differences in the outcomes between the BD and AD groups. Furthermore, this subgroup analysis clarified the concordance
rate of the prenatal and postnatal NG tube positions. The BD group was more susceptible to stomach transition than the AD group, so the concordance rate was lower than that of the AD group. Because most of the postnatally diagnosed CDH neonates had a sudden onset with a small defect size, stomach flip-up may have occurred even after birth, due to the increased abdominal pressure and negative intrathoracic pressure. In addition, the numbers of severe CDH patients were naturally low, which corresponded with the higher concordance rate and worse outcome in the AD group. Second, this study involved a multicenter database, so the accuracy of the prenatal diagnosis may have been biased. Third, some patients were enrolled before we implemented our standardized treatment protocol in 2017. Therefore, the indication of iNO and ECMO and the timing of operation may have differed among patients. Also, revision of our standardized protocol in future may be necessary to reduce the technical errors of NG tube insertion, because how to manipulate NG tube insertion has not yet discussed in our standardized protocol.

In conclusion, this study revealed that the position of the tip of the NG tube at postnatal X-ray was correlated with the mortality and morbidity and that the tip of the NG tube in the abdominal cavity was an independent predictive factor for the 90-day survival among postnatal variables. The assessment of the position of the NG tube via X-ray promptly after birth was very simple to perform and did not require a prenatal diagnosis. This approach is expected to be useful for patients who are not diagnosed prenatally or who are born in hospitals where imaging studies are difficult to perform.

**Abbreviations**

CDH, congenital diaphragmatic hernia; NG, nasogastric; BD, below diaphragm; AD, above diaphragm; LHR, lung area-to-head circumference ratio; o/eLHR, observed/expected lung area-to-head circumference ratio; LTR, lung-to-thorax transverse ratio; OI, oxygenation index; iNO, inhaled nitric oxide; ECMO, extracorporeal membrane oxygenation; OR, odds ratio; CI, confidence interval

**Declarations**

**Acknowledgement:** We thank Brian Quinn for English language editing. We also thank all members of the Japanese CDHSG for their commitments to CDH research.

**Authors’ contribution:** K.N. designed the study and, J.K. analyzed the data, and wrote the draft on the manuscript. K.T., S.A., K.T., N.I., Y.K., M.Y., T.O., Y.Y., H.O., M.H., T.F., K.M. A.Y., N.U. contributed to the data collection, data cleaning, interpretation. K.T., K.T., H.O., N.U., and T.T. critically reviewed this manuscript. The final version of the manuscript was approved by all authors.

**Funding:** This work was supported by a grant from the Ministry of Health, Labour and Welfare of Japan (Program Grant Number 20FC1017).
Conflict of interest: The authors have no conflicts of interest to disclose

Ethical approval: This study was approved by the ethics committee of Kyushu University (Ethical approval number 2020-759) and an institutional review board of all participating institutions.

Code availability: The datasets in this study are available from the corresponding author upon reasonable request.

References


Figure 1  flow chart of patients selection

Enrollment chart of patients in the Japanese CDH study group
Figure 2

The Kaplan–Meier analysis for recurrence

Supplementary Files

This is a list of supplementary files associated with this preprint. Click to download.

- 36Supplementarytable1.docx
- 37Supplementarytable2.docx