Published in final edited form as:

J Pediatr Surg. 2009 May ; 44(5): 918–923. doi:10.1016/j.jpedsurg.2009.01.036.

Predicting the Outcome of Newborns with Gastroschisis

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Abstract

Objective—Determine factors predicting outcome in newborns with gastroschisis

Methods—Retrospective analysis of 155 consecutive cases admitted from 1 January 1990 to 31 December 2007. Prenatal ultrasound findings were available for 89/155 (57%) patients and were compared to final outcome. Both univariate and multiple regression analyses were used.

Results—All patients survived to discharge home. The primary outcome measure was length of stay (LOS). Multiple regression identified four factors associated with LOS: 1) gestational age ($p=0.004$), 2) non-elective silo ($p<0.001$), 3) gastrointestinal (GI) complication (intestinal atresia, perforation, or resection) ($p<0.001$), and 4) non-GI anomaly ($p=0.029$). Non-GI anomalies occurred in 17/155 (11%) patients and tended to increase the risk of a non-elective silo or GI complication (59% vs. 39%, $p=0.190$). Dilated bowel (>10 mm) on prenatal ultrasound was associated with GI complications (22% vs. 3%, $p=0.010$). However, 78% of patients with dilated bowel on prenatal ultrasound did not have a GI complication. The absence of dilated bowel on prenatal ultrasound accurately predicted the absence of GI complications in 97% of cases.

Conclusion—Prematurity, non-elective silo, GI complications, and non-GI anomalies predict the short-term outcome of newborns with gastroschisis. Prenatal ultrasound serves primarily to predict the absence of GI complications.

Keywords

Newborn; Neonatal Intensive Care; Surgery; Gastroschisis; Prenatal Ultrasound

Introduction

Gastroschisis causes significant morbidity(1,2) and has increased in frequency over the past 20 years.(3,4) Although few patients die, treatment often involves an unpredictably variable and long length of hospital stay (LOS) that entails high treatment costs.(1,2,4,5) Outcome has been examined with regard to preterm delivery,(6) route of delivery,(7) labor,(8) rupture of amniotic membranes,(8) meconium staining of the amniotic fluid(9,10) maternal substance

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abuse,(11) and prenatal ultrasound.(12,13) Our experience, like that of others,(1,2) suggests that gastroschisis patients could be divided into two groups: simple cases with primary repair, and complex cases with either a small abdominal cavity or gastrointestinal (GI) complications (intestinal atresia, perforation, or resection). This study sought to expand on previous work by also examining the influence of non-GI anomalies on LOS.

Among all possible prenatal predictors of outcome, prenatal ultrasound has appeared the most promising. Obstetricians now diagnose many cases of gastroschisis before birth, leading to prenatal family consultation. However, prenatal ultrasound findings may over predict complications.(13,14) We propose that prenatal ultrasound findings serve best to identify patients at low-risk, rather than high-risk of GI complications.

Methods

Patient Data

This retrospective study included all gastroschisis patients who were born between 1 January 1990 and 31 December 2007 and admitted to the NICU of Children's Hospitals and Clinics of Minnesota-Minneapolis Campus NICU. The NICU serves as a regional referral, tertiary center for approximately 20,000 deliveries per year. The same, eight-person, pediatric surgical group treated all patients within the first few hours after delivery.

Patients were identified prospectively as part of an ongoing NICU outcome data collection and monitoring project. No patient was excluded from the study. Neonatal nurse practitioners prospectively collected demographic, diagnostic, treatment, and short-term outcomes data on all NICU patients. The database manager verified the collected data against the discharge summary, X-ray, and other reports to ensure data accuracy. Additional perinatal and surgical data were obtained by retrospective review of medical and surgical records. The Institutional Review Boards of Children's Hospitals and Clinics of Minnesota (No. 0502-011) and Abbott Northwestern Hospital (No. 2134-1X) approved the use of patient data in this study.

Clinical Definitions

Diagnosis was confirmed at surgery by the surgeon. Primary closure was attempted in all cases, but if the viscera could not be replaced into the abdominal cavity without excessive intra-abdominal pressure, a silo was placed as the first stage of a staged repair. Patients were categorized into three groups: primary repair, non-elective silo (for an abdominal cavity deemed too small to allow primary repair), and gastrointestinal (GI) complication (atresia, perforation, resection). Patients who received a silo for only a few hours, awaiting surgical repair and who then underwent complete repair, were considered as having had a primary repair. Patients with both a silo and a GI complication were categorized in the GI complication group.

Estimated gestational age was based on last menstrual period or early ultrasound evidence, if available. The gender-specific standards of Kramer, et al.(15) for birth weight (BW) < 10th percentile were used to classify patients as small for gestational age (SGA).(23) Delivery at < 37 completed weeks gestation was considered preterm. Undescended testes were considered to be related to the gastroschisis and were not included as a separate anomaly.

Prenatal Ultrasounds

Board-certified specialists in maternal-fetal medicine read all ultrasound exams. There were 89 patients with complete ultrasound data. The most recent complete exam that was obtained within four weeks of delivery was used for analysis. Fetal abdominal circumference and amniotic fluid index were estimated using published standards.(16,17)

Statistical Analysis

Normality of the data was examined using the Shapiro-Wilk test. Variables that were not normally distributed are summarized as median and range. Univariate analyses were performed using the Wilcoxon rank-sum or Fisher exact tests, as appropriate. Linear regression was used to determine the contribution of parenteral nutrition to LOS. Variables associated with LOS at a $p < 0.10$ were included in the multiple regression (Cox proportional hazards analysis of time to discharge). Data were analyzed using Stata, version 10.1 (Stata, Inc., College Station, Texas). A p -value of < 0.05 in multivariate analyses was considered statistically significant.

Results

Study Population Characteristics

There were 155 patients in this study. The gestational age was 36 ± 2 weeks (mean $\pm$ SD) and the birth weight was 2408 ± 507 grams. Demographic and descriptive features appear in Table 1 and were similar to those previously described. Non-GI anomalies occurred in 17/155 (11%) (Table 2). No patient had abnormal chromosome studies, but not all patients were tested. All patients survived to hospital discharge, although five were receiving parenteral nutrition at discharge and two are known to have died after discharge. There were 91 patients with primary repair, 37 with a non-elective silo and no GI complication, and 27 with a GI complication, of whom 8 also had a silo (Figure 1). The median LOS was 33 days (range = 8-188) and the median number of IV days was 26 (7-148). As expected, parenteral nutritional support explained 86% of variation in LOS ($R^2 = 0.856$).

Maternal and Neonatal Factors Associated with LOS

Multivariate analysis (Cox proportional hazards) confirmed a significant association with LOS for gestational age ($p = 0.004$), GI complication ($p < 0.001$), small abdominal cavity requiring a silo ($p < 0.001$), and non-GI anomaly ($p = 0.029$) (Figure 2). The most important predictor of LOS was GI complication (Figure 1). Factors not associated with LOS were maternal race, marital status, maternal age, duration of ruptured membranes, amount of amniotic fluid at delivery, cigarette use, small for gestational age, and outborn status (Table 1). Delivery by cesarean section and meconium or bile in the amniotic fluid at delivery both had a $p < 0.10$ in the univariate analysis, but were not significant in multivariate analysis ($p = 0.160$ - 0.647). Gestational age ($p = 0.004$), silo ($p < 0.001$), and GI complication ($p < 0.001$) also predicted IV days. Non-GI anomaly trended similarly, but did not reach statistical significance as a predictor of IV days ($p = 0.063$).

Non-GI Anomalies

There were 17/155 (11%) of patients with non-GI anomalies (Table 2). Five patients had cardiac anomalies, four had central nervous system, four had skeletal, and two had renal anomalies. Three patients had arthrogryposis of unknown etiology (Table 2). Patients with non-GI anomalies were somewhat more likely to require a non-elective silo or have a GI complication (59% vs. 39%), but this relationship was not significant ($p = 0.190$).

Prenatal Ultrasound

There were 89/155 (57%) patients who had prenatal ultrasound results obtained at ≤ 4 weeks of delivery (Table 3). We examined four potential predictors of adverse outcome: amniotic fluid volume, estimated abdominal circumference, dilated intestine ≥ 10 mm., and dilated intestine ≥ 18 mm. Low amniotic fluid volume and estimated abdominal circumference $< 5^{\text{th}}$ percentile had no predictive value for either GI complications or a silo (Table 3). Fetuses with dilated intestine ≥ 10 mm were more likely to have a GI complication ($N = 50$, 22% vs. 3%, $p = 0.010$). Similarly those with dilated intestine ≥ 18 mm were also more likely to have GI

complication (N=38, 26% vs. 4%, $p=0.003$). However, the many false-positive predictions so reduced the predictive power as to make dilated bowel unhelpful in predicting outcome. For example, of the 38 patients with dilated intestine ≥ 18 mm., 28 had no GI complication. Restricting the analysis only to patients with atresia and using a cutoff of ≥ 20 mm. of dilation did not improve the positive predictive power. Of 25 patients with intestinal dilation ≥ 20 mm., only 7 (28%) had intestinal atresia. However, the absence of dilated intestine ≥ 18 mm, correctly predicted the absence of GI complications in 96% of cases and primary repair in 71% of cases.

Discussion

This study examined the clinical course and outcome of 155 consecutively admitted newborns with gastroschisis. This relatively large series examined clinical findings affecting the short-term outcome as measured by LOS, which is largely driven by the duration of parenteral nutrition support. Our results, while largely similar to those of others,(1,18) are unique in suggesting a possible relationship between GI outcome and non-GI anomalies even after adjustment for other risk factors. The four factors that influenced outcome in this study were prematurity, non-elective silo, GI complication (intestinal atresia, perforation, or resection), and non-GI anomaly (Figure 1).

We also investigated the ability to predict outcome by prenatal ultrasound. Our study is one of the largest to address this issue. We examined four prenatal ultrasound findings. Amniotic fluid volume was studied because of our anecdotal observations that low amniotic fluid volumes were associated with GI complications. Abdominal circumference was studied because it intuitively should predict the size of the abdominal cavity and the requirement for a silo. Dilated intestine was included because it might predict atresia or other GI complication. Our findings confirm those of others indicating that prenatal ultrasound produces many false positive predictions of adverse outcome.(13,19,20) None of our findings reliably predicted GI complications or the need for a silo. The prenatal ultrasound may be helpful in predicting an uncomplicated, primary repair.

Prenatal ultrasound has many pitfalls as a predictive tool for gastroschisis. For example, dilated colon and dilated small intestine may have different implications and distinguishing between the two can be difficult on ultrasound. Furthermore, only ultrasounds shortly before delivery (≤ 4 weeks in this study) should be used for these predictions, since intestinal dilation often does not appear until 32-36 weeks gestation. Apparently, intestinal dilation often arises from temporary functional or mechanical obstructions that resolve after birth and surgical repair.

Unique to our investigation was the association of non-GI anomalies and increased LOS. The types of anomalies reported here correspond to those published previously by other investigators.(21-23) The mechanism by which non-GI anomalies might increase LOS remains unclear since many of the non-GI anomalies by themselves should not increase LOS (Table 3). The suggestion that non-GI anomalies might influence outcome deserves additional study in a larger data set.

The main limitation of our study is the fact that it is a single-site study. These findings should be confirmed in a multi-site study sample, such as the Canadian Pediatric Surgical Network. (2) Another limitation is that prenatal ultrasounds were read by different perinatologists without a prospective study protocol. However, ultrasound reports were remarkably complete, even going back over many years.

In summary, this study showed that the short-term outcome of gastroschisis patients depends on the patient's gestational age, the requirement for a silo, the presence of intestinal atresia, perforation, or resection, and non-GI anomalies. Prenatal ultrasound serves best to reassure families of an uncomplicated gastroschisis, not to predict a complicated gastroschisis.

Acknowledgments

This work was supported by the NICU Outcomes Fund of the Children's Hospitals and Clinics of Minnesota Foundation. The authors wish to thank the neonatal nurse practitioners, who collected clinical data and, especially, Ms. Martha Dugan, NNP, and Ms. Sam Olsen, who verified and entered the data, and Ms. Melissa Anderson, who collected much of the ultrasound data. Dr. Payne was supported during part of this project by perinatal epidemiology training grant 5 T-32 HD046377 to Michigan State University. John C. Connett, PhD, Department of Biostatistics, University of Minnesota, provided statistical advice.

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Abbreviations

AC	abdominal circumference
AFI	amniotic fluid index
BW	birth weight
GI	gastrointestinal
IV days	total days on which parenteral fluids were given intravenously
LOS	length of hospital stay from birth to discharge home
SD	standard deviation
SGA	small for gestational age

Figure 1. Length of Hospital Stay by Patient Group

This cumulative percentile graph of LOS shows the cumulative percent of patients discharged on the Y-axis and LOS on the X-axis. Group 1 patients received a primary repair without a silo, intestinal atresia, perforation, or resection. Group 2 patients required a silo, and group 3 patients had a major GI complication (atresia, perforation, or intestinal resection), with or without the need for a silo.

Figure 2. Regression Analysis (Hazard Analysis)

Hazard ratios indicate the effect on LOS of prematurity, need for a silo, GI complication (atresia, perforation, or intestinal resection), and non-GI anomalies. Hazard ratios to the left of 1 indicate that the presence of the selected finding lengthened LOS. The hazard ratio to the right of 1 indicates that increasing gestational age shortened LOS.

Table 1
Demographic and Clinical Characteristics and Their Relationship with LOS

Characteristic	N (%)	Median LOS (CI)	p-value
<u>Maternal race</u>			
White	128 (83)	31 (26-39)	0.217
Non-white	27 (17)	36 (27-54)	
<u>Marital status</u>			
Single	96 (62)	34 (27-41)	0.774
Married	59 (38)	29 (25-40)	
<u>Maternal age</u>			
≥ 21	81 (52)	30 (25-37)	0.147
< 21	74 (48)	36 (27-43)	
<u>Rupture of membranes</u>			
≤ 18 hrs	139 (90)	33 (26-38)	0.514
> 18 hrs	16 (10)	39 (16-97)	
<u>Amniotic fluid amount</u>			
Polyhydramnios	10 (6)	41 (28-77)	0.402
Oligohydramnios	14 (9)	34 (19-73)	
Normal	131 (85)	31 (26-38)	
<u>Cigarette use</u>			
Yes	45 (29)	30 (22-34)	0.436
No	110 (71)	25 (23-45)	
<u>SGA</u>			
Yes	51 (33)	36 (32-43)	0.131
No	104 (67)	29 (25-38)	
<u>Gender</u>			
Male	82 (53)	34 (27-39)	0.914
Female	73 (47)	32 (25-42)	
<u>Birth Location</u>			
Inborn	131 (85)	32 (26-38)	0.327
Outborn	24 (15)	39 (25-62)	
<u>Amniotic fluid appearance</u>			
Clear	70 (45)	26 (23-39)	0.087
Meconium/bile	85 (55)	36 (31-42)	
<u>Delivery route</u>			
Vaginal	94 (61)	27 (24-35)	0.025
C-section	61 (39)	39 (32-48)	
<u>Gestational age <37 weeks</u>			
Yes	97 (63)	39 (31-44)	0.006
No	58 (37)	27 (20-33)	
<u>Silo</u>			
Yes	37 (24)	40 (32-52)	0.003
No	118 (76)	27 (24-35)	
<u>GI complication</u>			

Characteristic	N (%)	Median LOS (CI)	p-value
Yes	27 (17)	97 (63-144)	<0.001
No	128 (83)	27 (25-32)	
<u>Non-GI anomaly</u>			
Yes	17 (11)	39 (29-117)	0.084
No	138 (89)	32 (26-36)	

Table 2
Non-Gastrointestinal Congenital Anomalies Seen in Gastroschisis Patients

Anomaly	Birth Weight	Gestational Age	LOS	Silo	GI Complication
Supernumerary digit, left hand	3100	36	15		
Arthrogryposis	3450	39	18		
Bicuspid aortic valve	2150	37	21		
Left ureteropelvic obstruction with hydronephrosis	2264	36	23		
Microcephaly	2800	38	29	Yes	
Ventricular septal defect	3000	39	29		
Arthrogryposis	1660	35	35		
Isolated cyst in filum terminale	1900	36	39	Yes	
Bilateral pyelectasis and inferiorly displaced left kidney	2900	36	39		
Bilateral talipes equinovarus deformity	1955	35	40	Yes	
Arthrogryposis	1988	35	73	Yes	
Supernumerary digit	2320	32	77	Yes	
Bicuspid aortic valve and aortic stenosis, megaureter with prune belly syndrome	1895	34	117	Yes	
Schizencephaly, anomalous systemic venous return into a left superior vena cava	2620	37	145		Intestinal atresia
Atrial septal defect	2677	36	153		Intestinal atresia, perforation, and resection
Absent distal left forearm (radial aplasia)	2820	35	157		Intestinal atresia
Cerebral dysgenesis, septooptic dysplasia, optic nerve hypoplasia, panhypopituitarism	2450	38	188	Yes	

Table 3
Prenatal Ultrasound as a Predictor of Outcome (N=89)

Outcome	Prenatal Ultrasound Findings							
	AFI* ≤ 5 th		AC** ≤ 5 th		AC** > 5 th		Intestine	Intestine
	Percentile	AFI* > 5 th Percentile	Percentile	Percentile	Percentile	Percentile	Intestine ≥ 10 mm	Intestine <10 mm
	N=8	N=81	N=44	N=45	N=50	N=39	N=38	N=51
Patients Requiring a Silo	2 (25%)	24 (30%)	14 (32%)	12 (27%)	12 (24%)	14 (36%)	12 (32%)	14 (27%)
Patients with GI Complication	0 (0%)	12 (15%)	6 (14%)	6 (13%)	11 (22%)	1 (3%)	10 (26%)	2 (4%)
Patients with Primary Repair	6 (75%)	49 (60%)	27 (61%)	28 (62%)	30 (60%)	25 (64%)	19 (50%)	36 (71%)

* AFI = amniotic fluid index¹⁷

AC = abdominal circumference