Pediatric Surgery International (2018) 34:743–748
https://doi.org/10.1007/s00383-018-4282-9

ORIGINAL ARTICLE

The factors associated with successful early enteral feeding in gastroschisis

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Accepted: 22 May 2018 / Published online: 25 May 2018
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Abstract

Background Gastroschisis is the most common congenital abdominal wall defect. Due to the exposure of midgut to amniotic fluid, the recovery of bowel function is often delayed. This study aimed to identify the factors associated with the successful early enteral feeding in gastroschisis and to develop further guidelines of treatment.

Methods A retrospective cohort study of gastroschisis babies from January 2006 to December 2015 was done. Exclusion criteria were incomplete data and death. Successful early enteral feeding was defined when full feeding was achieved within 21 days of life.

Results One hundred and five gastroschisis patients were divided into a successful early-feeding group ($n=56$, 53%) and a non-successful early-feeding group ($n=49$, 46%). In multivariable analysis, significant factors for successful feeding clustered by primary treatment were female (RR = 1.38, P value < 0.001), gestational age > 36 weeks (RR = 1.23, P value < 0.001), age at surgery less than 10 h (RR = 1.15, P value < 0.001), postoperative extubation time < 4 days (RR = 1.39, P value < 0.001), and age when feeding started less than 10 days (RR = 35.69, P value < 0.001).

Conclusion Several factors were found to be associated with successful early enteral feeding. The modifiable factors found in this study were surgery within 10 h, early postoperative extubation within 4 days, and feeding started before 10 days of life. These will guide the management of gastroschisis to achieve successful early enteral feeding.

Keywords Gastroschisis · Early enteral feeding · Successful feeding · Associated factors

Introduction

Gastroschisis is a Greek terminology originated from "gastros" (belly) and "schisis" (cleft) which is a congenital defect of the abdominal wall causing herniation of intraabdominal organs into the amniotic cavity [1].

The incidence of gastroschisis was four to five per 10,000 live births. The etiology of gastroschisis remains unclear. The main risk factor seems to be a young maternal age [1, 2]. The pathophysiology was uncertain. Some theories suggest that an early involution of the right umbilical vein causes the defects at the right site of umbilicus. Another theory was a vascular accident to the abdominal wall.

In gastroschisis, the intestine was bathed in amniotic fluid which caused intestinal abnormalities. These patients tend to have a slow onset of bowel function, no matter how quickly the defect is reduced or how normal the bowel appears [3].

There were no specific protocols for the determination of enteral feedings after gastroschisis closure [2]. Previously, starting enteral feedings was postponed due to the belief of delayed bowel function. However, during the past 20 years early enteral feeding was introduced and showed an improvement of the treatment outcomes [4]. Walter-Nicolet et al. performed a prospective study of the early trophic feeding within 5 days after surgery and found faster full enteral feeding leads to faster bowel function than the others [5]. Singh et al. reported that enteral feeding within 10 days after closure had a significantly lower incidence of sepsis,

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duration of TPN and hospital stay [6]. The previous data collection in our institute found that hospital stay and duration of total parenteral nutrition used were significantly longer in the patient treated with silo bag which could archive early enteral feeding than in the primary abdominal wall closure.

This study was aimed to clarify the factors associated with the successful early enteral feeding in gastroschisis which reflected the effective treatment outcomes. We expected the advantage of this study will help in further developing a feeding protocol of the newborns with gastroschisis.

Materials and methods

This study was a retrospective cohort analysis approved by the Ethics Committee of Chiang Mai University (CMU) Hospital. Our population was all infants with gastroschisis (ICD-10 codes Q79.3) treated in Maharaj Nakorn Chiang Mai Hospital from January 2006 to December 2015. The electronic database reviews included characteristic data, associated anomalies, peri-operative, postoperative data and feeding data. We excluded patients with incomplete electronic data, and patients who died. The patients were divided into two groups: those were successful with early enteral feeding and unsuccessful feeding groups.

The standard treatment was performed in the patients who met the above criteria by the pediatric surgeons and pediatricians in Chiang Mai University Hospital. The main treatments were primary fascial closure or silo closure according to the abdomino-visceral proportion. The feeding was started according to our feeding protocol which was the resume of normal bowel function. Normal bowel function was determined by the presence of normal bowel sound, passage of the stool, reduction of the nasogastric content and the disappearance of the bilious content aspiration from nasogastric tube. The patients who had continuous feeding without an episode of feeding intolerance until full feeding within 21 days of life were defined as successful feeding [7].

Statistical analysis was performed with commercial statistical software (STATA 11.0; StataCorp LP, College Station, TX, USA). The categorical data were reported in count and percent. The continuous data were reported in mean and standard deviation or median and interquartile range according to data distribution. The univariable analysis was done by Fisher's exact test for categorical data and Student's *t* test or Mann–Whitney *U* test for continuous data. The multivariable analysis was performed, choosing variables with a *P* value of <0.2 in univariable analysis, by use of an exponential risk regression model with stepwise variable selection, to identify factors associated with successful enteral feeding in gastroschisis patients and reported by risk ratio (RR) clustered by primary treatment. The statistical significance level was set as two tailed with *P* values ≤ 0.05.

Results

One hundred and twenty-one gastroschisis patients were treated in CMU from January 2006 to December 2015. Sixteen patients were excluded from the study; eight patients had incomplete data and eight patients died. One hundred and five gastroschisis patients remained in the study as shown in Fig. 1. The numbers of newborns with successful early feeding vs unsuccessful feedings were 56 and 49, respectively. The factors that influenced the successful early feeding were analyzed by the univariable (Tables 1, 2, 3, 4) and multivariable (Table 5) analyses. In the univariable model, the significant factors for successful early feeding were age at the surgery, primary repair, extubation hour, presence of electrolyte imbalance and age of enteral feeding start. After multivariable analysis was done, we found that the significant factors for successful early feeding clustered by primary treatment were female

Fig. 1 Flow of the study

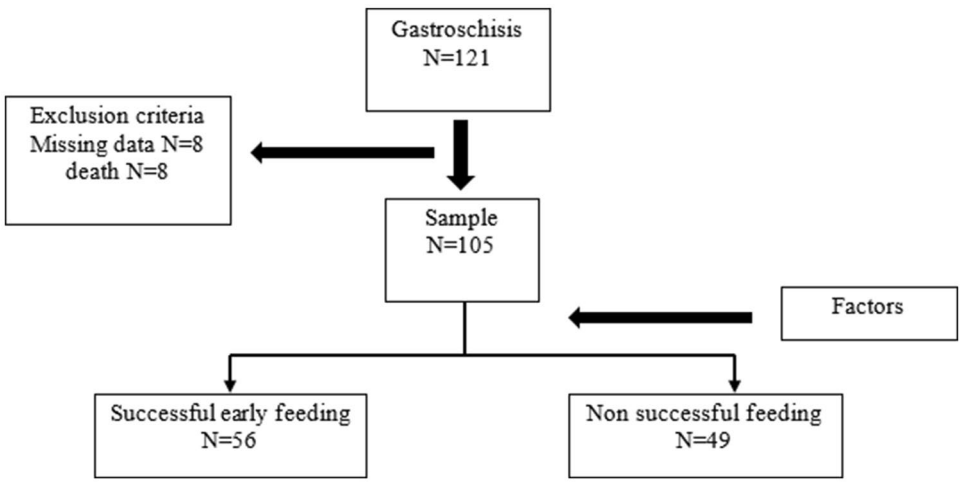

Table 1 Baseline characteristics (demographics and symptoms) of newborns with successful early feeding ($n=56$) and non-successful early feeding ($n=49$) in gastroschisis

Characteristics	Successful early feeding *N* (%)	Non-successful feeding *N* (%)	*P* value
Sex			
Male	21 (50.00)	21 (50.00)	0.690
Female	35 (55.56)	28 (44.44)	
Maternal age[a] (years)	22.49 ± 5.65	21.25 ± 4.93	0.232
Prenatal diagnosis	25 (48.08)	27 (51.92)	0.846
Mode of delivery			
Vaginal delivery	34 (44.16)	43 (55.84)	0.508
Cesarean section	15 (53.57)	13 (46.43)	
Gestational age[a] (weeks)	36.51 ± 2.11	35.68 ± 2.50	0.071
APGAR at 1 min[a]	7.65 ± 2.09	8.11 ± 2.18	0.280
APGAR at 5 min[a]	8.86 ± 1.65	9.23 ± 1.26	0.190
Birth weight[a] (g)	2361.37 ± 496.02	2293.64 ± 537.35	0.503
Length[a] (cm)	44.85 ± 2.35	44.31 ± 2.65	0.271
Size of defect[a] (cm)	3.10 ± 1.27	3.09 ± 1.02	0.986
Bowel matting	4 (36.36)	7 (63.64)	0.534
Associated anomalies	12 (38.71)	19 (61.29)	0.391
Bowel atresia	1 (16.67)	5 (83.33)	0.212

[a]Mean ± standard deviation

Table 2 Peri-operative data

Characteristics	Successful early feeding *N* (%)	Non-successful feeding *N* (%)	*P* value
Age at surgery[a] (h)	7 (4–10)	11 (6–16)	0.012
Duration of surgery[b] (h)	1.43 ± 0.34	1.52 ± 0.46	0.248
Intraoperative body temperature (°C)	35.62 ± 0.86	35.59 ± 1.12	0.882
Treatment			
Primary repair	49 (62.82)	29 (37.18)	< 0.001
Silo placement	0 (0.00)	26 (100.00)	
Blood loss[a] (ml)	2.5 (0–5)	1 (0–5)	0.338
Fluid administration[a] (ml)	45 (34.5–65.5)	46 (33–58)	0.984

[a]Median (interquartile range)

[b]Mean ± standard deviation

Table 3 Postoperative data

Characteristics	Successful early feeding *N* (%)	Non-successful feeding *N* (%)	*P* value
Extubation[a] (h)	2.78 ± 2.32	5.21 ± 7.17	0.025
First spontaneous stool evacuation[b] (day)	1 (1–2)	1 (1–2)	0.107
Serum albumin[a] (g/dl)	2.36 ± 0.54	2.26 ± 0.45	0.356
Presence of electrolyte imbalance	17 (35.42)	32 (57.14)	0.032
Duration of postoperative acidosis[b] (h)	6 (2–24)	8 (0–28)	0.736

[a]Mean ± standard deviation

[b]Median (interquartile range)

Table 4 Feeding data

Characteristics	Successful early feeding *N* (%)	Non-successful feeding *N* (%)	*P* value
Start of enteral feeding[a] (day of life)	8 (7–9)	16 (12-21.5)	< 0.001
Initial volume[b] (ml/kg/day)	9.5 ± 5.99	9.71 ± 5.52	0.8534
Type of feeding			
Bolus	44 (45.36)	53 (54.64)	0.701
Continuous	4 (57.14)	3 (42.86)	
Type of milk			
Breast	24 (42.11)	33 (57.89)	0.712
Formula	1 (50.00)	1 (50.00)	
Mixed	23 (51.11)	22 (48.89)	

[a]Median (interquartile range)

[b]Mean ± standard deviation

Table 5 Multivariable risk ratio of newborns with successful early enteral feeding in gastroschisis clustered by primary treatment

Characteristics	Crude risk ratio (95% confidence interval)	*P* value	Multivariable risk ratio (95% confidence interval)	*P* value
Female	1.11 (0.87–1.40)	0.396	1.38 (1.22–1.55)	< 0.001
GA > 36 weeks	1.57 (0.79–3.09)	0.196	1.23 (1.12–1.34)	< 0.001
Age at surgery < 10 h	1.88 (0.50–7.03)	0.349	1.15 (1.11–1.19)	< 0.001
Postoperative extubation < 4 days	2.05 (0.27–15.52)	0.489	1.39 (1.32–1.46)	< 0.001
Age at start feeding < 10 days	38.07 (4.84–299.53)	0.001	35.69 (5.57–228.69)	< 0.001

GA gestational age

(RR = 1.38, $P < 0.001$), gestational age (GA) > 36 weeks (RR = 1.23, $P < 0.001$), age at surgery < 10 h (RR = 1.15 $P < 0.001$), postoperative extubation < 4 h (RR = 1.39, $P < 0.001$), and age when feeding started < 10 days (RR = 35.69, $P < 0.001$).

In 56 newborns with unsuccessful early enteral feeding, three patients also had a necrotizing enterocolitis (NEC) whereas there were no NEC patients in the successful early enteral feeding group. The hospital stay was statistically lower in the successful early-feeding group (P value < 0.001). The necrotizing enterocolitis has no significant different between two groups (success vs non-success group; 3 vs 0 cases, P value = 0.246). Median length of stay in patient who had successful early feeding was 22 days (interquartile range 19–27 days) whereas in non-success group was 43 days (interquartile range 29–65 days).

Twenty-nine patients were in the primary closure group with failure to proceed to successful enteral feeding; 9 were males and 20 were females. Most of them were preterm vaginal deliveries ($N = 23$, 79.31%). In this group, there were associated anomalies ($N = 10$, 34.48%), bowel atresia ($N = 3$, 10.34%), bowel gangrene ($N = 1$, 3.45%), NEC ($N = 2$, 6.90%). None of the silo-closure group had successful early enteral feeding.

Discussion

This study showed that there were many factors associated with the successful early enteral feeding. The significant factors associated with successful early enteral feeding in our study were female, GA > 36 weeks, age at surgery < 10 h, postoperative extubation < 4 days and age at start of enteral feeding < 10 days.

No one of the surgical treatment options for gastroschisis patient was suitable for every patient [8]. Primary closure was still considered to be the ideal correction if it could be done [9]. Delayed closure was associated with a high rate of sepsis, delayed feeding and other complications [10]. In our study, as mentioned before, primary repair had better successful enteral feeding outcomes. The silo treatment group referred to the larger viscero-abdominal disproportion and could not be closed which could be the cause of delayed feeding. However, many studies provided different aspects in the closure of gastroschisis defect. They suggested that staged closure or silo treatment had also fewer days on mechanical ventilation, decreased time to full enteral feeding, decreased length of hospital stay, morbidities and cost of treatment [11, 12]. Schmidt et al. [13] found that staged closure when

using an intraoperative intravesical pressure (IVP) below 20 cmH_2O did not increase length of hospital stay or frequency of complications. A meta-analysis by Kunz et al. [12] reported that with the least selection bias, silo closure was associated with better outcomes.

Some studies showed that compromised bowel such as atresia or ischemia was the predictor of a complicated postoperative course. The time to achieve full enteral feeding and the length of stay could be longer. The risk of sepsis was also presented in the gastroschisis patient with intestinal atresia or other intestinal damage before closure [14]. Our study also showed shorter length of stay in successful early-feeding group.

Many studies showed no relationship between gender and outcome of treatment in gastroschisis. Snyder et al. stated that sex was not a significant predictor of intestinal function [15]. In our study, gender was one of the factors associated with the successful early enteral feeding. Female newborns were more likely to achieve the goal of treatment as shown in multivariable analysis.

Giving an appropriate gestational age of delivery was also controversial in the management of a newborn with gastroschisis [1, 16]. Some studies suggested that limiting the exposure of the bowel to amniotic fluid by preterm delivery with Cesarean section might improve the outcome of treatment [16]. Moir et al. prospectively studied that earlier delivery (GA 34.2 vs GA 37.7 weeks) had no bowel compromise and earlier establishment of full enteral feeding and shorter length of stay [1]. Schmidt et al. [13] suggested that GA < 35 weeks was a feasible time to undergo the primary repair, whereas Maramreddy et al. stated that the exposure to amniotic fluid had not always been correlated with bowel damage (the intestinal peel, a collection of fibrin and collagen: pathognomonic sign of intestinal damage). As a matter of fact, the morbidity associated with preterm delivery was a concern [17]. Ergun et al. also reported the delivery before 36 weeks was associated with longer hospitalization by the preterm birth complications and delayed achievement of full feeds by significant delaying in the return of intestinal function [18]. Vilela et al. found that gastroschisis newborns with GA less than 37 weeks and birthweight less than 2500 g had an increased risk of death [17, 19]. In our study, we found that the delivery at GA > 36 weeks supported successful early feedings.

Many studies were performed to determine the effects of time from delivery to the surgery in gastroschisis. Nevertheless, none of them revealed this relationship. Singh et al. concluded that the time to closure of the defect should be balanced with the time to stabilization and should not be hurried [6]. Walter-Nicolet et al., on the other hand, was the one who had a significantly different data in the study. They found that the early feeding of gastroschisis newborns had a median time to surgery at 2.8 h of life while the control group had median time to surgery at 3 h [5]. From our results, the age at the surgery of less than 10 h tended to have a greater success in early enteral feeding. However, our study had a place of birth as a confounding factor. Some patients were born outside Chiang Mai University Hospital and had been referred in. Time from delivery to the operating room might have been increased due to this factor.

Accordingly, patients with respiratory problems might develop delayed bowel function due to blood oxygenation to bowel and can be related to the difficulty in reduction which caused delayed enteral feeding. The prolonged extubation time might be used for the prediction of the successful enteral feeding. Our study showed that gastroschisis in newborns with postoperative extubation within 4 days of life was a significant factor promoting successful early enteral feeding. Only few studies mentioned about the time of extubation after the operation and did not affect the outcomes of gastroschisis treatment [5].

The benefits of early enteral feeding were provision of trophic substance to the gastrointestinal tract, increase of GI motor activity, and protection of bacterial translocation across the gut mucosa [4, 20, 21]. Early trophic enteral feeding was widely recommended to reduce length of stay and shorten the duration of TPN [1, 6]. Sharp et al. stated that each day of delay in enteral feeding increased the length of stay and TPN duration [4]. Walter-Nicolet et al. prospectively studied the early trophic feeding within 5 days after the abdominal wall closure and found that full enteral feeding was reached faster than the others [5]. Singh et al. also reported that gastroschisis with enteral feeding within 10 days of operation had a significantly lower incidence of sepsis, duration of TPN and hospital stay [6]. Our study also supported these statements. There were good results in the gastroschisis newborns who started enteral feeding within 10 days of life. These patients tended to succeed in early full feeding within 21 days, had lower complications and a shortened length of hospital stay.

Patients in the primary closure group with failure to proceed to successful enteral feeding had no significant data to describe the results of these cases. Subgroup analysis or additional studies are needed to gain more details about this topic.

Limitations of our study were this was a retrospective study, and choice of surgery and protocol for feeding depended on the clinician. However, data were well recorded. There were multidisciplinary team of surgeon, neonatologist, pediatrician and patient care teams who initiated feeding in similar and appropiate protocol as described above.

Conclusion

Several factors were found to be associated with successful early enteral feeding. The modifiable factors found in this study were surgery within 10 h, early postoperative extubation within 4 days, and starting to feed before 10 days of life. These will guide the management of gastroschisis to achieve successful early enteral feeding.

Compliance with ethical standards

Conflict of interest We report no conflicts of interest in this work.

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