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分担研究報告書

Outcomes of congenital diaphragmatic hernia among preterm infants: inverse probability of treatment weighting analysis

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研究要旨

日本の多施設研究のデータを用いて、CDH の重症度をマッチさせた早産児と満期産児の退院時の生存率と無傷生存率を評価した。その結果、CDH の早産児の退院時生存率および無傷生存率は、満期産児よりも有意に低かった。この結果は、胎児診断技術の発達、人工呼吸器や薬剤の進歩、外科的治療や術後管理を含む治療戦略の改善によるものと考えられた。

A. 研究目的

先天性横隔膜ヘルニア（CDH）を有する早産児の生存率と無傷生存率を評価すること。

B. 研究方法

日本の CDH 研究グループ 15 施設で 2006 年から 2020 年に出生した 849 例の多施設レトロスペクティブコホート研究。逆確率治療重み付け（IPTW）法で調整した多変量ロジスティック回帰分析を用いた。また、CDH の正期産児と早産児の無傷生存率の傾向を比較した。

C. 研究結果

CDH 重症度、性別、5 分後の APGAR スコア、帝王切開分娩について IPTW 法で調整した結果、妊娠月齢と生存率は有意に正の相関があり［決定係数（COEF）3.40、95%信頼区間（CI）1.58-5.21、p 値 <0.001］、無傷生存率は高かった［COEF 2.39、95%CI、1.73-4.06、p 値 0.005］。早産児と正期産児の無傷生存率の傾向は有意に変化していたが、早産児の改善は正期産児よりもはるかに小さかった。

D. 考察

本研究では、CDH を有する早産児は、CDH の重症度が一致していても、退院時の医療の必要性が高いことがわかった。

E. 結論

未熟児は、CDH 重症度の調整にかかわらず、CDH 児の生存率および無傷生存率の有意な危険因子であった。

F. 研究発表

1. 論文

Imanishi Y, Usui N, Furukawa T, Nagata K, Hayakawa M, Amari S, Yokoi A, Masumoto K, Yamoto M, Okazaki T, Inamura N, Toyoshima K, Terui K, Okuyama H. Outcomes of congenital diaphragmatic hernia among preterm infants: inverse probability of treatment weighting analysis. J Perinatol. 2023 Jul;43(7):884-888.

ARTICLE

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Outcomes of congenital diaphragmatic hernia among preterm infants: inverse probability of treatment weighting analysis

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OBJECTIVES: To evaluate the survival and intact-survival rates among preterm infants with congenital diaphragm hernia (CDH).
STUDY DESIGN: Multicenter retrospective cohort study of 849 infants born between 2006 and 2020 at 15 Japanese CDH study group facilities. Multivariate logistic regression analysis adjusted using inverse probability treatment weighting (IPTW) method was used. We also compare trends of intact-survival rates among term and preterm infants with CDH.
RESULTS: After adjusting using the IPTW method for CDH severity, sex, APGAR score at 5 min, and cesarean delivery, gestational age and survival rates have a significantly positive correlation [coefficient of determination (COEF) 3.40, 95% confidence interval (CI), 1.58–5.21, *p* value <0.001] and higher intact-survival rate [COEF 2.39, 95% CI, 1.73–4.06, *p* value 0.005]. Trends of intact-survival rates for both preterm and term infants had significantly changed, but improvement in preterm infants was much smaller than in term infants.
CONCLUSION: Prematurity was a significant risk factor for survival and intact-survival among infants with CDH, regardless of adjustment for CDH severity.

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INTRODUCTION

Congenital diaphragmatic hernia (CDH) is a fetal abnormality that occurs in 2.7–4.9 per 10,000 live births [1]. The pathophysiology of CDH is a diaphragmatic defect accompanied by complications, such as lung hypoplasia, pulmonary hypertension, and cardiac dysfunction which may occur and significantly affect a child's life [2]. Although the survival rate has improved dramatically over the years, owing to prenatal diagnosis and advances in various treatments [3–5], there are still several problems to be solved, including severe cases and complications.

Prematurity is an essential factor among the various factors that affect the prognosis of CDH. Preterm births have gotten worse for survival rates and newborn developmental outcomes. Survival rates for preterm births are improving worldwide, and as the survival rate increases, the proportion of children who require long-term medical care increases [6–9]. Although data in the U.S. showed that the prognosis for preterm CDH naturally improves with increasing weeks of gestation [10]; however, this is not the case in Japan.

It is unknown how many preterm infants with CDH will require medical care. Many cases have reported life expectancy; however, complications have not yet been reported. Preterm birth outcomes have improved over the years, but there are no data on changes over time. Additionally, these data do not account for disease severity, and the evidence is insufficient.

In this study, we hypothesized that preterm infants with CDH would have a lower survival rate and require additional medical care than term infants with CDH. The survival rate of preterm infants with CDH and extent of medical care needed at discharge were examined using the Inverse Probability treatment of Weighting (IPTW) method according to the severity of CDH.

MATERIALS AND METHODS

Study design and population

This multicenter, retrospective cohort study was conducted among infants with CDH born between 2006 and 2020 at 15 Japanese CDH study group facilities. The study enrolled 1037 infants with CDH registered in the Japanese CDH group database. Outborn infants, those receiving palliative care, and those with an unknown gestational age (GA) were excluded. We first excluded those who were outborn because of lack of markers to assess CDH severity, such as lung area to head circumference ratio (LHR) and liver-up. We also excluded patients who underwent fetal endoscopic

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