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ORIGINAL ARTICLE

Analysis of risk factors of long-term complications in congenital diaphragmatic hernia: A single institution's experience

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Summary *Objective:* To establish better management practices to reduce morbidities in survivors with congenital diaphragmatic hernia (CDH).
Methods: Of 60 patients treated for CDH at our institution between 1991 and 2011, 49 patients without severe anomalies were retrospectively reviewed.
Results: Since 2004, gentle ventilation (GV) has been the main treatment for CDH. Patients were divided into the following two groups: the non-GV group ($n = 29$) who were treated before GV treatment was implemented, and the GV group ($n = 20$). The overall survival rate was 62.1% (18/29) and 95% (19/20) in the non-GV and GV groups, respectively ($p = 0.016$). Despite the high survival rate, the incidence of long-term complications in survivors was still high (14/19, 73.7%) in the GV group. In the GV group, liver-up ($p = 0.106$) and the need for patch repair ($p = 0.257$) tended to be associated with the development of long-term complications, but did not reach statistical significance. The presence of perioperative complications was associated with the development of long-term complications ($p = 0.045$) in the GV group.
Conclusion: Patients who developed short-term complications seemed to be at risk of long-term complications. Therefore, to minimize long-term morbidities in CDH survivors, the prevention of short-term complications might be important.

Conflicts of interest: The authors declare no conflicts of interest associated with this manuscript.

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1. Introduction

Congenital diaphragmatic hernia (CDH) is one of the most challenging anomalies faced by pediatric surgeons and neonatologists. Recently, especially over the past 2 decades, many innovative techniques, including high-frequency oscillation (HFO), inhaled nitric oxide, extracorporeal membrane oxygenation, and gentle ventilation (GV), have been introduced as suitable options for CDH treatment.[1–5] In addition, prenatal diagnosis has also contributed to improvement in the outcome of CDH.[2,3] Currently, reports from a number of highly qualified centers show remarkable improvement in the survival rates, reported to be as high as 80%.[1,5,6] By contrast, in follow-up studies of infants with CDH, many complications, such as pulmonary damage, cardiovascular diseases, gastrointestinal diseases, failure to thrive, neurocognitive defects, and musculoskeletal abnormalities, have been described.[7–12] With improved management of infants with CDH, there has been an increase in morbidities among long-term survivors. Thus, we must now concentrate not only on the survival of infants with CDH but also on morbidities in surviving patients. Although some reports have addressed the issue of long-term outcomes for CDH survivors,[7–11,13–16] the variations in patient populations, management, and length of follow up make it difficult to draw firm conclusions about the quality of life of these patients. The aim of this study is to show the long-term functional impact of CDH repair on the survivors in a single-institution cohort of newborns over a 20-year period.

2. Methods

A retrospective chart review was conducted on isolated prenatally diagnosed CDH patients born during the period between 1991 and 2011. Inclusion criteria were the presence of a CDH without associated life-threatening or chromosomal anomalies. From 2004 to the present, a combination of GV and a delayed operation was the main treatment after birth. GV was performed based on the protocol presented by one of the study authors.[4] The patient was intubated just after birth. The initial settings of HFO were as follows: frequency, 15 Hz; mean airway pressure, 15 cmH_2O; stroke volume, 15 mL; and inspired O_2 fraction (FiO_2), 1.0. The pre-SpO_2 (saturation of peripheral oxygen) was maintained at $>$90% and the pre-$PaCO_2$ (pressure of arterial carbon dioxide) was maintained at $<$65 mmHg. In addition, the pre-PaO_2 (pressure of arterial oxygen) was maintained above 60 mmHg, if possible.

Liver position was determined at the time of surgery. A systematic review was conducted including the following data: gestational age at diagnosis, position of the liver, postnatal treatment, need for patch repair, duration of ventilation, perioperative complications, long-term complications, and survival. Liver position is considered to be "up" if any portion of the liver is in the chest above the normal level of the diaphragm, and "down" if it is completely within the abdomen. Major morbidities at discharge included the need for respiratory support (supplemental oxygen, mechanical ventilation, and tracheostomy), nutritional support (tube feeding and parenteral nutrition), or circulatory support (use of vasodilators).

Statistical analysis was performed to assess the patients' backgrounds in the non-GV and GV groups using the Wilcoxon signed-rank test and Fisher exact test. Univariate analyses were also performed for comparison of the outcomes in the non-GV and GV groups using the Wilcoxon signed-rank test and Fisher exact test. A p value <0.05 was defined as significant. The values are expressed as the mean $\pm$ standard deviation. This study design was approved by the Ethical Committee of our university.

3. Results

We retrospectively reviewed 60 neonates with CDH treated at our institution from 1991 to 2011. Of these neonates, one who became symptomatic more than 24 hours after birth, and 10 with fatal anomalies were excluded, leaving 49 patients for review in this study. The patients were divided into two groups, namely, the non-GV group ($n = 29$) who were treated before GV was implemented and the GV group ($n = 20$) who were treated after GV was implemented.

3.1. Survival

Table 1 shows the outcomes in both groups. The overall survival rate improved with GV treatment (non-GV group 62.1%, GV group 95%; $p = 0.016$). The 90-day survival rate also improved with GV treatment, but did not reach statistical significance (non-GV group 72.4%, GV group 95%; $p = 0.064$). In the non-GV group, eight patients died before 90 days of life. The causes of deaths were heart failure in four cases, severe persistent pulmonary hypertension in one case, pneumonia in one case, and diffuse intravascular coagulation in two cases. Six of these eight cases were outborn deliveries and two of them were already in a state of cardiopulmonary arrest when they arrived at our institution. Only one patient died in the GV group, due to catheter infection-related sepsis at 68 days of life after the surgery. There were three late death cases after 90 days of life in the non-GV group and are attributed to the following causes: pneumonia at 1 year of age, severe enteritis at 1 year of age, and tracheostomy trouble at 16 years of age. There were no late death cases in the GV group.

3.2. Perioperative and long-term complications

The perioperative and long-term complications in both groups are listed in Tables 2 and 3, respectively. The incidence of perioperative complications was 13/29 (44.8%) patients and 9/20 (45.0%) patients in the non-GV and GV groups, respectively. The incidence of long-term

Table 1 Outcome in study groups.

	Non-GV group	GV group	p
Overall survival	62.1 (18/29)	95.0 (19/20)	**0.016**
Survived at 90 d of birth	72.4 (21/29)	95.0 (19/20)	0.064

Values in bold indicate values with significant difference.
Data are presented as % (n).
GV = gentle ventilation.