World J Surg (2018) 42:2668–2673
https://doi.org/10.1007/s00268-018-4509-x

ORIGINAL SCIENTIFIC REPORT

Neonatal Gastric Perforation: Case Series and Literature Review

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Published online: 1 February 2018

Abstract

Purpose We reported clinical findings of neonatal gastric perforation in a tertiary children's hospital.

Patients and methods Retrospective chart reviews were conducted for neonatal gastric perforation between 1980 and 2016. Factors including sex, gestational age, birth weight, age, main symptoms and signs, white blood cell count (WBC), surgical intervention time (time between development of main symptom and surgical intervention), surgical findings, pathologic results, clinical outcomes, and causes of death were collected.

Results Sixty-eight patients were identified. In total, 76.5% were male infants, the median age was 4 days, median birth weight was 2500 g, and 42.6% were premature. Abdominal distention and vomiting were the most common symptoms, and pneumoperitoneum was the most common radiographic finding. The median surgical intervention time was 51 h (range 8–312). In total, 73.5% of perforations occurred in the great curvature, 17.6% in the lesser curvature, and 8.9% unspecified. The median perforation size was 4 cm (range 0.2–16). Associated gastrointestinal anomalies were found in 20.6% of patients, and the most common anomaly was intestinal malrotation. Of the 51 patients with pathologic results, 11 showed the presence of musculature in the perforated gastric wall, while 40 showed the absence of musculature. Of the 66 patients with known clinical outcomes, 26 (39.4%) died, 23 of who died of infection. Among those aforementioned factors, WBC has a significant impact on survival. The mortality for four arbitrary divided year groups (1980–1989, 1990–1999, 2000–2009, and 2010–2016) was 100, 50, 31.6, and 16.7%, respectively.

Conclusions The mortality of neonatal gastric perforation is constantly decreasing. Associated gastrointestinal anomalies and the presence of musculature are found in a minority of this condition.

Introduction

Neonatal gastric perforation is a rare entity and life-threatening condition [1, 2]. In 1825, Siebold reported the first case of neonatal gastric perforation. In 1943, Herbut reported the first case of neonatal gastric perforation with a congenital defect of the musculature of the perforated gastric wall. It was not until 1950 that the survival of an infant operated upon for this disease was first reported [3]. Most of the previous reports about neonatal gastric perforation are limited case series and case report studies. Much of the discussion regarding this rare entity centers on the

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causes and etiology [3–14]. Nonetheless, the causes and etiologies remain debated and elusive. Recently, studies have focused on the investigation of possible prognostic factors for clinical outcomes. However, the relative importance of these possible factors to neonatal gastric perforation is unclear and controversial [15, 16].

In this retrospective study, we reviewed all patients with neonatal gastric perforations who underwent surgery at a pediatric tertiary hospital during a 36-year period. We try to describe the overall clinical findings of neonatal gastric perforation and investigate the correlation of possible prognostic factors with outcomes.

Patients and methods

The medical database (1980–present) in our institution was available for search. Patients were identified through admitting and discharge diagnosis. Children diagnosed with gastric perforations between January 1980 and February 2016 in the Guangzhou Women and Children's Medical Center were identified. However, only neonates (age $\leq$ 30 days) who were surgically confirmed to have gastric perforations were included in the current study.

Parameters retrieved were sex, gestational age, date of birth, birth weight, mode of delivery, respiratory distress at birth, age, gastric tube insertion and mechanical ventilation prior to the onset of gastric perforation, main symptoms and signs, preoperative abdominal radiographic findings, time between the development of main symptom and surgical intervention (surgical intervention time), site of perforation, size of perforation, associated gastrointestinal anomalies and conditions, surgical procedures, pathologic findings, and survival status.

Pathologic characteristics of neonatal gastric perforation were well defined and can be classified into the absence or presence of musculature [5, 6, 17]. The absence of musculature was defined in the following manner. Microscopic examination of the perforated gastric tissue found that, for a distance away from the perforation, there was an absence of gastric musculature. The stomach wall in such areas was usually composed only of mucosa, muscularis mucosa, and the loose connective tissue of the submucosa and subserosa [6, 7]. In contrast, the presence of musculature was confirmed by the pathology reports documenting gastric musculature in the perforated gastric tissue. Possible prognostic factors, including gestational age, birth weight, WBC, surgical intervention time, perforation location, perforation size, pathology subtype, for clinical outcomes were chosen based on both the literature and surgical experiences.

We used a standard abstraction form, which had a logical organization similar in flow to the format of the original medial charts, to collect data. A trained data abstractor, who was blinded to the study hypothesis, independently reviewed the original medical charts and collected data. Explicit criteria for abstracting variables were applied. Any discrepancies in coding variables were reviewed jointly and discussed to clarify any issues. This study was approved by the Institutional Review Board of Guangzhou Women and Children's Medical Center (Guangzhou, China), which waived the need for informed consent for the retrospective collection of demographic, clinical, and hospital outcome data. All patient records/data were anonymized and de-identified prior to analysis.

Statistical analysis

Continuous variables were presented as either means and standard deviations (SD) or medians with ranges. Categorical variables were presented as frequencies and percentages. Predictors for mortality were analyzed by using logistic regression analyses. Differences were considered statistically significant with a 2-sided $p < 0.05$. Statistical analyses were performed using SPSS 19.0 (SPSS Inc., Chicago, IL).

Results

Study population

From January 1980 to February 2016, eighty-eight patients were diagnosed as gastric perforations in our institution. Thirteen patients were older than 30 days, and seven neonates were clinically diagnosed with gastric perforations without surgical laparotomy, and these 20 patients were excluded. Thus, a total of 68 neonates (age $\leq$ 30 days) who were surgically diagnosed as gastric perforation were included in the current study. Further investigation identified two neonates for whom further treatment was withdrawn after surgery without specific reasons, and these two patients were included in the study but not in the logistic regression analysis.

Demographic characteristics of the study population

This report included 68 cases of surgically diagnosed neonatal gastric perforation between January 1980 and February 2016 (Table 1). The majority of patients were male neonates (76.5%), and the male/female ratio was approximately 3:1. Nearly half of the patients were premature (42.6%) and were low-birth-weight (<2500 g) neonates (48.5%). The median birth weight was 2500 (range 1100–3600) g. The median age at presentation was 4 (range 1–30) days. Fifty-six (82.3%) cases of neonatal

Table 1 Demographic characteristics of patients

Characteristics	No. of patients ($n = 68$)
Sex	
Male	52 (76.5)
Female	16 (23.5)
Gestational age	
Full term	39 (57.4)
Prematurity	29 (42.6)
Mode of delivery	
Cesarean section	33 (48.5)
Natural delivery	35 (51.5)
Birth weight	
Normal (2.5–4.0 kg)	35 (51.5)
Low birth weight (<2.5 kg)	33 (48.5)
Age (day)[a]	4 (1–30)
Birth weight (g)[a]	2500 (1100–3600)
Clinical outcomes ($n = 66$)[b]	
Death	26 (39.4)
Discharge from hospital	40 (60.6)

Percentages in parentheses unless indicated otherwise

[a]Values are median (range)

[b]Two patients were withdrawn from further treatment after surgery and were excluded from the clinical outcome analysis

Table 2 Clinical characteristics and radiologic findings

Characteristics	$N = 68$ (%)
Respiratory distress at birth	9 (13.2)
Gastric tube insertion prior to perforation	6 (8.8)
Mechanical ventilation prior to perforation	7 (10.3)
Symptoms and signs	
Abdominal distention	59 (86.8)
Vomiting	27 (39.7)
Lethargy	3 (4.4)
Bloody stool	3 (4.4)
Fever	2 (2.9)
Hematemesis	1 (1.5)
WBC[a]	6.7×10^9/L (1.4–29.0)
Preoperative radiographic findings ($n = 66$)	
Pneumoperitoneum	57 (86.4)
Bowel obstruction	11 (16.7)
Others	4 (6.1)

Percentages in parentheses unless indicated otherwise

[a]Median and range

Table 3 Surgical findings and operative procedures

	$N = 68$ (%)
Surgical intervention time (h)[a]	51 (8–312)
Site of perforations	
Great curvature	50 (73.5)
Lesser curvature	12 (17.6)
Unspecified	6 (8.9)
Perforation size (cm)[a]	4 (0.2–16)
Surgical procedures	
Gastrorrhaphy	64 (94.1)
Gastrorrhaphy + gastrostomy	3 (4.4)
Gastroduodenostomy + gastrostomy	1 (1.5)
Associated gastrointestinal anomalies	15 (22.1)
Pathologic findings ($n = 51$)	
Absence of musculature	40 (78.4)
Presence of musculature	11 (21.6)

Percentages in parentheses unless indicated otherwise

[a]Median and range

gastric perforations occurred within the first week of life, eight (11.8%) cases within the second week, and four (5.9%) patients after two weeks of age. Of the 66 patients with known clinical outcomes, 26 died and 40 were discharged from the hospital with a full recovery.

Clinical features and radiographic findings

The clinical characteristics and radiographic findings of patients are shown in Table 2. Nine patients had a history of respiratory distress at birth, six patients had gastric tube insertion, and seven patients were mechanically ventilated prior to the onset of gastric perforation. Abdominal distention and vomiting were the most common presenting symptoms, documented in 87 and 40% of the patients, respectively. The median WBC was 6.7×10^9/(range 1.4–29.0). Pneumoperitoneum was detected in 57 of 66 patients with preoperative abdominal radiography available for analysis.

Surgical findings and operative procedures

Sixty-eight neonates underwent surgical laparotomy, and the operative findings and surgical techniques are shown in Table 3. The median time between development of main symptom and surgical intervention was 51 (range 8–312) hours. Fifty cases perforations occurred in the greater curvature of the stomach (73.5%), 12 in the lesser curvature (17.6%), and 6 were unspecified. The median perforation size is 4 (range 0.2–16) cm. Gastrorrhaphy alone was used in 64 patients (94.1%), gastrorrhaphy combined with gastrostomy in three patients, and gastroduodenostomy plus gastrostomy in one patient due to extensive necrosis over the antrum area.

Sixteen gastrointestinal tract anomalies were found in 14 (20.6%) patients, with two patients having two kinds of anomalies. Intestinal malrotation and Meckel's diverticulum were the most common associated anomalies, accounting for 44% (8/18) and 11% (2/18), respectively. Others included jejunal atresia, intestinal volvulus, heterotaxy (liver on the left, spleen on the right), ectopic pancreatic tissue of the ileum, duodenal web, and annular pancreas. One patient had associated meconium peritonitis and distal ileum perforation. All patients underwent concurrent surgical correction for the associated gastrointestinal anomalies, except one patient with intestinal malrotation.

Fifty-one patients had pathologic examination of the perforated gastric tissue, which was taken during the laparotomy. Forty were classified as having a congenital absence of musculature, while 11 cases showed the presence of musculature.

Clinical factors and outcomes

Of the 66 patients with outcomes, 26 patients died and 40 patients were discharged from the hospital with a full recovery. Twenty-three patients died of severe infection, one died of aspiration pneumonia, one died of massive intraoperative bleeding, and one died of respiratory failure caused by inappropriate ventilator weaning. As for possible prognostic factors in predicting outcomes (Table 4), logistic regression analysis showed that age, birth weight, surgical intervention time, gestational age, associated anomaly, perforation location, pathology subtype were not statistically correlated with mortality. WBC has a significant impact on the overall survival.

Patients were arbitrarily divided into four groups chronologically for the evaluation of changes in mortality rates over time. The four groups were 1980–1989, 1990–1999, 2000–2009, and 2010–2016. The mortality for the four groups was (5/5) 100%, (12/24) 50%, (6/19) 31.6%, and (3/18) 16.7%, respectively. A significant trend of decreased mortality based on arbitrary chronological classification was observed (Table 5).

Discussion

This study represents the largest cohort of neonatal gastric perforation patients. The surgical management remained largely unchanged during the study period. However, the overall mortality is constantly decreasing, from 100% in 1980s to 16.7% in 2010s.

The causes and etiology of neonatal gastric perforations remain controversial and unclear. Congenital defect of the musculature of the perforated gastric wall is considered as a possible cause by many authors in the mid-twentieth

Table 4 Logistic regression analysis of risk factors

Risk factors	Univariate logistic regression			Multivariate logistic regression		
	OR	95% CI	*p* value	OR	95% CI	*p* value
Age	1.054	[0.935–1.186]	0.390	1.012	[0.832–1.232]	0.903
Birth weight	1.477	[0.466–4.679]	0.508	1.826	[0.185–18.002]	0.606
WBC	1.067	[0.978–1.164]	0.145	1.315	[1.012–1.710]	0.041
Surgical intervention time	0.999	[0.989–1.008]	0.767	1.006	[0.982–1.030]	0.635
Gestational age						
Premature	1	Reference	N/A	1	Reference	N/A
Mature	0.811	[0.300–2.193]	0.679	1.423	[0.139–14.542]	0.766
Associated anomaly						
Without associated anomaly	1	Reference	N/A	1	Reference	N/A
With associated anomaly	0.968	[0.299–3.137]	0.956	1.025	[0.125–8.409]	0.982
Perforation location						
Greater curvature	1	Reference	N/A	1	Reference	N/A
Lesser curvature	1.645	[0.392–6.904]	0.496	0.911	[0.072–11.561]	0.943
Unspecified	0.000	[0.000–Inf]	0.991	0.000	[0.000–Inf]	0.992
Pathology subtype						
Intact musculature	1	Reference	N/A	1	Reference	N/A
Absence of musculature	0.575	[0.131–2.520]	0.463	0.521	[0.043–6.362]	0.610
Unspecified	0.422	[0.082–2.160]	0.300	0.209	[0.007–6.273]	0.367

Table 5 Comparison of survival among different arbitrary divided year groups

Year groups	Total ($n = 66$)	Survived ($n = 40$)	Death ($n = 26$)	p value
1	5 (7.58)	0 (0.00)	5 (19.23)	0.002
2	23 (34.85)	11 (27.50)	12 (46.15)	
3	19 (28.79)	13 (32.50)	6 (23.08)	
4	19 (28.79)	16 (40.00)	3 (11.54)	

Parentheses indicate percentage

1 = 1980–1989, 2 = 1990–1999, 3 = 2000–2009, 4 = 2010–2016

century [3, 5–7, 17–19]. However, experimental studies suggest that these muscular changes may only be the result of gastric distention [9, 20]. The majority of our pathologic findings demonstrate the absence of gastric wall musculature. However, the presence of musculature of the perforated gastric wall is also noted in some neonates.

High gastric acidity in combination with local ischemia is also considered a significant etiologic factor in neonatal gastric perforation [8, 21, 22]. Animal studies show a marked reduction in the blood flow of the mucosa of the gastrointestinal tract during experimental asphyxia [11], supporting gastric tissue ischemia secondary to hypoxia as a reasonable explanation [10, 12, 18, 21, 23–25]. However, some authors specifically denounce the theory of hypoxia-induced ischemia and subsequent gastric perforation, because necrotizing enterocolitis (NEC) has seldom been reported in neonates with gastric perforation [20]. We found no NEC in the eighteen associated gastrointestinal anomalies, and respiratory distress at birth was not common. It seems unlikely that hypoxia-induced gastric ischemia is the primary etiologic factor in neonatal gastric perforation [26].

Along with the identification of associated gastrointestinal anomalies, increased gastric pressure due to distal gastrointestinal anomalies is postulated as a possible mechanism for neonatal gastric perforation [20, 27]. Associated gastrointestinal anomalies were observed in 20.6% of patients in our study, with intestinal malrotation and Meckel's diverticulum being the most common anomaly. However, we should note that both asymptomatic malrotation and Meckel's diverticulum can be commonly seen in healthy population. Other studies have also revealed a variety of gastrointestinal anomalies concomitantly associated with neonatal gastric perforation [14, 15, 27]. However, most of the associated gastrointestinal anomalies are unlikely to cause gastric outlet obstruction and produce enough gastric pressure leading to gastric perforation [16].

Although being attributed to varying causes, neonatal gastric perforation is more likely the result of a variety of causes acting either alone or in combination. Unfortunately, it is inappropriate for us to generate a possible causative relationship based on this retrospective observational study.

The surgical strategy remains unchanged over time; prompt surgical laparotomy is encouraged and lifesaving. Gastrorrhaphy alone or combined with gastrostomy is the most commonly performed techniques. As for the associated gastrointestinal anomalies, concurrent or delayed surgical correction should be decided based on the specific situation of patients.

Among the risk factors we investigated, gestational age, birth weight, surgical intervention time, associated anomaly, perforation location, and pathologic findings seem to have no significant prognostic impact on the overall mortality. Results from other studies also show contradictory effects of gestational age and birth weight on predicting mortality [2, 16]. WBC seems to have a significant impact on the overall survival. The most common causes of death in this study are severe infection. Overall mortality has decreased over time, which may mainly due to the considerable improvements in the intensive care for critically ill neonates [28].

This is a retrospective study and as such inevitably has several limitations. For example, the changes in intensive medical care for neonates over time undoubtedly affect the overall clinical outcomes and may act as confounder when we look for prognostic factors for the outcomes. Moreover, we were unable to suggest a causational inference for neonatal gastric perforation due to the absence of a control group.

Conclusions

In conclusion, the overall mortality of neonatal gastric perforation is constantly decreasing over time. Gastric perforation is evenly distributed among mature and immature neonates. Most of the neonatal gastric perforations occur within the first week of life. Associated gastrointestinal anomalies and the presence of musculature of the perforated gastric wall are observed in some patients,

but do not seem to be a causative factor in gastric perforation.

Funding This study was funded by National Natural Science Foundation of China (Grant No. 81602199), Guangzhou Science Technology and Innovation Commission (Grant No. 201607010395), Natural Science Foundation of Guangdong Province, China (Grant No. 2016A030313496).

Compliance with ethical standards

Conflict of interest There are no conflicts of interest to declare.

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