



Necrotizing enterocolitis in patients with congenital heart disease: A single center experience

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ABSTRACT

Purpose: The purpose of this study was to evaluate the characteristics of patients with congenital heart disease (CHD) who developed necrotizing enterocolitis (NEC).

Methods: A retrospective review of neonates with CHD at a tertiary care center between January 2006 and January 2016 was performed. Diagnosis of NEC was based on modified Bell's criteria. Patients were grouped by Risk Adjustment for Congenital Heart Surgery (RACHS-1) or by ductal-dependent (DD) lesions that require a patent ductus arteriosus to supply pulmonary or systemic circulation.

Results: Of 1811 neonates with CHD, 3.4% (n = 61) developed NEC. Eighteen (30%) of these required surgical management. The rate of NEC among DD patients was 5% (n = 33/653), compared to 2.4% (n = 28/1158) in the non-DD group (p = 0.003). RACHS-1 score > 2 had a higher rate of NEC 6.2% (41/658) compared to RACHS-1 ≤ 2 cases, 1.7% (20/1153) (p = 0.005). DD patients and complex patients with RACHS-1 > 2 were more likely to develop NEC after cardiac surgery. Hypoplastic left heart syndrome patients had a rate of 9% (n = 16/185). Surgical NEC was more prevalent in the non-DD group. Mortality was similar among groups.

Conclusion: CHD patients with ductal-dependent lesions or complex cases (RACHS-1 score > 2) have higher rates of NEC than non-ductal-dependent patients or RACHS-1 score of 2 or less. Mortality is similar regardless of ductal dependence, but surgical NEC was more prevalent in non-DD patients.

Level of Evidence: Level IIb.

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Necrotizing enterocolitis (NEC) continues to be one of the most life-threatening conditions that affect neonates. Mortality rates of this condition can be as high as 20 to 30% in those for which surgical intervention is necessary [1]. Although the classic presentation of NEC is in premature infants born 29–32 weeks of gestation, there are forms of NEC that are prevalent in other neonatal populations. Term infants that develop NEC usually have other associated factors that predispose them to the disease such as low Apgar scores, prolonged rupture of membranes, exchange transfusions, neural tube defects and congenital heart disease (CHD) [2]. Patients with CHD have been reported to have a 3.3%–11% risk of developing NEC [3,4], which is much higher than other full term infants. The pathophysiology of NEC in CHD

patients is still unknown, but it is theorized that infants with CHD have lower diastolic pressures leading to lower bowel perfusion pressures and as well as lower systemic oxygenated blood flow, contributing to an overall state of bowel hypo-perfusion and ischemia [5–7].

There exists a broad spectrum of severity among patients with CHD. Patients who have ductal dependent (DD) CHD are at a higher risk of mesenteric hypo-perfusion and ischemia owing to a steal phenomenon [5,6]. One classification scheme that has been used to assess the severity of disease among CHD is the Risk Adjustment for Congenital Heart Surgery-1 (RACHS-1) score. RACHS-1 helps to create a better understanding of the mortality risk among those patients undergoing congenital heart surgery in a pediatric population. Patients with high RACHS-1 scores have life threatening CHD that will likely require surgical intervention in the immediate postnatal period. These patients are likely to also suffer from the aforementioned risks for NEC. The purpose of this study was to evaluate the characteristics of patients with CHD that

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develop necrotizing enterocolitis at a larger tertiary care institution. We hypothesized that patients with ductal-dependent lesions and RACHS-1 scores higher than 2 would have a higher incidence of NEC and a higher need for surgical intervention for NEC.

1. Methods

1.1. Inclusion criteria

The study was approved by Baylor College of Medicine's Institutional Review Board, Houston, Texas (H-34662).

A retrospective review of all neonates with CHD at Texas Children's Hospital from January 2006 to January 2016 was performed. Patients with CHD who were diagnosed with NEC were included in the study. NEC was defined using modified Bell's criteria which are based on clinical findings of abdominal distention, feeding intolerance, and standard radiographic findings including the presence of pneumatosis intestinalis, portal venous gas and/or pneumoperitoneum.

1.2. Data collection

Patients' medical records were reviewed for demographic data, gestational age at birth, birth weight, and types of cardiac anomalies. Cardiac anomalies were defined as anomalies other than patent ductus arteriosus or a patent foramen ovale. Patient's CHD was stratified by their Risk Adjustment for Congenital Heart Surgery (RACHS-1) or by the presence of Ductal-dependent (DD) lesions requiring the presence of a patent ductus arteriosus to supply pulmonary or systemic circulation. Clinical data such as the age of onset of NEC, the time of surgical repair for CHD, the amount of time on cardiac bypass, duration of aortic clamping, the rate of enteral feeds, presence of vasopressors, and need for transfusion the day of or prior to onset of NEC were collected. Outcomes of interest included stage of NEC, the need for surgical intervention for NEC, in-hospital mortality and length of hospital stay. Surgical NEC was defined as the need for placement of a bedside drain or exploratory laparotomy in a NEC patient. NEC totalis was defined as global bowel necrosis involving more than 80% of gastrointestinal tract at the time of exploratory laparotomy or autopsy.

1.3. Statistical analysis

IBM SPSS Package version 24 (IBM Corporation, Armonk, NY) was used for the statistical analysis in this study. Student-t test and Mann-Whitney U test were used for parametric and nonparametric continuous variables respectively. Categorical variables were analyzed using Chi-square analysis. A p-value less than 0.05 was considered statistically significant.

2. Results

2.1. Patient Demographics

A total of 1811 neonates with CHD were identified from January of 2006 to January 2016. Of these, 61 patients were found to have developed necrotizing enterocolitis (3.4%). Fifty-seven percent ($n = 35$) of the NEC patients were male. The average maternal age was 27 ± 6.75 years by the time of birth. The average gestational age at birth was 34 ± 4.68 weeks with an average birth weight 2034 ± 911 g. A total of 48 (79%) of the NEC patients were born at our institution. The median day of diagnosis of NEC was 25 (1–93) days of life. The overall survival in this cohort was 74% ($n = 45$). Most patients fit the description of modified Bell's stage II ($n = 26$, 43%), while there were 19 cases (31%) of NEC stage I and 16 (26%) of NEC stage III. NEC totalis was diagnosed in five patients and eighteen patients needed a surgical intervention for NEC. Of those patients that survived, their median length of stay was 80.5 (20–245) days.

Table 1

Type of cardiac disease.

Cardiac lesion	No. of patients (n = 61)
HLHS	16
Atrial Septal Defect	7
Ventricular Septal Defect	6
TGA	5
DORV	5
Coarctation of the aorta	3
Atrioventricular canal	3
Hypoplastic right ventricle	3
Truncus Arteriosus	2
ASD + VSD	2
Pulmonary atresia	2
Interrupted aortic arch	1
TAPVR	1
Coronary fistula	1
Aortic stenosis	1
Pulmonary stenosis	1
Shone Complex	1
Tetralogy of Fallot	1

Distribution of patients with various cardiac anomalies.

HLHS: Hypoplastic left heart syndrome, TGA: Transposition of the great arteries, DORV: Double outlet right ventricle, ASD: Atrial septal defect, VSD: ventricular septal defect, TAPVR: Total anomalous pulmonary venous return.

2.2. Cardiac characteristics

The categories of CHD with NEC in our study population are shown in Table 1. Patients with hypoplastic left heart syndrome (HLHS), comprised 26% ($n = 16$) of the study group. The overall rate of NEC among HLHS patients during this study period was 9% ($n = 16/185$). Patients with NEC totalis had the diagnosis of: hypoplastic right ventricle ($n = 1$), HLHS ($n = 1$), DORV with TGA ($n = 1$), VSD with ASD ($n = 1$) and DORV ($n = 1$).

Of the patients with ductal dependent lesions, 33 had NEC, giving an incidence of NEC of 5% ($n = 33/653$), compared to 2.4% ($n = 28/1158$) with non-DD lesions ($p = 0.003$). No difference was appreciated in maternal age and gender of the patients with DD and non-DD lesions. However, patients who had non-DD lesions were significantly more premature and had smaller birth weights than those with DD lesions, (Table 2). Patients with non-DD and DD lesions developed NEC after 3 weeks of life. Most of the patients with DD lesions developed NEC after surgery. There was no difference in the bypass time and aortic clamp time among these two groups. The rate of surgical NEC was much higher among patients with non-DD lesions (46% vs 15%, $p = 0.011$), although there was no difference between the mortality among these groups.

While organizing the data by the complexity operation using RACHS-1 scores, patients with scores >2 had a higher rate of NEC 6.2% ($n = 41/658$) compared to RACHS-1 ≤ 2 cases, 1.7% (20/1153) ($p = 0.005$). Patients with RACHS-1 ≤ 2 were more premature and had lower birth weights compared to the more complex counterparts (Table 2). The age at the diagnosis of NEC was not significantly different among these two groups but those with higher scores had a median age of diagnosis 10 days later compared to those with lower scores. No patients developed NEC after cardiac surgery in those patients with RACHS-1 ≤ 2 . There was no difference in the rate of surgical NEC despite differences in RACHS-1 scores, as well as no difference in mortality.

While looking at other characteristics among these patients, majority of the patients were on enteral feeds at the time of the diagnosis of NEC (82% in non-DD group and 91% in DD group, $p = 0.59$). Those with DD lesions were more likely to be on full enteral feeds by the time of diagnosis compared to the non-DD patients (Table 3). No differences were observed in the rate of feeds, the presence of parenteral nutrition (TPN), the need for vasopressors and for blood transfusion at the time of diagnosis of NEC. The overall length of hospital stay for those who survived was also similar among groups, with those with

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