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Multi-institutional practice patterns and outcomes in uncomplicated gastroschisis: a report from the University of California Fetal Consortium (UCfC)

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Abstract

Background/Purpose—Gastroschisis is a resource-intensive birth defect without consensus regarding optimal surgical and medical management. We sought to determine best–practice guidelines by examining differences in multi-institutional practices and outcomes.

Methods—Site-specific practice patterns were queried, and infant-maternal chart review was retrospectively performed for gastroschisis infants treated at 5 UCfC institutions (2007–2012). The primary outcome was length of stay. Univariate analysis was done to assess variation practices and outcomes by site. Multivariate models were constructed with site as an instrumental variable and with sites grouped by silo practice pattern adjusting for confounding factors.

Results—Of 191 gastroschisis infants, 164 infants were uncomplicated. Among uncomplicated patients, there were no deaths and only one case of necrotizing enterocolitis. Bivariate analysis revealed significant differences in practices and outcomes by site. Despite wide variations in practice patterns, there were no major differences in outcome among sites or by silo practice, after adjusting for confounding factors.

Conclusions—Wide variability exists in institutional practice patterns for infants with gastroschisis, but poor outcomes were not associated with expeditious silo or primary closure, avoidance of routine paralysis, or limited central line and antibiotic durations. Development of clinical pathways incorporating these practices may help standardize care and reduce health care costs.

Keywords

gastroschisis; outcome; uncomplicated; silo; practice

INTRODUCTION

Gastroschisis is a common birth defect that is increasing in prevalence in the United States [1]. Considerable variability in the surgical and medical management of infants with gastroschisis has been noted [2, 3], and a consensus is lacking for the optimal surgical repair method [2–7], ventilation and paralysis strategies [2], pain management [2], antibiotic and central line duration [3], and feeding regimens [8]. Not only do different centers use varying management strategies, but variability within single institutions is also prevalent.

Survival rates for infants with gastroschisis are as high as 90–97% [9–11], but the costs of treating the disease remain significant [12]. Infants often remain hospitalized for more than 30 days [4, 12, 13], and the average hospital charge for an infant with gastroschisis has been reported to be over $180,000 [4]. Surgical literature demonstrates a significant benefit of clinical care pathways for improving quality of care [14–16], yet published protocols are lacking for treatment of gastroschisis [2]. This study aims to evaluate differences in practice patterns and outcomes for infants with gastroschisis in a multi-institutional setting in order to determine best–practice guidelines.

METHODS

Overview

This is a retrospective cohort study of infants with gastroschisis who were evaluated antenatally and born at any of the five University of California Fetal Consortium sites (UCfC: UC San Francisco, UC Davis, UC Los Angeles, UC Irvine, and UC San Diego) during the years 2007–2012. A multi-institutional review board reliance registry provided approval for the study (IRB #10-04093). Patients were identified and maternal and neonatal data were gathered by chart review at each site directly. Infants born at outside institutions were not included because our goal was to evaluate practice patterns within the 5 consortium sites and not the potential confounding impact of outborn delivery, variations in outside hospital management, and transfer. Neonatologists and pediatrics surgeons at each site were asked to provide information regarding standard gastroschisis management practices at their site. In order to preserve site confidentiality, site number was de-identified in the results.

Patients

Complicated gastroschisis was defined as the presence of intestinal atresia, stricture, ischemic bowel prior to closure, or severe pulmonary hypoplasia. Patients with complicated gastroschisis were not included in the analysis because they represented outliers whose response to postnatal institutional practice and ultimate outcomes likely differ from those with uncomplicated gastroschisis. Furthermore, we chose to focus on outcomes in a homogenous population of uncomplicated patients. Data were collected by chart review. Maternal information included self-reported smoking and/or illicit drug use during pregnancy. Infant information collected included gestational age (GA), birth weight standardized for GA (z-score based on 2003 Fenton growth curves) [17], surgical history/ complications, and associated major congenital anomalies. The primary outcome was length of stay. Secondary outcomes were ventilator days, weight gain (grams/day averaged across hospitalization), age at achieving full feeds (100kcal/kg/day or exclusive breastfeeding), cholestasis (direct bilirubin ≥2mg/dL), days with central line in place, total antibiotic exposure days, and bacteremia (defined as positive blood culture requiring treatment for ≥ 5 days).

Site Practices

Representative physicians from each participating site, one neonatologist and one pediatric surgeon, were asked to provide information about their site's preferred practice patterns during the study period for infants with uncomplicated gastroschisis. Representatives were responsible for confirming their responses with their respective faculty. Physicians were asked about preferred method of surgical closure, use of routine intubation/paralysis, duration of prophylactic antibiotics and opiates, feeding practices, and central line use. Results were analyzed by site. For minor discrepancies between representatives, surgeons' answers were used for surgical practices and neonatologists' answers for medical practices.

Data Analysis

Associations between categorical variables were assessed using Pearson's chi-squared or Fisher's exact test as appropriate. To compare the difference in means or distributions of continuous outcomes between the five sites, ANOVA or Kruskal Wallis tests were used (Stata 12.0, College Station, TX). For each outcome, we performed two multivariate analysis Cox proportional hazards models; one with site as an instrumental variable adjusted for confounding factors (with Site 5, the largest site, held as the referent site) and the second with sites grouped by silo practice pattern and adjusted for confounding factors. Logistic regression models were constructed for binary outcomes. Confounding factors included fixed infant characteristics, to account for potential differences in patient populations; these factors were gestational age, birth weight z-score, sex, and maternal smoking and/or drug exposure. Variations in practice were accounted for in the site variable. In addition, we sought to adjust for the degree of visceroabdominal disproportion. We observed that patients who had silos placed at institutions that preferred primary closure generally required at least 5 days of silo prior to definitive closure. Therefore, silo days ≥5 days was used as a marker of gastroschisis severity. P-values <0.05 were considered statistically significant.

RESULTS

Cohort characteristics

We identified 191 infants born with gastroschisis within the UCfC from 2007 to 2012. Twenty-three infants were excluded for complicated gastroschisis, including 19 with bowel atresia or stricture requiring reoperation (10%), two with ischemic bowel prior to definitive closure (1%), and two with severe pulmonary hypoplasia (1%). There were three deaths in these complicated cases. All occurred within the first 9 days of life in premature infants (30–36 week GA). Two of the infants had evisceration of the entire liver and severe pulmonary hypoplasia; one of these two infants also had multiple other anomalies. The third death had an in utero volvulus, jejunal atresia, and congenital heart disease; care was withdrawn by parents. Necrotizing enterocolitis (NEC) developed in one complicated infant and only one uncomplicated infant (born at 34 weeks GA and managed medically).

The cohort of 168 uncomplicated patients used for the analysis had a mean GA of 36.5±1.7 weeks. The majority of infants were preterm (58%) and male (55%). Seven percent of infants had other major anomalies, consistent with prior reports [18]. Fifteen percent of the cohort (n=26) was exposed to maternal smoking or illicit drug use.

Site Practices

All five sites reported that their institutional practices were either similar between providers or protocolized during the study period. Two of the sites reported a preference for primary closure, while the other three sites preferred the use of silos (Table 2). Surgeons reported a wide variety of factors influencing the decision to place a silo, including time/day, defect size, bowel appearance, concern for the development of necrotizing enterocolitis, and patient stability. Three of the five sites practiced "routine intubation" prior to all silo placements; no sites attempted extubation prior to silo closure. No sites paralyzed infants for the duration of silo placement, and only one site reported a policy of routine paralysis for silo reduction.

The reported use of antibiotic prophylaxis following either primary closure or closure following silo reduction varied widely between sites from ≤3 days to >14 days. Four of five sites reported the standard use of ampicillin and gentamicin; one site reported use of cefotaxime and metronidazole. All sites preferred to begin with trophic feeds of breast milk, though there were minor variations in advancement schedules. Only two institutions report altering parenteral nutrition, particularly Intralipid-20%® (Fresenius Kabi, Uppsala, Sweden) administration, in infants requiring prolonged parenteral nutrition to prevent cholestasis during the study period.

Univariate results

The primary outcome, length of stay, was significantly different between sites with means ranging from 31 to 42 days (p<0.001, Figure 1). Among all sites, 42% of patients (n=70) had a primary closure and 58% (n=98) had a silo placed, although this varied by site (p<0.001) (Table 2). Time spent in a silo also varied by site (p<0.001). Despite wide variation in reported preference for antibiotic duration following closure, the actual days of antibiotics received was less variable with means ranging from 10 to 15 days (p=0.04). Duration of central line use ranged from an average of 20 to 34 days (p=0.001). Ventilator days also varied significantly between sites (p<0.001) (Figure 2). Those sites that reported routinely intubating all infants receiving silo had a higher mean duration of ventilation than those who did not (7.9 ± 7.0 versus 5.6 ± 5.2 days, p=0.003). Age at achieving full feeds also varied significantly between sites (Table 2).

Multivariate results

For the multivariate analysis using site as an instrumental variable, Site 5 was the reference group since this site had the largest number of patients. Overall, site was not associated with longer length of stay (p=0.07) after adjusting for potential confounding factors (sex, GA, birth weight z-score, smoke/drug exposure, and silo ≥5 days). When analyzing the data by closure strategy, routine silo placement was not predictive of prolonged length of stay (p=0.17). Regardless of the statistical model, female sex, lower gestational age, and lower birth weight z-score were significantly associated with prolonged length of stay.

In contrast, site was significantly associated with greater ventilator days after adjusting for confounding factors (P<0.001) with Sites 1, 2, and 4 having decreased ventilator days. Two of these three sites use primary closure as their preferred strategy; the other had the lowest mean silo days. When grouping the sites by silo practice pattern, routine use of silos was associated with longer ventilation (Hazard Ratio 2.0, p<0.001). Other neonatal factors including sex, GA, birth weight z-score, and smoke/drug exposure were not associated with duration of ventilator support (Table 3).

Neither site nor silo practices were predictive of age at reaching full feeds (p=0.41 and p=0.41) after adjusting for confounding factors. However, female sex and lower gestational age were predictive of older age at reaching full feeds (p=0.009 and p=0.03). Of note, female sex was also associated with a 4 gram/day lower weight gain as compared to males (p=0.01).

Silo placement ≥5 days was significantly associated with prolonged length of stay, prolonged ventilation, increased time to full feeds, and cholestasis. When looking only at the subset of infants with silo in place <5 days, number of silo days was associated with increased ventilator days (p=0.001), but not with increased length of stay (p=0.74), cholestasis (p=0.07), or reaching full feeds (p=0.44).

DISCUSSION

The optimal surgical and neonatal management of gastroschisis remains an area of debate. Despite abundant literature on the subject, consensus regarding best practice has not been reached. The current study is a large, contemporary, multi-institutional report on both preferred practice patterns and outcomes for infants with uncomplicated gastroschisis. The study confirms the existence of wide variability in institutional practice patterns, but importantly demonstrates that poor outcomes were not associated with expeditious silo or primary closure, avoidance of routine paralysis, or limited central line and antibiotic durations.

Despite wide institutional variation in use of silo, duration of silo, intubation/paralysis strategies, and medication use, we have found no institutional differences in our primary outcome of length of stay after adjusting for confounding neonatal characteristics. Institutions with less invasive approaches to intubation and paralysis as well as institutions using expeditious closure (either primarily or with silo) also appear to have a lower overall duration of ventilation. One institution preferring longer duration of silo reported a concern for NEC and increased mortality with earlier closure. Both in the overall cohort and in the uncomplicated gastroschisis, NEC was much less common (1.6% and 0.6%) than previously reported [19]. Furthermore, the survival rate for the uncomplicated cases was 100%, and overall survival was 98.4% for the entire cohort. Given the absence of adverse effects seen with expeditious closure and the increased cost and potential adverse effects of prolonged ventilation, closure in a timely manner is warranted. Furthermore, the lack of poor outcomes with decreased use of paralytics, opiates, and antibiotics suggests that a "less is more" approach will not result in worse prognosis.

When comparing surgical closure method, our study showed no significant differences in most outcomes based on method. The debate of silo versus primary closure has been ongoing for decades with no clear superior choice based on the literature [1–7]. While silo placement may be associated with increased ventilator days, there was no effect on age reaching full feedings or overall length of stay (LOS). Additionally, among those infants treated with a silo for a limited time (<5 days), the amount of time spent in a silo also did not correlate with poor outcomes other than increased ventilator days. Alternatively, use of a silo for ≥5 days was a significant predictor of multiple poor outcomes including prolonged LOS, prolonged ventilation, increased time to full feeds, and cholestasis. This may be secondary to inherently worse disease preventing earlier closure in patients with silo ≥5 days having a greater degree of visceroabdominal disproportion or other feature of more severe forms of gastroschisis. However, an additional explanation is that practice patterns that favor slow reduction of the silo may contribute to prolonged ventilator days and length of stay.

We suspect that both severity of disease and practices favoring slow silo reduction may contribute to the poor outcomes associated with silo ≥5 days.

Although management strategies are not well correlated with particular outcomes, fixed neonatal characteristics were associated with poor outcomes. As expected, lower gestational age and lower birth weight z-scores were associated with prolonged LOS and delayed time to full feeds. However, we unexpectedly found that male infants had shorter LOS, faster time to full feeds, and superior weight gain to their female counterparts. Sex-related outcomes in gastroschisis have not specifically been extensively examined; however, two studies showed inferior outcomes (increased cost in one and increased mortality in the second) for male sex [12, 20]. No studies have demonstrated worse prognosis for female infants, and the cause of the association found here remains unclear.

This study is primarily limited by its retrospective nature. Specifically, reported practice-pattern preferences should be interpreted with caution as these may not accurately reflect actual practice. One such example is that the reported duration of antibiotic prophylaxis following silo reduction is shorter than the observed total antibiotics days. This may be secondary to the treatment of an infection beyond or after the period of prophylaxis resulting in an increased mean antibiotic days rather than inaccurate reporting of practice patterns. We did observe a high concordance between surgeon- and neonatologist- reported practices. Other potential limitations include the exclusion of outborn patients and the relatively small sample size, particularly when comparing individual sites; however, this study represents one of the largest reported cohorts to date.

Despite wide variations in practice patterns in this multi-institutional study, there were no major differences in outcome among sites or by silo practice. Although the mortality rate is extremely low in gastroschisis, the morbidity and cost of the disease remain high. Implementation of clinical care pathways have demonstrated success in quality improvement and cost reduction in surgical fields [14–16]. Therefore, development of a multi-institutional clinical pathway may be the most effective management strategy to decrease morbidity for gastroschisis. In order to develop a clinical pathway, a multidisciplinary working group of UCFC members was established to provide consensus recommendations for the management of gastroschisis:

1. Expeditious surgical closure, whether by primary closure or silo, when clinically feasible.

2. Shorter duration of intubation and avoidance of routine paralysis should be considered.

3. Judicious use of opiates with consideration of adding non-opiate medications for supplemental pain management

4. Reduction in the number of days of antibiotic prophylaxis when no definitive infectious risk factors are present.

Our plan is to implement these guidelines across the UC sites with the goal of standardizing care, improving outcomes, decreasing costs, and providing evidence to support these recommendations.

Acknowledgments

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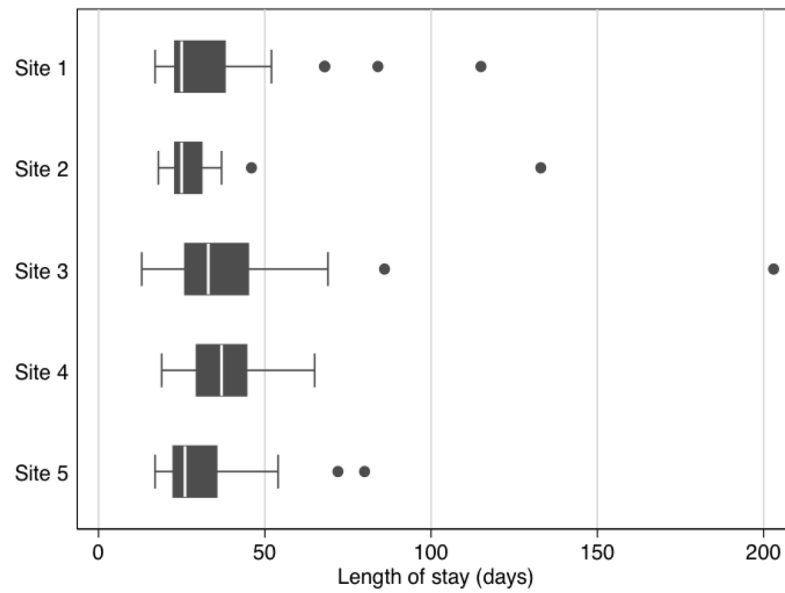
Figure 1. Length of stay by site
These boxplots demonstrate the distribution of the primary outcome, length of stay, among the five sites. The box represents the interquartile range with the median as the line within the box. Points beyond the whiskers represent outlying data.

Figure 2. Ventilator days by site
These boxplots demonstrate the distribution of ventilator days among the five sites. The box represents the interquartile range with the median as the line within the box. Points beyond the whiskers represent outlying data.
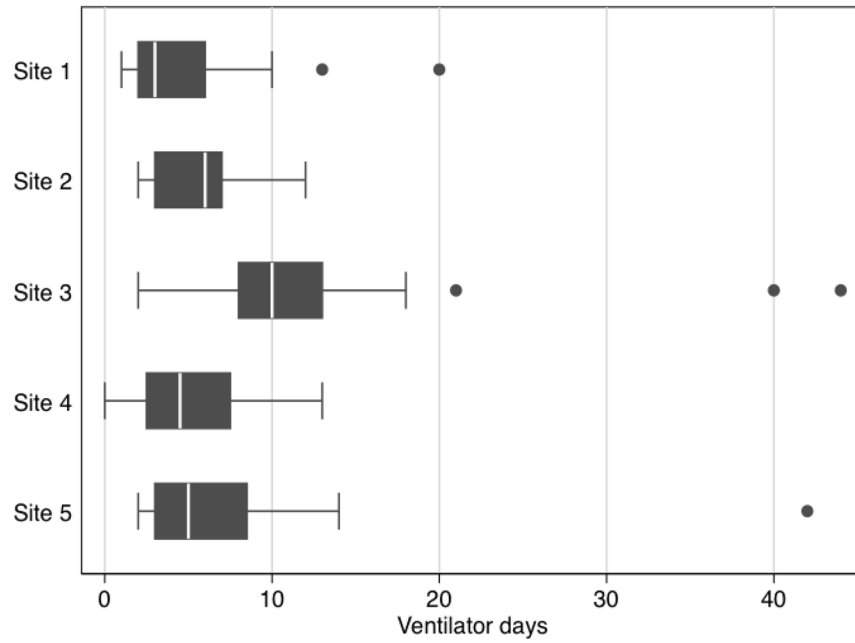
Table 1

Baseline cohort characteristics.

	All sites	Site 1	Site 2	Site 3	Site 4	Site 5	p value[*]
	n=168	n=42	n=13	n=29	n=36	n=48	
Maternal smoking/drug use	15% (26)	24% (10)	0% (0)	21% (6)	19% (7)	6% (3)	0.05
Gestational age (weeks)	36.5 ± 1.7	36.0 ± 1.4	36.8 ± 1.8	37.3 ± 1.6	36.8 ± 1.7	36.2 ± 1.7	0.67
Birth weight (kilograms)	2.5 ± 0.5	2.5 ± 0.4	2.6 ± 0.4	2.6 ± 0.5	2.4 ± 0.5	2.5 ± 0.5	0.67
Male sex	55% (92)	50% (21)	62% (8)	59% (17)	50% (18)	58% (28)	0.85
Other congenital anomalies	7% (11)	5% (2)	8% (1)	0% (0)	11% (4)	8% (4)	0.38

[*] Comparisons made using analysis of variance for continuous variables, and chi squared test or Fisher's exact for categorical variables. Data is presented as %(N) or mean ± SD.

Table 2

Practices and outcomes by site (univariate analysis)

	All sites	Site 1	Site 2	Site3	Site 4	Site 5	p value*
	N=168	N=42	N=13	N=29	N=36	N=48	
Site Practices							
Routine silo placement	-	No	Yes	Yes	No	Yes	-
Routine intubation prior to silo placement	-	No	Yes	Yes	Yes	No	-
Routine paralysis during silo reduction	-	No	No	Yes	No	No	-
Antibiotic prophylaxis following silo reduction §	-	4–7 d	7–14 d	≤3 d	7–14 d	≤3 d	-
Opiate use with silo		4–7 d	7–14 d	≥14 d	≥14 d	≤3 d	
Opiate use with primary closure		4–7 d	4–7 d	7–14 d	≥14 d	≤3 d	
Characteristics							
Silo (yes/no)	58% (98)	17% (7)	77% (10)	93% (27)	39% (14)	83% (40)	<0.001
Number of silo days¶	4.9 ± 3	6.3 ± 1.3	4.7 ± 2.7	6.3 ± 3.1	5.9 ± 1.6	3.5 ± 2.9	<0.001
Silo ≥5 days†	36% (60)	17% (7)	46% (6)	72% (21)	33% (12)	29% (14)	<0.001
Antibiotic days	11 ± 7	10 ± 8	12 ± 8	15 ± 9	12 ± 8	10 ± 5	0.04
Central line days	26 ± 15	26 ± 16	26 ± 18	34 ± 18	26 ± 11	20 ± 10	<0.001
Outcomes							
Length of stay (days)	35 ± 21	33 ± 20	36 ± 30	43 ± 36	38 ± 10	31 ± 13	<0.001
Ventilator days	6.7 ± 6.2	4.2 ± 3.8	5.5 ± 2.9	12.1 ± 9.4	5.4 ± 3.4	6.8 ± 6.1	<0.001
Age at full feeds (days)	29 ± 19	30 ± 15	28 ± 19	39 ± 37	26 ± 10	26 ± 9	<0.001
Cholestasis	21% (35)	12% (5)	31% (4)	17% (5)	33% (12)	19% (9)	0.16
Bacteremia	12% (20)	17% (7)	8% (1)	17% (5)	14% (5)	4% (2)	0.25
Gastrostomy tube	2% (3)	2% (1)	8% (1)	3% (1)	0% (0)	0% (0)	0.15

*
Comparisons made using analysis of variance or Kruskal Wallis test for continuous variables and Chi squared or Fishers exact test for categorical variables. Data is presented as %(N) or mean ± SD.

§
Antibiotic prophylaxis for primary closure was the same as for silo prophylaxis at all sites except site 2 (4–7 days following primary closure).

¶
Mean number of days in silo among those with silo placement.

†
Proportion of total patients who had a silo in place for ≥5 day.

Table 3

Multivariate analysis.

Covariate	Length of Stay			Ventilator Days			Cholestasis		
	Hazard Ratio	95% CI	p value[*]	Hazard Ratio	95% CI	p value[*]	Odds Ratio	95% CI	p value[*]
Routine silo placement	0.77	(0.57, 1.10)	0.17	2.00	(1.41, 2.77)	<0.001	0.71	(0.32, 1.57)	0.34
Silo ≥5 days	1.75	(1.25, 2.43)	0.001	6.25	(4.12, 9.49)	<0.001	2.54	(1.12, 5.74)	0.03
Male sex	0.58	(0.42, 0.81)	0.002	0.88	(0.64, 1.23)	0.47	1.08	(0.49, 2.40)	0.84
Gestational age (weeks)	0.91	(0.84, 0.98)	0.02	0.93	(0.84, 1.02)	0.13	0.79	(0.63, 1.00)	0.05
Birth weight z-score	0.80	(0.66, 0.97)	0.02	1.15	(0.94, 1.40)	0.17	0.86	(0.51, 1.44)	0.56
Smoke or drug exposure	0.75	(0.48, 1.16)	0.19	1.01	(0.65, 1.58)	0.95	0.43	(0.12, 1.57)	0.20

[*] Cox proportional hazards was used for time dependent outcomes and logistic regression for binary outcomes.