Incidence and Risk Factors of Necrotizing Enterocolitis Following Gastroschisis Repair in Correlation with Modes of Abdominal Wall Closure and Umbilical Management at Siriraj Hospital: an 11-Year Retrospective Review

Mongkol Laohapensang, M.D.*, Duangkamol Puthakunraksa, M.D., Niramol Tantemsapya, M.D.***

**Department of Surgery, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok 10700, **Department of Surgery, Chareonkrung Pracharak Hospital, Bangkok 10120, Thailand.*

ABSTRACT

Objective: We investigated the correlation between umbilical management and NEC in infants with gastroschisis as well as the incidence and potential risk factors of NEC in patients with gastroschisis at Siriraj Hospital from 2005 to 2016.

Methods: A retrospective chart review was conducted of patients with gastroschisis who were surgically repaired at Siriraj Hospital from January 2005 to January 2016. The baseline characteristics, umbilical management, and short-term outcomes were analyzed in relation to NEC complications to determine the associated correlations and potential risk factors.

Results: Overall, 106 patients were enrolled. The incidence of NEC following gastroschisis repair was 16% (17/106). Umbilical preservation was a significant potential risk factor for NEC ($p = 0.009$; hazard ratio = 5.14; 95% CI = 1.51-17.42). There were no significant differences between the NEC and non-NEC group for gender, median Apgar scores, gestational ages, and birth weight. The short-term outcomes were significantly higher for the NEC than the non-NEC group, with a time to first oral feeding of 15 vs. 9 days ($p = 0.006$), duration of total parenteral nutrition, 22 vs. 12 days ($p < 0.001$), and length of stay, 32 vs. 23 days ($p = 0.01$) respectively.

Conclusion: Umbilical preservation following gastroschisis repair was associated with a higher incidence of NEC, even in term infants. Thus, NEC should be carefully monitored after abdominal fascial closure with umbilical preservation.

Keywords: NEC; gastroschisis; umbilical preservation (Siriraj Med J 2019; 71: 261-267)

INTRODUCTION

Gastroschisis is a congenital, abdominal-wall defect with eviscerated abdominal content. Usually, the defect is less than 4 cm in width and is located on the right of the umbilicus. The incidence varies from 2-4.9 per 10,000 live births.[1–3] Necrotizing enterocolitis (NEC) is a well-recognized and serious complication, particularly after gastroschisis repair, and is responsible for increased morbidity and occasional mortality.[4–6] The incidence of NEC has ranged from 4%–18.5% in infants with gastroschisis following abdominal wall closure.[4–7]

Previous studies have reported the association of NEC in infants with gastroschisis with a lower birth weight[5,8] and prematurity[5], although the association is

Corresponding author: Mongkol Laohapensang
E-mail: mongkol.lao@mahidol.ac.th
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ORCID ID: http://orcid.org/0000-0002-0774-5705
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unclear following the initiation of enteral feedings.[4–5] The predisposing factors for NEC in normal term infants have been speculated to be the combination of reduced mesenteric perfusion and feeding with artificial formula.[9] The risk factors for NEC in infants with gastroschisis have rarely been documented.

The current definitive surgical management of gastroschisis is by early return of the eviscerated abdominal content into the abdomen through the primary abdominal fascia and skin closure.[3,4] If primary abdominal closure is impossible due to visceral-abdominal disproportion or increased intraabdominal hypertension, an artificial pouch or silo is placed with a subsequent serial reduction of the extra-abdominal content[3,4] and a succeeding definitive closure.

The difference in umbilical cord management during and after abdominal closure depends on individual surgeons' preferences. Several previous studies have demonstrated the advantages of umbilical preservation in cosmetic outcomes, and most did not report any major complications such as cellulitis or omphalitis.[10–12] Conversely, research by Komuro et al. revealed a possible association between umbilical preservation and wound infection.[13]

Concerns about periumbilical necrotizing fasciitis led to umbilical cord and urachal remnant excision, as reported by Kosloske and Bartow.[14] The infection was speculated to spread along the umbilical arteries and vein as well as the urachal remnant. However, the association between umbilical preservation and NEC has not yet been defined.

Objectives

The purpose of this study was to determine the association between umbilical cord preservation and NEC in infants with gastroschisis. The incidence and risk factors of NEC in infants with gastroschisis were also evaluated.

Keywords and variables in the study

Preterm refers to a baby born before 37 weeks of pregnancy have been completed. Preterm infants experience a greater risk of morbidity and mortality than term infants due to immaturity-related complications.[15]

Low Apgar score is defined as a score of less than 7 at 1 minute.[16]

Low birth weight is defined as a birth weight of less than 1,500 grams.

Modes of surgical treatment for gastroschisis were classified into:

- ***Primary fascial closure with umbilical preservation***: closure of the abdominal fascial wall, either immediately or in the first operation, with preservation of the umbilical cord.
- ***Primary fascial closure with umbilical cord removal***: closure of the abdominal fascial wall, either immediately or in the first operation, with an umbilical cord excision followed by an umbilicoplasty.
- ***Staged abdominal wall closure***: a salvage technique providing temporary intestinal coverage, which allows for the gradual reduction of the contents, followed by a definitive closure and an umbilical cord excision.

Umbilical cord excision: the excision of the umbilical cord from a newborn by cutting the umbilical arteries, umbilical vein, and urachal remnant at the level of the peritoneum.

NEC Staging: classified according to the modified Bell's clinical staging criteria.[17]

MATERIALS AND METHODS

A retrospective clinical-chart review was conducted of patients with gastroschisis who had been surgically repaired at Siriraj Hospital January 1, 2005-January 31, 2016. The inclusion criterion was neonates with gastroschisis operated at Siriraj Hospital during the 11-year study period. Excluded were patients who had undergone a definitive operation at another hospital or who had incomplete medical records.

In all, 110 patients with gastroschisis were identified as having been treated at Siriraj Hospital from 2005 to 2016. Complete medical records of 108 of the patients were available and formed the basis of the retrospective review. However, as two of those patients were subsequently found to have undergone definitive surgical repair at other hospitals, they were excluded. The patients' demographic and clinical data that were collected comprised gender, gestational age, birth weight, Apgar score, type of delivery, mode of surgical treatment, comorbidities, operative findings, and umbilical management. The variables of the NEC and non-NEC groups were compared. The significant variables were reanalyzed to find the potential risk factors for NEC. The short-term outcomes (time to first oral feeding, duration of total parenteral nutrition [TPN], and length of stay) were reviewed with respect to overall complications, sepsis, wound infections, necrotizing enterocolitis, morbidities, and mortalities.

The statistical analyses were performed using SPSS Statistics for Windows, version 17 (SPSS Inc., Chicago, Ill., USA). The data were presented as mean, median, mode, min, max, and standard deviation. Student's t-test was used for normally distributed data, and the Mann–Whitney U test was employed for deviated distribution or non-parametric tests in comparative quantitative data analysis. The qualitative data were compared using the Chi-square test, and if the sample size was deemed too small, a two-tailed Fisher's exact test was used. Statistical significance was determined by a p-value of less than 0.05. The significant factors from the univariate analysis were reanalyzed in a stepwise selection of variable and logistic regression processes.

Ethics approval

The institute's ethics review board approved the review of the medical records undertaken by the present research (Si 341/2015).

RESULTS

A total of 106 infants with gastroschisis were studied. There were 50 male and 56 female patients (47% vs. 53%), as summarized in Table 1. Sixty five percent of the cases were preterm infants, mainly weighing more than 1,500 grams (92.5%) and mostly with good Apgar scores (73.6%). The most common associated anomaly was bowel atresia with or without volvulus, with an incidence of 12.3% of the study population. In this study, 70 out of 106 patients (66.1%) underwent primary fascial closure, which included 17% of the cases with umbilical preservation and 49% with umbilical cord excision. Thirty six out of 106 patients underwent staged fascial closure, accounting for 34% of the cases with delayed umbilical cord removal. The incidence of NEC in this study was 16% (17/106), and the mortality rate was 7.5% (8/106). All mortalities were not related to NEC (1 abdominal compartment syndrome, 2 bowel atresia with complications, 1 midgut volvulus, 2 sepsis, 1 pneumothorax, and 1 congenital heart disease and associated hydranencephaly).

There were 13 complicated patients with gastroschisis with associated bowel atresia or midgut volvulus. Twelve patients had associated intestinal atresia, of which 9 underwent fascial closure with constructed ostomy and 3 underwent fascial closure with primary anastomosis. There were two mortalities from the ostomy group. One died from very short bowel syndrome, with a jejunal length of 12 cm. Another died of complicated anastomotic dysfunction after operative ileostomy closure.

A univariate analysis to identify the potential risk factors of NEC in infants with gastroschisis is presented in Table 2.1. There were no significant differences between some of the parameters of the NEC and non-NEC groups (gender, median gestational age, Apgar score, and birth weight). However, the univariate analysis showed that umbilical management (including umbilical preservation), umbilical excision, and delayed umbilical resection during staged abdominal wall closure were significantly different between the NEC and non-NEC groups, with a p-value of 0.001. The significant variables were reanalyzed in a stepwise logistic regression, as detailed in Table 2.2. Umbilical preservation was identified as a potential risk factor for NEC in infants with gastroschisis, with a p-value of 0.009 (hazard ratio = 5.13; 95% CI = 1.512-17.42), and staged closure showed a tendency towards a preventive effect of NEC, but with no statistical significance (adjusted odds ratio = 0.378; 95% CI = 0.078-1.937).

Excluding 8 mortalities, the short-term outcomes were compared between the NEC and non-NEC groups. Table 3 details the comparison of the outcomes (the median time to first oral feeding, duration of TPN, and length of stay), all of which were significantly higher in the NEC than the non-NEC group (p-values = 0.006, 0.000, and 0.01, respectively).

The overall postoperative complications were intestinal obstruction, respiratory complications, and NEC (Table 4). There were no significant differences between the groups with different umbilical management in terms of the overall complication rate, sepsis, and wound complications. The infants with gastroschisis who underwent a staged abdominal wall closure with delayed umbilical resection had the highest overall complication rate (58.3%). This incidence was similar to the figure of 55.6% for a primary fascial closure with a preserved umbilicus group. The primary fascial closure with umbilical removal group had the lowest overall complications (36.5%) and wound complication rate (9.6%). The incidence of sepsis was highest in the staged closure with a delayed umbilical resection group (27.8%).

The incidence of NEC was analyzed based on umbilical management, which was classified according to the modified Bell's clinical staging criteria. The analysis found significant differences between the 3 umbilical management groups, with a p-value of 0.01 (Table 5). The primary fascial closure with preserved umbilicus group had the highest NEC incidence of 44.4%. The umbilical removal approaches (primary fascial closure or staged closure) had significantly lower incidences of NEC (13.5% and 5.6%, respectively).

TABLE 1. Demographic data of 106 neonates with gastroschisis treated 2005–2016 (n = 106).

Parameter	Category		Incidence	%
Gender	Male/Female		50/56	47.1/52.8
Mean GA (weeks)	< 37/≥ 37		69/37	65/34.9
Birth weight (g)	≤ 1,500/> 1,500		8/98	7.5/92.5
Apgar	< 7/≥ 7		28/78	26.4/73.6
Comorbidities	Bowel atresia/volvulus		13	12.3
Umbilical management	Primary closure	Preserve umbilicus	18	17
		Remove umbilicus	52	49
	Staged closure (remove umbilicus)		36	34
NEC			17	16
Mortality			8	7.5

TABLE 2.1. Univariate analysis of potential risk factors for NEC in infants with gastroschisis (n = 106).

Variable	NEC (n = 17)	Non-NEC (n = 89)	P-value
Gender (M:F)	7:10	43:46	0.59
Median GA (weeks; range)	37 (34–39)	36 (30–44)	0.71
Median Apgar score (range)	9 (7–10)	10 (5–10)	0.97
Median birth weight (g; range)	2,340 (1,730–3,647)	2,060 (1,200–3,700)	0.08

TABLE 2.2. Logistic regression analysis of potential risk factors for NEC in infants with gastroschisis (n = 106).

Variable	NEC (n = 17)	Non-NEC (n=89)	P-value	Adjusted odds ratio (95% CI)	Hazard ratio (95% CI)
Umbilical management			0.001		
Preserve umbilicus	8 (47.7%)	10 (11.2%)	0.009		5.143 (1.512–17.42)
Remove umbilicus	7 (41.2%)	45 (50.6%)			1
Staged closure (remove umbilicus)	2 (11.8%)	34 (38.2%)	0.24	0.378 (0.078–1.937)	

TABLE 3. Comparison of short-term outcomes of NEC and non-NEC groups (excluding 8 mortality cases; n = 98).

Variable		NEC (n = 17)	Non-NEC (n = 81)	P-value
Time to feeding	Median (min-max)	15 (6–45)	9 (4–73)	0.006
TPN duration	Median (min-max)	22 (12–45)	12 (0–100)	0.000
LOS	Median (min-max)	32 (19–67)	23 (9–365)	0.01

Abbreviations: TPN = total parenteral nutrition, LOS = length of stay, P-value of < 0.05 considered statistically significant

TABLE 4. The complication rates of each mode of treatment and umbilical management (n = 106).

	Primary closure		Staged closure (n = 36)	P-value
	Preserve umbilicus (n = 18)	Remove umbilicus (n = 52)		
Complications	10 (55.6%)	19 (36.5%)	21 (58.3%)	0.97
Sepsis	3 (16.7%)	9 (17.3%)	10 (27.8%)	0.44
Wound complications	4 (22.2%)	5 (9.6%)	8 (22.2%)	0.21

P-value of < 0.05 considered statistically significant

TABLE 5. The incidence of NEC for each mode of treatment, classified according to the modified Bell's clinical staging criteria[17] (n = 106).

	Primary closure		Staged closure (n = 36)	P-value
	Preserve umbilicus (n = 18)	Remove umbilicus (n = 52)		
NEC stage	8 (44.4%)	7 (13.5%)	2 (5.6%)	0.011
IA	4	3	1	
IB	3	4	1	
IIB	1	0	0	

P-value of < 0.05 considered statistically significant

DISCUSSION

Necrotizing enterocolitis occurring in infants after gastroschisis repair is not uncommon. It tends to occur later in the clinical course, although it can often be successfully managed nonoperatively.[4] In this study, the incidence of NEC was 16%, which is similar to the findings of previous studies that reported incidences ranging from 4%-18.5%.[4–7] Most cases were diagnosed early in stages I-II, and they were successfully treated nonoperatively by fasting and intravenous empirical antibiotics. Comprehensive studies by Snyder[7] and Eggink et al.[18] reported lower NEC incidences of 4% and 9%, respectively, which illustrates the reduction is a consequence of more advanced stage inclusion criteria.

NEC in infants with gastroschisis is a distinctive condition in that no significant relationship has been established with any known predisposing conditions, such as prematurity, low birth weight, or low Apgar score.[4,18] Conforming to previous reports, our study found no significant association between NEC and gestational age, birth weight, or Apgar score. However, substantial studies by Oldham et al.[4] and Suttiwongsing et al.[8] acknowledged the combination of low birth weight, compromised intestinal vascular perfusion, and associated gastrointestinal anomalies as predisposing factors for NEC after gastroschisis repair.

A study by Komuro et al.[13] reported the disadvantages of umbilical preservation as a possible cause of wound infections, omphalitis, cellulitis, and the development of ventral hernia. This corresponds to earlier reports by Kosloske and Bartow,[14] which emphasized the importance of umbilical cord and urachal excision in complicated periumbilical necrotizing fasciitis infants where there were concerns of an infection spreading along the umbilical vessels and urachal remnant. Based on those reports, it can be speculated that the concept of infection spreading along the umbilical vessels and urachal remnant may be related to the development of NEC in infants with gastroschisis. The hypothesis is that umbilical preservation results in bacterial colonization in the area of the umbilical insertion; consequently, spread through the fascial defect, together with operative fascial closure procedures, may lead to impaired tissue perfusion, reduced mucosal blood flow, and cellular hypoxia. Therefore, intestinal mucosal injury and break-down precipitates the development of NEC. Our study showed that umbilical preservation was highly correlated to the development of NEC in infants with gastroschisis, accounting for 47% of the NEC cases. Accordingly, the incidence of NEC in the 18 patients who underwent primary fascial closure with umbilical preservation was as high as 44.4%, which is the highest compared to both primary and staged umbilical resection, with 13.5% and 5.6% respectively. As a result, umbilical preservation was identified as a predisposing factor for NEC in infants with gastroschisis after surgical repair (p-value = 0.009; hazard ratio = 5.13; 95% CI = 1.512-17.42). Further additional pathophysiological studies may be required.

Alternatively, various studies[10,11] have advocated umbilical preservation as it offers better cosmetic results. Nagaya et al.[11] reported the approach in later gastroschisis cases, following complaints about the subsequent absence of the umbilicus in earlier cases. In the 5 patients who underwent fascial closure with umbilical preservation, the procedure provided excellent cosmetic results with no complicated omphalitis or cellulitis. Those studies[10,11] did not identify the incidence of NEC or its correlation to umbilical preservation; in addition, they had fairly small sample sizes. Our study found no difference in the incidences of overall complications, including sepsis and wound complications, in the different umbilical management groups. Nevertheless, the highest overall complication rate of 58.3% in the staged fascial closure group may be a consequence of a more critical population group, for which a primary closure is impractical. Furthermore, wound infections are common and likely to occur with a staged fascial closure. As to the research by Fonkalsrud,[19] it found a much smaller percentage of patients (31%) undergoing a primary fascial closure (compared to 66% in the current study) and cited a higher incidence of complications in those with a staged silo repaired. It was postulated by Fonkalsrud that the significant visceral-abdominal disproportion precluded a primary closure.

With respect to the incidence of sepsis, aside from the higher risk of wound infections in staged fascial closure wounds, a delay in the time to the first oral feeding results in the prolonged use of a central venous catheter, which in turn can ultimately predispose the patient to septicemia more than any other reason.[20] In the present study, the significantly longer time to first oral feeding, prolonged duration of TPN, and length of hospital stay of the NEC group were due to the early detection and treatment of the condition. When NEC was suspected, the patient would be fasted and promptly provided empirical intravenous antibiotics as well as parenteral nutrition. Not only was NEC diagnosed early (no later than stage IIB), all cases were successfully managed nonoperatively. Only one severe case developed pneumatosis intestinalis, and it was in the umbilical preservation group.

Several earlier studies[4,7] included either only definite NEC cases or cases from stages IIA upwards. This contrasts with the current study, in which the majority of cases

were in stages IA and IB, with only 1 case in stage IIB. As to the diagnosis of stage I, some of the cases of NEC may actually have been a delayed gut function, which is common in patients with gastroschisis; however, this is one of the limitations of conducting a retrospective review. Despite the fact that most studies[4,7,8] reported higher incidences (18%-18.5%) of NEC in infants with gastroschisis, including only definite NEC cases, the declining rate of NEC[8] over the past 2 decades has presumably been the result of early detection and the availability of more efficient antimicrobial agents. The lower incidence of NEC in the staged fascial closure group in the present study (5.6%) was consistent with the conclusion of Schlatter et al.[21] that the improved outcome was attributable to lower intraabdominal pressure following the initial preformed silo coverage, allowing sufficient intestinal perfusion.

The current study identified only one significant predisposing factor for NEC in infants with gastroschisis, which is the preservation of the umbilicus. The patients in the primary fascial closure with preserved umbilicus group had 5 times the risk of developing NEC than those in the umbilical removal groups over the study period. A staged fascial closure conveyed the lowest incidence of NEC, despite having the highest incidence of wound infections, sepsis, and overall complications. Nevertheless, the decision to perform any method of fascial closure depends on a patient's condition rather than the prevention of wound complications. Therefore, NEC should be closely monitored when preserving the umbilicus for a patient.

CONCLUSION

Umbilical preservation following gastroschisis repair was strongly associated with the development of NEC, with no correlation to gestational age. Thus, NEC should be carefully monitored after abdominal fascial closure with umbilical preservation. NEC may lead to a prolonged time to the first oral feeding, an extended duration of TPN, and a lengthened hospital stay. Staged fascial closure showed a tendency towards a preventive effect of NEC, but with no statistical significance.

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The limitations of this study were those of a retrospective analysis, a single center, and a relatively small sample size. In addition, the study provided only short-term outcomes of patients with gastroschisis; a long-term study period may provide a more extensive illustration of the outcomes and complications.

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