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# Clinical factors associated with in-hospital death in pediatric surgical patients admitted to the neonatal intensive care unit: a 15-year single tertiary center experience☆

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ABSTRACT

*Background/purpose:* The purpose of this study was to explore clinical characteristics and primary surgical diagnoses associated with in-hospital death in pediatric surgical patients admitted to the neonatal intensive care unit (NICU) of a tertiary hospital.
*Methods:* This retrospective study includes all patients admitted to our NICU for pediatric surgical diseases between January 2001 and December 2015. Univariate and multivariate binary logistic regression were performed to assess independent factors associated with in-hospital death.
*Results:* A total of 440 cases were included and 334 (83.5%) patients underwent one or more surgeries. Thirty six patients (8.2%) died while hospitalized in the NICU. The 5 most common surgical diagnoses were intestinal atresia/stenosis, anorectal malformation, congenital diaphragmatic hernia (CDH), esophageal atresia, and urinary system disorder. Necrotizing enterocolitis (NEC) had the highest mortality rate. Using logistic regression, in-hospital death was predicted by extremely low birth weight (ELBW) (odds ratio (OR) = 6.594; P = 0.006), CDH (OR = 13.954; P < 0.001), and NEC (OR = 8.991; P = 0.049).
*Conclusions:* This study describes CDH, NEC, and ELBW are independent predictive factors associated with in-hospital death of pediatric surgical patients in our NICU. Novel approaches for those conditions are required to improve the survival.
*Type of study:* Prognostic
*Levels of evidence:* II.



Pediatric surgery in Japan in the 1950s was far less advanced than in Western countries [1]. Since then, advances in perinatal and neonatal care have significantly reduced mortality rates of infants admitted to neonatal intensive care units (NICU(s)) [2]. The overall infant mortality rate has now decreased to less than 10% in Japan [1,3]. Advances in pediatric surgery, pediatric anesthesia, and neonatal physiology, technological advances allowing improved monitoring, advances in airway management and mechanical ventilation, the introduction of total parenteral nutrition, the discovery of antibiotics, and the establishment of NICUs are primarily responsible for the improvement in mortality [4]. Further risk identifications and improvements are necessary to further reduce the mortality rate.

Previous reports show that preterm birth, outborn status, congenital anomalies, and surgery are associated with mortality in NICUs [2,3,5]. Attempts to stratify risks for individual congenital disorders such as necrotizing enterocolitis (NEC), congenital diaphagmatic hernia (CDH), and gastroschisis have been described [6–9], and efforts have also been made to identify perioperative risk factors for major complications or death after pediatric surgery [10,11].

The purpose of this study was to explore the clinical factors associated with in-hospital death in pediatric surgical patients admitted to the NICU over 15 years in our hospital. Identifying clinical characteristics and primary surgical diagnoses might allow for more directed interventions in high risk patients and it might lead to reduced mortality in pediatric surgical patients admitted to the NICU.

☆ **Conflict of interest statement:** The authors report no conflicts of interest in the study design, collection, analysis and interpretation of data, writing of the report, and the decision to submit the paper for publication.

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## 1. Materials and methods

### 1.1. Study design

This was a retrospective chart review of all patients admitted to our NICU for pediatric surgical diseases between January 2001 and December 2015. The study population was not limited only to neonates, but also included older infants who remained hospitalized in the NICU. The study population included all infants hospitalized in the NICU with suspected non-cardiac surgical diseases. Patients were identified through our NICU hospitalization ledger of all non-cardiac surgical cases. Patients were followed until discharge or in-hospital death. The primary outcome was discharge or in-hospital death. This study was approved by the hospital institutional review board (#1608). Because of the young age of our patients, written informed consent was obtained from the patients' parents per the IRB ethical guidelines.

### 1.2. Study variables

Collected clinical characteristics included: gender, gestational age, birth weight, presence of prenatal diagnosis, location of delivery, mode of delivery, Apgar score at 1 min, presence of a chromosomal abnormality, presence of congenital heart disease, and whether the operation was emergent. The presence of congenital heart disease was defined as that requiring a pediatric cardiologist's evaluation and care while hospitalized in the NICU. The diagnoses were collected and categorized: intestinal atresia/stenosis, anorectal malformation, congenital diaphragmatic hernia, esophageal atresia, urinary system disorder, intestinal perforation, Hirschsprung disease, omphalocele, meconium-related intestinal obstruction, gastroschisis, gastroesophageal reflux disease, inguinal hernia, meconium peritonitis, ovarian cyst, necrotizing enterocolitis, hepatobiliary disorder, intestinal malrotation, hypertrophic pyloric stenosis, and others.

### 1.3. Data analysis

All statistical analyses were performed with SPSS version 22.0 software (IBM Corp., Armonk, NY, USA). Univariate and multivariate binary logistic regression were performed to assess independent factors associated with in-hospital death. Multivariate analysis included variables that yielded P values of 0.05 or lower in the univariate analysis. A P value of $<0.05$ was regarded as statistically significant.

## 2. Results

In total, 440 cases were included in this study. The clinical characteristics of the patients included in this study are summarized in Table 1. Chronological changes in the number of our patients or primary diagnoses were not observed over the study period. The male-to-female ratio was high, at 1.53-fold more males than females. Thirty extremely preterm (less than 28 weeks gestation) infants (6.8%) and 32 extremely low birth weight (ELBW) (<1000 g) infants (7.3%) were included. One hundred sixty-two patients were inborn and 278 patients were outborn. Three hundred thirty four patients (83.5%) got one or more operations and 82 patients (20.5%) underwent more than one operation. Emergent operations were performed in 179 patients (40.7%). Twenty-six patients (5.9%) had chromosomal abnormalities and 45 patients (10.2%) had congenital heart diseases. Thirty-six patients (8.2%) died while hospitalized in the NICU during the study period.

Primary diagnosis of the study patients is detailed in Table 2. Intestinal atresia/stenosis and anorectal malformation ranked first and second in our study. All NEC cases were surgical and NEC cases had the highest mortality rate (66%) in our study (Table 2). The group of "Other" included: 7 congenital pulumonary airway malformation cases, 7 stoma-associated complication cases, 7 lymphangioma cases, 5 ventilatory impairment cases who needed the creation of tracheostomy, 4 milk allergy cases, 4 tracheomalacia cases, 4 idiopathic small intestinal tortion, 4 idiopathic constipation cases, 2 ventriculoperitoneal shunt-related peritonitis cases, 2 teratoma cases, 2 neonatal melena cases, 2 umbilical cord cyst cases, 1 segmental intestinal dilatation case, 1 laryngotracheoesophageal cleft case, 1 aphallia case, 1 epididymitis case, 1 pyriform sinus fistula case, 1 perineal lipoma case, 1 intrahepatic portal vein aneurysm case, 1 interstitial emphysema case, 1 pneumothorax case, 1 subglottic stenosis case, 1 congenital central hypoventilation syndrome case and 1 pseudoexstrophy case.

Study variables listed in Table 1, the 5 most common surgical diagnoses and the diagnosis of NEC were subjected to univariate and multivariate logistic regression analyses to identify independent predictive factors associated with in-hospital death. On univariate analysis, extremely preterm birth, ELBW, cesarean delivery, a 1-min Apgar score less than 7, CDH, and NEC were found to be predictive factors associated with in-hospital death (Table 3). On multivariate analysis, CDH ($P < 0.001$; OR, 13.945; 95% CI, 5.114–38.078), NEC ($P = 0.049$; OR, 8.991; 95% CI, 1.005–80.475), and ELBW ($P = 0.006$; OR, 1.548; 95% CI, 0.384–6.239) were independent predictive factors associated with in-hospital death (Table 3).

## 3. Discussion

In this report, we analyzed the data obtained from a 15-year single-center experience beginning in 2001. Based on a nationwide Japanese surveillance program, the overall mortality rate in neonatal surgery ranged from 6.6% to 12% [3]. The mortality rate while hospitalized in

**Table 1**
Clinical characteristics of the patients.

| | Total (n = 440) |
|---|---|
| Gender (female/male) | 174/266 |
| Gestational age <28 weeks, n (%) | 30 (6.8) |
| Body weight <1000 g, n (%) | 32 (7.3) |
| Prenatal diagnosis, n (%) | 148 (33.6) |
| Outborn, n (%) | 278 (63.2) |
| Cesarean delivery, n (%) | 183 (41.6) |
| 1-min Apgar score less than 7, n (%) | 122 (27.7) |
| Chromosomal disorder, n (%) | 26 (5.9) |
| Congenital heart disease, n (%) | 45 (10.2) |
| Need for surgery, n (%) | 334 (83.5) |
| Need for more than one surgery, n (%) | 82 (20.5) |
| Emergent operation, n (%) | 179 (40.7) |
| In-hospital death, n (%) | 36 (8.2) |

**Table 2**
Primary diagnosis of the patients.

| | Total (n = 440) | In-hospital death n (%) | |
|---|---|---|---|
| **Intestinal atresia/stenosis** | **56** | **3** | **(5)** |
| **Anorectal malformation** | **53** | **0** | **(0)** |
| **Congenital diaphragmatic hernia** | **40** | **15** | **(38)** |
| **Esophageal atresia** | **29** | **2** | **(7)** |
| **Urinary system disorder** | **27** | **0** | **(0)** |
| Intestinal perforation | 24 | 6 | (25) |
| Hirschsprung disease | 19 | 1 | (5) |
| Omphalocele | 18 | 0 | (0) |
| Meconium-related intestinal obstruction | 16 | 4 | (25) |
| Gastroschisis | 15 | 0 | (0) |
| Gastroesophageal reflux disease | 13 | 0 | (0) |
| Meconium peritonitis | 11 | 0 | (0) |
| Inguinal hernia | 11 | 1 | (9) |
| Ovarian cyst | 7 | 0 | (0) |
| **Necrotizing enterocolitis** | **6** | **4** | **(67)** |
| Hepatobiliary disorder | 6 | 0 | (0) |
| Intestinal malrotation | 5 | 0 | (0) |
| Hypertrophic pyloric stenosis | 3 | 0 | (0) |
| Others | 81 | 0 | (0) |