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Original article

Predictors of prognosis in neonates with congenital diaphragmatic hernia: experience of 12 years

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Abstract

Introduction: Congenital diaphragmatic hernia (CDH) is a severe malformation, displaying relevant mortality and morbidity rates in newborns.

Aim: To characterize clinically and demographically all neonatal cases of CDH admitted to a level III Neonatal Intensive Care Unit during a 12-year period and to evaluate the predictive value of baseline characteristics on mortality and morbidity at discharge.

Methods: Maternal/infant clinical and electronic records were retrospectively reviewed. All neonates with posterolateral CDH admitted between January 2003 and December 2014 were included.

Results: Fifty-three newborns were included. Overall mortality during hospitalization was 22/53 (41.5%). Clinical characteristics associated with mortality were the presence of intrathoracic liver ($p = 0.005$), intrathoracic stomach ($p = 0.015$), elevated arterial pCO_2 or lower pH values at admission (respectively, $p = 0.001$ and $p < 0.001$), pre-ductal oxygen saturation < 85% at admission ($p = 0.012$) and surgical repair with prosthetic patch ($p = 0.041$). Morbidity at discharge was reported in 7 (22.6%) survivors. Stomach herniation and sepsis were associated with higher morbidity (respectively, $p = 0.012$ and $p = 0.029$). In a logistic regression, patch repair was the only variable with predictive value for death during hospitalization, with an odds ratio (OR) of 15 (95% CI 0.98-228.9), and intrathoracic stomach was a predictor of morbidity at discharge (OR = 15.7, 95% CI 1.4-174.2).

Conclusion: Structural characteristics, namely defect size and presence of intrathoracic stomach, remain the primary determinants of neonatal prognosis in CDH. Although post-natal approaches have progressively proven their value in increasing survival and improving management of high-risk cases, future researches should continue focusing on the definition of

foetal anatomical markers of severity and prenatal treatment of CDH.

Keywords

Congenital diaphragmatic hernia, congenital abnormality, newborn infant, prognosis, mortality, morbidity.

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Introduction

Congenital diaphragmatic hernia (CDH) is characterized by the passage of abdominal viscera into the thorax, due to a defective embryological development of the diaphragm [1, 2].

This fetal anomaly affects from 1.7 to 5.7 per 10,000 live births [3]. Herniation of the posterolateral area (Bochdalek hernia) of the left hemidiaphragm constitutes 85-90% of cases [4]. Anterior (Morgagni hernia) and central diaphragmatic regions are less frequently involved and are associated with a distinct genetic and embryologic background [5, 6]. A serous membrane acting as a herniation sac is also an uncommon feature [2, 4]. Diaphragmatic eventration, described as a cephalic dislocation of the diaphragm, is a congenital abnormality that should be differentiated from CDH since it does not share the same pathogenic mechanisms [3].

The displacement of abdominal structures into the thoracic cavity does not allow a normal development of alveoli and pulmonary vasculature [7]. These mechanical limitations, associated with reduced airway pressure in the fetal stage, ultimately lead to hypoplasic lungs and pulmonary hypertension [3].

Other malformations, syndromic or chromosomal anomalies are concomitant with CDH in 10% to 50% of patients [8]. Congenital heart disease can be found in one third of cases [2].

In the past two decades, encouraging results were reported in CDH post-natal management approaches such as inhaled nitric oxide (iNO), sildenafil, high frequency oscillatory ventilation and extracorporeal membrane oxygenation, when applied in selected cases [3]. Nevertheless, CDH remains a complex and severe entity in neonatal intensive care units (NICU), displaying over-all mortality rates of 30% to 50% and relevant morbidity at discharge [8].

The aims of the following study were to clinically and demographically characterize all neonatal cases of posterolateral CDH admitted in our NICU during a 12-year period and to evaluate the predictive value of baseline characteristics on mortality and morbidity at discharge.

Materials and methods

Patients

Neonates with posterolateral CDH admitted to the NICU of "Centro Hospitalar São João" between January 2003 and December 2014 were included in the study. The NICU of "Centro Hospitalar São João" is a Portuguese level III unit. Patients with diaphragmatic eventration (6 cases) or with anterior/central CDH (5 cases) were excluded from this study.

Research design

The authors conducted a retrospective review of accessible maternal/infant clinical and electronic records, in order to analyze prenatal, demographic and clinical characteristics and to describe medical/surgical treatments during hospitalization and preoperative/postoperative complications on the NICU. The authors defined mortality during hospitalization and morbidity at discharge as objective endpoints.

Variables

Diagnosis and laterality of CDH was confirmed by postnatal chest radiography. Data from surgical descriptions and post-mortem records of non-operated newborns was privileged over imaging reports when determining which abdominal organs were dislocated into the chest. Hernia location and the presence of herniation sac were referred on surgical and post-mortem descriptions.

Major congenital anomalies were defined as abnormalities with relevant impairment of function

and quality of life or that require specific surgical/medical intervention [9]. Chromosomopathies were evaluated by amniocentesis, chorionic villus sampling or postnatal karyotyping. Newborns underwent echocardiography to detect and evaluate congenital heart disease and pulmonary hypertension. Pulmonary artery pressure estimation was based on the gradient between the right ventricle and atrium, through tricuspid regurgitation (assuming the right atrium pressure as 15 mmHg) [10, 11]. Classification of congenital heart disease was divided in pathophysiological categories according to Thiene et al. [12].

Since 2003, a new post-natal management protocol has been used in all patients admitted with CDH in our center. Guidelines include elective intubation, permissive hypercapnia, total daily water intake of 80 ml/kg until enteral feeds with a perfusion of dopamine of 5 mcg/kg/min until after surgery, a policy of delayed surgery after preoperative stabilization and sedation with or without paralysis. High frequency oscillatory ventilation was used as a rescue modality in cases of refractory hypoxia and/or hypercapnia. iNO was administered after echocardiography and if the oxygenation index (mean airway pressure x fraction of inspired oxygen x 100/partial arterial pressure of oxygen) was over 20. Sildenafil was indicated in iNO-refractory pulmonary hypertension. A perfusion of dobutamine 5 mcg/kg/min was performed if there were signs of myocardial dysfunction at echocardiographic assessment [10, 11]. Extracorporeal membrane oxygenation was primarily used in our unit in 2010, according to recommendations of the CDH EURO Consortium Consensus [13, 14].

CDH was surgically approached by invasive techniques – abdominal laparotomy or thoracotomy – or minimally invasive surgery – thoracoscopy. Invasive abdominal approach was accessible through right subcostal or median supra-umbilical incisions. A prosthetic patch (GORE-TEX®) was applied in larger hernias [15].

Concerning complications during NICU stay, hydrothorax was confirmed by chest ultrasound. Proven neonatal sepsis was defined as any systemic infection documented by a positive blood culture [16]. Chylothorax was defined according to the criteria proposed by Buttiker et al. and gastro-esophageal reflux disease according to Vandenplas et al. [17, 18]. Pulmonary hypertension was categorized as "severe" when pulmonary artery pressure was higher than 60 mmHg [10, 11]. The grade of intraventricular haemorrhage was based on the presence of ventricular dilatation (grade III) and parenchymal involvement (grade IV) in cranial ultrasounds [16]. Cystic periventricular leukomalacia was diagnosed when hypoechoic cysts were detected in the periventricular white matter [16].

Patients with morbidity at discharge (respiratory and/or gastrointestinal impairment) included those discharged on oxygen supply and/or pharmacological treatment for gastro-esophageal reflux disease (ranitidine, domperidone) and/or pulmonary hypertension (sildenafil).

Ethics

This study was approved by the Ethics Committee of our institution.

Statistical analysis

Data collection and statistical analysis were performed using IBM SPSS® statistics 23. Categorical variables were described as absolute and relative frequencies, continuous variables with symmetric distribution by mean (± standard deviation) and continuous variables with asymmetric distribution by median (minimum-maximum). Chi-square or Fisher's exact test were applied to compare categorical variables and Independent t test and Mann-Whitney U test were used for symmetric and asymmetric continuous variables, respectively. A multivariate analysis by logistic regression was performed to evaluate predictors. A p-value < 0.05 was considered statistically significant.

Results

A total of 53 neonates with posterolateral CDH were admitted during the selected 12-year period of study. Thirty-nine (73.6%) had prenatally been diagnosed with CDH, mostly on the third trimester. Postnatal diagnosis generally occurred after immediate postpartum respiratory distress. General characteristics of the study population are summarized in **Tab. 1**.

All newborns were mechanically ventilated and supplied with oxygen during hospitalization. In 13 (24.5%) cases, an exchange from conventional mechanical modes to high frequency oscillatory ventilation was necessary, mainly due to refractory hypoxia and hypercapnia. An isolated dose of exogenous surfactant was given to 5 (9.4%)

Table 1. General characteristics of the study population.

	n = 53
DEMOGRAPHIC AND PRENATAL CHARACTERISTICS	
Male, n (%)	29 (54.7)
Maternal age (years), mean (± SD)	30.17 ± 5.8
Multiple pregnancy, n (%)	1 (1.9)
Antenatal steroids, n (%)	7 (13.2)
Tracheal plug, n (%)	3 (5.7)
BIRTH AND NEONATAL PERIOD	
C-section, n (%)	40 (75.5)
Endotracheal tube, n (%)	44 (83)
Severe pulmonary hypertension (PAP > 60 mmHg), n (%)	23 (46.9)
Chromosomal anomaly, n (%) [a]	1 (1.9)
NICU MANAGEMENT	
Conventional mechanical ventilation (days), median (min-max)	8 (1-121)
High frequency oscillatory ventilation, n (%)	13 (24.5)
Days, median (min-max)	3.5 (1-16)
Oxygen supply (days), median (min-max)	9 (1-167)
Extracorporeal membrane oxygenation, n (%)	2 (3.8)
Days, median (min-max)	12 (7-17)
Exogenous surfactant, n (%)	5 (9.4)
Inotropic support, n (%)	37 (69.8)
Days, median (min-max)	6 (1-65)
Inhaled nitric oxide, n (%)	22 (41.5)
Days, median (min-max)	9 (2-120)
Sildenafil, n (%)	13 (24.5)
Days, median (min-max)	32 (1-150)
Need for paralysis during sedation, n (%)	15 (28.3)
Total parenteral nutrition, n (%)	43 (81.1)
Days, median (min-max)	13 (2-121)
NICU stay (days), median (min-max)	16 (1-167)
SURGERY	
Operated patients, n (%)	41 (77.4)
Age at surgery (days), median (min-max)	4 (2-42)
Preoperative stabilization (days), median (min-max)	3 (1-41)
Surgical technique	
Abdominal laparotomy, n (%)	28 (68.3)
Thoracotomy, n (%)	5 (12.2)
Thoracoscopy, n (%)	8 (19.5)

PAP: pulmonary arterial pressure; NICU: neonatal intensive care unit.
[a] Trisomy 18 (47 XX, +18), postnatal diagnosis.

preterm newborns during the first hour of life. Extracorporeal membrane oxygenation was used in 2 (3.8%) neonates who died during NICU hospitalization.

All survivors were operated. Preoperative complications included 4 (7.5%) cases of pneumothorax and 2 (3.8%) cases of sepsis. The remaining complications were developed after surgery and hydrothorax was the most frequent postoperative condition (31.7%). Six (11.3%) patients required phenobarbital or oral morphine for opioid withdrawal syndrome. We also reported 1 (1.9%) case of in-hospital recurrence of hernia which was preceded by a thoracoscopy.

Results from a univariate analysis for in-hospital mortality are displayed in **Tab. 2**. Overall mortality during NICU stay was 22/53 (41.5%). Death occurred at a median age of 4 days. Twelve (54.5%) patients died before surgery. No intraoperative deaths were reported. Twelve (54.5%) non-survivors were submitted to necropsy examination and pneumonia was the main finding; it was identified in 8 (66.7%) autopsies and was followed by aspiration of meconium (33.3%), acute tubular necrosis (33.3%) and infant respiratory distress syndrome (33.3%).

Table 2. Comparison of clinical characteristics between survivors and non-survivors (univariate analysis).

	Total (n = 53)	Survivors (n = 31)	Non-survivors (n = 22)	p-value
Laterality, n (%)				
Right-sided hernia	10 (19.2)	4 (12.9)	6 (28.6)	0.282[a]
Left-sided hernia	42 (80.8)	27 (87.1)	15 (71.4)	0.282[a]
Hernia contents, n (%)				
Bowel	48 (92.3)	29 (93.5)	19 (90.5)	> 0.999[a]
Spleen	35 (71.4)	21 (67.7)	14 (77.8)	0.453[b]
Stomach	29 (55.8)	13 (41.9)	16 (76.2)	**0.015**[b]
Liver and gallbladder	24 (52.2)	10 (35.7)	14 (77.8)	**0.005**[b]
Pancreas	4 (7.8)	1 (3.2)	3 (15)	0.287[a]
Kidney	1 (2)	1 (3.2)	0 (0)	> 0.999[a]
Coexisting major anomalies[e], n (%)	11 (20.8)	4 (12.9)	7 (31.8)	0.168[a]
Congenital heart disease	7 (63.6)	2 (50)	5 (71.4)	0.576[a]
Ventricular septal defect with right-to-left shunt	5 (71.4)	1 (50)	4 (80)	> 0.999[a]
Ventricular septal defect with left-to-right shunt	2 (28.6)	1 (50)	1 (20)	> 0.999[a]
Prenatal diagnosis, n (%)	39 (73.6)	20 (64.5)	19 (86.4)	0.075[b]
Gestational age (weeks), median (min-max)	27.5 (19-39)	28.5 (19-39)	24 (19-38)	0.218[d]
Polyhydramnios, n (%)	16 (30.2)	10 (32.3)	6 (27.3)	0.697[b]
Outborn, n (%)	11 (20.8)	8 (25.8)	3 (13.6)	0.327[a]
Gestational age at birth (weeks) median (min-max)	38 (29-40)	38 (32-40)	38 (29-40)	0.335[d]
Birth weight (grams), median (min-max)	2,820 (880-3,770)	2,900 (1,680-3,725)	2,724 (880-3,770)	0.125[d]
Apgar score, n (%)				
1st min: < 7	24 (45.3)	11 (35.5)	13 (59.1)	0.089[b]
5th min: < 7	12 (22.6)	5 (16.1)	7 (31.8)	0.202[a]
ABG at admission, median (min-max)				
pO_2 (mmHg)	65 (12-200)	65 (12-200)	54.5 (26-149)	0.242[d]
pCO_2 (mmHg)	58 (13-120)	48 (29-74)	66 (13-120)	**0.001**[d]
HCO_3^- (mmHg)	22 (6-31)	24 (15-31)	22 (6-28)	0.166[d]
pH	7.25 (6.50-7.47)	7.31 (7.04-7.42)	7.16 (6.50-7.47)	**< 0.001**[d]
Pre-ductal SaO_2 at admission (%), median (min-max)	95.5 (44-100)	97 (52-100)	89 (44-100)	**0.012**[d]
Surgically confirmed herniation sac, n (%)	10 (25)	7 (23.3)	3 (30)	0.689[a]
Patch repair, n (%)	12 (30)	6 (20)	6 (60)	**0.041**[a]
Hydrothorax during hospitalization, n (%)	13 (24.5)	10 (32.3)	3 (13.6)	0.121[b]
Pneumothorax during hospitalization, n (%)	11 (20.8)	5 (16.1)	6 (27.3)	0.493[a]
Sepsis during hospitalization, n (%)	9 (17)	7 (22.6)	2 (9.1)	0.277[a]
Chylothorax during hospitalization, n (%)	5 (9.4)	3 (9.7)	2 (9.1)	> 0.999[a]
Intraventricular hemorrhage ≥ III, n (%)	4 (9.3)	1 (3.3)	3 (23.1)	0.075[a]
Cystic periventricular leukomalacia, n (%)	1 (2.3)	0 (0)	1 (7.7)	0.302[a]

NICU: neonatal intensive care unit; ABG: arterial blood gas.
[a]Fisher's exact test; [b]Chi-square test; [c]Independent t test; [d]Mann-Whitney U test.
[e]Congenital heart disease (7), cystic hygroma (1), cleft palate (1), polydactyly (1), ambiguous genitalia (1).

Thirty-one (58.5%) patients were alive at discharge: 19 (61.3%) had domiciliary discharge, 3 (9.7%) were transferred to another institution and 9 (29%) were hospitalized in CHSJ Pediatric Unit. Morbidity at discharge was reported in 7 (22.6%) patients. Five (16.1%) survivors were discharged on domiciliary oxygen. Three (9.7%) survivors developed gastro-esophageal reflux disease during hospitalization and were discharged on anti-reflux medication. We reported 1 case of recurrent vomiting with desaturation and weight loss, 1 patient with esophagitis and 1 case requiring Nissen fundoplication and surgical repair for paraesophageal hernia. Intrathoracic stomach was observed in all cases of gastro-esophageal reflux disease ($p = 0.238$). One (3.2%) infant was discharged on sildenafil for pulmonary hypertension developed during NICU stay. A comparison between patients with and without morbidity at discharge was performed (**Tab. 3**). Stomach herniation and sepsis during hospitalization were significantly associated with higher morbidity at discharge (respectively, $p = 0.012$ and $p = 0.029$).

Finally, a logistic regression was performed and surgical repair with prosthetic patch was the only factor with a predictive value for death during NICU stay, with an odds ratio (OR) of 15 (95%CI 0.98-228.9). Intrathoracic stomach was a predictor of morbidity at discharge (OR = 15.7, 95%CI 1.4-174.2).

Discussion

According to several series, presence of liver herniation is one of the strongest independent predictors of mortality in CDH [19-22]; that notion was reinforced recently by two meta-analyses [23, 24]. A significant association between death and liver herniation was observed in our study, however this was not supported by logistic regression.

This study also revealed a prognostic association between stomach displacement and either mortality or morbidity at discharge, which is equally supported by current papers [21, 25, 26]. One of our major findings was that intrathoracic stomach is an independent predictor of morbidity at discharge. This was not unexpected as the presence of this abdominal organ in the thorax was probably responsible for the development of gastro-esophageal reflux disease [27].

Sepsis during hospitalization was also associated with morbidity at discharge, although it is more likely that neonatal infections were a consequence of long periods of oxygen supply and anti-reflux medication (particularly ranitidine) rather than a cause of respiratory and gastrointestinal morbidity [28, 29].

Elevated arterial pCO_2, lower pH values and pre-ductal oxygen saturation < 85% at admission were significantly associated with mortality, as it would be expected due to ventilation-oxygenation disturbances before stabilization [30].

In our study, a significant correlation between mortality and patch repair was also reported. Previous studies stated that presence of patch was an independent predictor of mortality, gastro-esophageal reflux disease and oxygen supply at discharge [15]. Even though corrective surgery with patch was not associated with morbidity at discharge in our study, it had predictive value for death during hospitalization, probably due to the fact that use of a prosthetic patch is an indirect marker of defect size [15].

A tendency for poorer prognosis in right congenital diaphragmatic hernias (RCDH) was observed, even though these results were not statistically significant ($p = 0.282$); this tendency can be explained by liver herniation observed in all RCDH cases. A meta-analysis published in 2000 (including 51 studies and 2,980 patients) revealed significantly increased mortality rates in RCDH and these results were similar to those obtained by Mayer et al. in 2011 (meta-analysis of 90 studies with 602 fetuses), that correlated prenatally assessed left-sided hernias (LCDH) with survival [23, 31]. However, the most recent retrospective and prospective works with large sample sizes (reaching 498 cases) failed to show a significant difference on mortality or oxygen-dependency at discharge between RCDH and LCDH [32-34].

Presence of other major malformations or congenital heart disease were not associated with mortality, contrarily to what has been published in several retrospective reviews and meta-analysis [31, 35-38]. However, it is remarkable that: i) in a CDH study group report with 3,100 patients, differences in concomitant severe cardiac anomalies between survivors and non-survivors were not significant; ii) a recent prospective study showed a significant association between mortality and complex cardiac abnormalities, but this lost significance in milder cases; iii) in a more recently published study, the presence of additional anomalies was not independently correlated with survival [34, 39, 40].

Concerning prenatal diagnosis, a recent study from 2015 revealed the importance of gestational

Table 3. Morbidity at discharge in survivors (n = 31).

	Survivors (n = 31)	Morbidity at discharge		p-value
		Without morbidity (n = 24)	With morbidity (n = 7)	
Laterality, n (%)				
Right-sided hernia	4 (12.9)	3 (12.5)	1 (14.3)	> 0.999[a]
Left-sided hernia	27 (87.1)	21 (87.5)	6 (85.7)	> 0.999[a]
Hernia contents, n (%)				
Bowel	29 (93.5)	23 (95.8)	6 (85.7)	0.406[a]
Spleen	21 (67.7)	15 (62.5)	6 (85.7)	0.379[a]
Stomach	13 (41.9)	7 (29.2)	6 (85.7)	**0.012**[a]
Liver and gallbladder	10 (35.7)	7 (33.3)	3 (42.9)	0.674[a]
Pancreas	1 (3.2)	0 (0)	1 (14.3)	0.226[a]
Kidney	1 (3.2)	1 (4.2)	0 (0)	> 0.999[a]
Coexisting major anomalies[e], n (%)	4 (12.9)	2 (8.3)	2 (28.6)	0.212[a]
Congenital heart disease	2 (50)	0 (0)	2 (100)	0.333[a]
Ventricular septal defect with right-to-left shunt	1 (50)	0 (0)	1 (50)	-
Ventricular septal defect with left-to-right shunt	1 (50)	0 (0)	1 (50)	-
Prenatal diagnosis, n (%)	20 (64.5)	14 (58.3)	6 (85.7)	0.372[a]
Gestational age (weeks), median (min-max)	28.5 (19-39)	29.5 (19-39)	26.5 (22-30)	0.321[d]
Polyhydramnios, n (%)	10 (32.3)	8 (33.3)	2 (28.6)	> 0.999[a]
Outborn, n (%)	8 (25.8)	7 (29.2)	1 (14.3)	0.642[a]
Gestational age at birth (weeks) median (min-max)	38 (32-40)	38 (32-40)	39 (35-39)	0.662[d]
Birth weight (grams), median (min-max)	2,900 (1,680-3,725)	2,880 (1,680-3,725)	2,930 (2,080-3,400)	0.906[d]
Apgar score, n (%)				
1st min: < 7	11 (35.5)	8 (33.3)	3 (42.9)	0.676[a]
5th min: < 7	5 (16.1)	4 (16.7)	1 (14.3)	> 0.999[a]
ABG at admission, median (min-max)				
pO_2 (mmHg)	65 (12-200)	71 (12-200)	51.5 (17-71)	0.106[d]
pCO_2 (mmHg)	48 (29-74)	44 (29-74)	51.4 (40-69)	0.395[d]
HCO_3^- (mmHg)	24 (15-31)	23.5 (15-31)	24.2 (21-25)	0.558[d]
pH	7.31 (7.04-7.42)	7.31 (7.04-7.42)	7.30 (7.15-7.32)	0.468[d]
Pre-ductal SaO_2 at admission (%), median (min-max)	97 (52-100)	97 (91-100)	74.5 (52-97)	0.288[d]
Surgically confirmed herniation sac, n (%)	7 (23.3)	5 (21.7)	2 (28.6)	> 0.999[a]
Patch repair, n (%)	6 (20)	3 (13)	3 (42.9)	0.120[a]
Hydrothorax during hospitalization, n (%)	10 (32.3)	6 (25)	4 (57.1)	0.172[a]
Pneumothorax during hospitalization, n (%)	5 (16.1)	2 (8.3)	3 (42.9)	0.062[a]
Sepsis during hospitalization, n (%)	7 (22.6)	3 (12.5)	4 (57.1)	**0.029**[a]
Chylothorax during hospitalization, n (%)	3 (9.7)	2 (8.3)	1 (14.3)	0.550[a]
Intraventricular hemorrhage ≥ III, n (%)	1 (3.3)	0 (0)	1 (14.3)	0.233[a]

ABG: arterial blood gas.
[a]Fisher's exact test. [b]Chi-square test. [c]Independent t test. [d]Mann-Whitney U test.
[e]Congenital heart disease (2), cleft palate (1), polydactyly (1).

age at diagnosis as a predictor for postnatal outcomes, since early diagnosis (probably due to abdominal organs that were already dislocated into the fetal chest at the beginning of gestation) was significantly associated with higher morbi-mortality rates [41]. Our study showed a tendency for poorer outcomes with earlier gestational age at diagnosis, however no significant association was reported (p = 0.335).

Outborns did not have prenatal diagnosis, except for 1 case that required extracorporeal membrane oxygenation in our NICU. A tendency

for increased survival was noticed in outborns (p = 0.327), contrarily to the most recent large-sample study (2,140 hernias) that established a significant difference between inborn and transported patients, the latter displaying elevated mortality rates [35].

The presence of a herniation sac was thought to be protective, due to physical restriction of abdominal viscera movement into the thorax. A recent report comparing a group of hernias with sac (n = 30) and without sac (n = 107) showed no significant difference on mortality, which was similar to our results [42].

Limitations and future directions

Although our study presented certain advantages (eg. the uniformity of cohort management granted by a protocol of medical treatment), it also showed some limitations, namely its retrospective nature and relatively reduced sample size.

Furthermore, the use of prosthetic patch is not a direct indicator of defect size. Thererfore, it would have been important to consider standardized classifications, such as the defined scheme from the CDH study group, as a systematic recording process in hospitalized cases of posterolateral hernia [36].

Conclusion

Standardized protocols, namely The CDH EURO Consortium Consensus, provided better outcomes and major advances in medical and surgical approach of CDH. Since 2003, our NICU treats all patients with CDH according to similar guidelines.

Although mortality and morbidity rates in our center have improved with these recent guidelines of management, approximately 2 out of 5 patients still do not survive during hospitalization and 1 out of 5 survivors displays respiratory or gastrointestinal morbidity at discharge.

Patch repair is an independent predictor of mortality during NICU stay, since it is an indirect marker of larger hernias. The presence of an intrathoracic stomach has predictive value for respiratory and/or gastrointestinal morbidity at discharge due to its close relation with development of gastro-esophageal reflux disease during hospitalization. Since anatomical features remain the primary determinants of neonatal prognosis, future researches should continue focusing on the definition of prenatal criteria for CDH severity and the prenatal management of this condition.

Declaration of interest

The Authors declare that there is no conflict of interest.

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