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Effect of Time to Surgical Evaluation on the Outcomes of Infants with Gastroschisis

Brian T. Bucher, MD, Ioanna G. Mazotas, BS, Brad W. Warner, MD, and Jacqueline M. Saito, MD

Division of Pediatric Surgery, Departments of Surgery; St. Louis Children's Hospital, Washington University School of Medicine, St. Louis, MO

Abstract

Purpose—Our goal is to identify the impact of time to surgical intervention on the outcomes of infants with gastroschisis.

Methods—After IRB approval, we performed a retrospective review of the medical records of all infants admitted to our institution from 2001-2010. Transport, bowel stabilization, and closure times were defined as the time from birth to admission, admission to the first documented operative intervention, and first operative intervention to abdominal closure, respectively. Outcomes included age at full enteral feeds, total parental nutrition days, ventilator days, and hospital length of stay. Multivariate analysis was used to identify independent predictors of the outcomes.

Results—One hundred and eighteen infants with gastroschisis were included in our study. Transport time and bowel stabilization time were not predictive of any outcome. However, the time to abdominal wall closure and postnatal gastrointestinal complications were independently predictive of age at full enteral feeds, total parenteral nutrition days, and hospital length of stay.

Conclusion—Time to surgical evaluation/bowel stabilization was not predictive of any clinically relevant outcomes in infants with gastroschisis. These data demonstrate that potential benefits from prenatal regionalization of infants with gastroschisis are not supported by decreased time to operative intervention.

Keywords

gastroschisis; transport; outcome

Introduction

Occurring in approximately 1 in 4000 live births, gastroschisis is the most common abdominal wall anomaly in the neonate.[1] Following delivery of a child with gastroschisis,

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Corresponding Author: Brian T. Bucher, MD, Department of Surgery, Washington University School of Medicine, Box 8235, 660 South Euclid Ave. St. Louis, MO 63110, Phone: (314) 454-6022, Fax: (314) 454-4224, bucherb@wudosis.wustl.edu.

Request for Reprints: Jacqueline M. Saito, MD, Assistant Professor of Surgery, Department of Surgery, Washington University School of Medicine, Box 8235, 660 South Euclid Ave. St. Louis, MO 63110, Phone: (314) 454-6022, Fax: (314) 454-4224, saitoj@wudosis.wustl.edu

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the exposed bowel and subsequent evaporative fluid losses require urgent resuscitation and surgical evaluation. In addition, since the majority of fetuses with gastroschisis are diagnosed prenatally by ultrasound, expectant mothers can be referred to a tertiary care center for prenatal evaluation and counseling, and newborns can have care potentially expedited following delivery. [2]

The damaging effects to the intestine from *in utero* amniotic fluid exposure have been well documented in animal models. [3] Intestinal damage may decrease motility and absorptive capacity, thereby causing affected infants to require prolonged parenteral nutrition after birth. In addition, several maternal (younger maternal age), prenatal (dilated bowel on ultrasound), and postnatal factors (gastrointestinal complications) have been associated with the need for prolonged TPN and longer hospital stays. [4-6] However, it is unclear whether duration of intestinal exposure after birth contributes to intestinal dysfunction. The goal of the current project is to evaluate the impact of times to surgical evaluation/bowel stabilization and abdominal wall closure on the outcomes of infants with gastroschisis.

Methods

Setting

St. Louis Children's Hospital (SLCH) is a 250 bed, academic tertiary care center affiliated with Washington University School of Medicine. SLCH is located in the metropolitan St. Louis area and has a 300-mile radius referral base in southeastern Missouri and southwestern Illinois.

Study Design

We performed a retrospective cohort study by identifying all patients who were treated at SLCH from January 1, 2001, until December 31, 2010 and had discharge diagnosis international classification of diseases-9th edition (ICD9) code of 756.76 "Other congenital anomalies of the abdominal wall." In addition, we identified an independent cohort of patients from our institutional neonatal intensive care unit database that had a diagnosis of gastroschisis. Subjects from both cohorts were included in the present study if they were primarily treated at our institution or were immediately transferred to our institution after birth. Upon review of the clinical record, subjects were excluded if the patient did not have gastroschisis, had delayed transfer after birth, or was transferred from our institution prior to discharge home. Approval was obtained from the Washington University Institutional Review Board; a waiver of informed consent was requested and granted (HRPO #10-12713).

Data Collection

Medical records, including inpatient, operative, and laboratory reports were reviewed retrospectively by two of the investigators (BTB, IGM). Data on demographics, transportation, operative procedures, and hospitalization course were collected for each patient. Clinically relevant dates and times including birth, admission, and first and subsequent operative interventions were also collected.

Definitions

The prenatal complications variable was a composite definition which included preeclampsia, maternal hypertension, gestational diabetes, maternal drug abuse, maternal smoking, intrauterine growth restriction (IUGR), and/or Group B Streptococcus (GBS) infection. Inborn patients were those delivered at our adjacent labor and delivery unit in Barnes-Jewish Hospital. The congenital anomalies variable was a composite definition which included central nervous system, cardiac (excluding ASD, PFO), respiratory,

genitourinary, and/or musculoskeletal anomalies. Prenatal gastrointestinal (GI) complications included intestinal atresia, congenital stricture, or necrosis on initial examination. Postnatal GI complications included intestinal volvulus, acquired necrosis, perforation, or necrotizing enterocolitis. Abdominal wall defect size was categorized into small (<2.5cm), medium (2.5-5cm), or large (>5cm). Transport, bowel stabilization, and closure times were defined as the time from birth to admission, admission to the first documented operative intervention, and first operative intervention to abdominal wall closure, respectively.

Outcomes

The primary outcome was age at full enteral feeds defined as the time from birth to the patient receiving 100 kcal/kg/day. Secondary outcomes included time from abdominal wall closure until full enteral feeds, total parental nutrition days, total ventilator days, hospital length of stay, and the development of major complications which included death or ongoing requirement for TPN at the time of discharge. The hospital complication variable was a composite definition which included wound infection, catheter-associated sepsis, urinary tract infection, hospital-acquired pneumonia, or aspiration.

Data Analysis

Data analysis was performed using SAS Version 9.2 (Cary, NC). Categorical variables were compared using χ^2 analysis. Continuous variables were compared using student t-test or Wilcoxon rank sum test for normally or non-normally distributed variables, respectively. All statistical tests were 2-tailed, and a p-value of <0.05 was considered significant. Clinically relevant statistically significant variables with a p-value of <0.1 from univariate analysis were used to create a Cox proportional hazard model. The final model consisted of the following variables: maternal prenatal complications, prenatal and postnatal gastrointestinal complications, amniotic fluid character, transport time, stabilization time, and closure time. We subsequently used these variables to develop a generalized linear model for total TPN days, total ventilator days, and hospital length of stay. In addition, we modeled the primary and secondary outcomes using log-transformed time variables which did not change the findings presented in this study. For simplicity and ease of interpretation, non-transformed variables were used in the final model.

Results

One hundred eighteen neonates were included in the present study, and univariate analysis of the entire cohort is shown in Table 1. The majority of neonates was male, Caucasian, and prenatally diagnosed with gastroschisis. The mean maternal age was 22 years, and the majority of mothers experienced at least one prenatal complication. The most common prenatal complications were IUGR (28%), maternal smoking (23%), and GBS infection (16%). The median gestational age of the cohort was 36 weeks with a mean birthweight of 2412 grams. The majority (71%) of patients was inborn to our local hospital system. The most common method of delivery was spontaneous vaginal (43%), and the amniotic fluid character was most commonly meconium-stained (47%). A minority of neonates (9%) had other associated congenital anomalies; however, 14% of the cohort experienced prenatal GI complications, and 27% experienced postnatal GI complications. The majority of defects (62%) was between 2.5-5cm, and the majority of infants (86%) underwent delayed closure after placement of an abdominal silo. The initial operation was most commonly performed in the NICU (75%). The median (interquartile range, IQR) time from birth to admission to our institution (Transport time) was 57.5 (110) minutes. The median (IQR) time from admission to bowel stabilization (Stabilization time) was 65 (73) minutes. The median (IQR) time from bowel stabilization to final abdominal closure was 129 (92) hours.

The overall survival of our cohort was 95%. Fourteen patients (12%) experienced hospital complications, and eight patients (7%) required TPN upon hospital discharge. The median (IQR) hospital length of stay was 55 (64) days. The median (IQR) age at the time to the start and full enteral feeds was 18 (13) and 44 (59) days, respectively. The median (IQR) TPN and ventilator days were 36 (42) and 5 (11) days, respectively.

We next used relevant patient variables to develop a Cox proportional hazard model to identify independent predictors of clinically relevant outcomes. Our primary outcome was subject age at full enteral feeds. Hazard ratios for independent predictors of age at full enteral feeds are shown in Table 2. Older age to reach full enteral feeds was independently associated with longer time to closure ($p=0.0005$), presence of either prenatal ($p=0.002$) or postnatal gastrointestinal complications ($p<0.0001$), or amniotic fluid stained with meconium ($p=0.002$) or blood ($p=0.01$). The presence of maternal prenatal complications was associated with a younger age to reach full enteral feeds ($p=0.006$). Time from abdominal wall closure to full enteral feeds was also associated with closure time, prenatal and postnatal gastrointestinal complications, amniotic fluid character, and maternal complications (Table 2). Both transport time and stabilization time were not independently associated with the either age at full enteral feeds or time from closure to full enteral feeds. In a separate analysis, age at stabilization was not independently associated with either time from birth or from closure to full enteral feeds.

We next used a generalized linear model to identify independent predictors of our secondary outcomes: total TPN days, total ventilator days, and hospital length of stay. (Table 3A/B). On analysis of total TPN days, the presence of postnatal GI complications ($p=0.003$) and longer time to abdominal wall closure ($p<0.0001$) were independently associated with a longer duration of TPN. On analysis of total ventilator days, only longer time to abdominal wall closure ($p<0.0001$) was independently associated with prolonged need for mechanical ventilation. Hospital length of stay was independently associated with the presence of postnatal GI complications ($p=0.0008$) and longer time to abdominal wall closure ($p<0.0001$). In a separate analysis, age at stabilization was not independently associated with TPN days, ventilator days, or length of stay.

Discussion

The purpose of the current study was to assess the impact of time from delivery to surgical evaluation on the outcomes of infants born with gastroschisis. We retrospectively identified a cohort of 118 infants with gastroschisis treated at our institution from 2001-2010. On multivariate analysis, abdominal wall closure time was independently associated with time to full enteral feeds, total TPN days, total ventilator days, and hospital length of stay. Other significant findings of the current study include the effect of prenatal and postnatal gastrointestinal complications on the time to full enteral feeds, TPN days, and hospital length of stay.

The current study failed to show an impact of time to surgical evaluation on the outcomes of infant with gastroschisis. The time to evaluation included both the time from birth to admission to a tertiary care hospital, and the time from admission to bowel stabilization. Previous reports from the Canadian Pediatric Surgery Network have documented improved outcomes of infants with gastroschisis born at tertiary care hospitals. [7] The data from the current study does not refute this data; however, any added benefit from prenatal referral to a tertiary care medical center is not associated with decreased time to surgical evaluation. Other factors related to care at tertiary care facilities may account for improved outcomes, such as specialized obstetric, neonatal, and surgical expertise in treating infants with gastroschisis.

Previous reports have documented the correlation of longer time to abdominal wall closure with duration of intestinal dysfunction. [5, 8, 9] In each of these reports, the primary comparison was between infants who underwent primary closure and those treated with silo placement/delayed closure. The placement of a silo resulted in longer times to abdominal wall closure, delayed start of enteral feeds, prolonged duration of TPN, and longer hospital stays. In Baynard *et al.*, the patients who underwent silo placement took approximately 3 days longer to achieve abdominal closure but were hospitalized 6 days longer. These results indicate that lead-time bias does not likely account for the advantage of primary closure compared to silo placement. The observation of faster recovery with primary closure may reflect treatment bias; that is, neonates with features such as non-edematous bowel may be more likely have a rapid recovery regardless of timing of abdominal wall closure. Some authors still advocate silo placement for selected infants. [10] Indeed, a small, randomized trial of primary versus delayed closure resulted in equivocal outcomes in both groups. [11] Our current study does not seek to address whether primary or delayed closure is optimal. The present study shows that the time to abdominal wall closure and gastrointestinal complications were the strongest predictors of age at full enteral feeds. In an attempt to eliminate lead-time bias, we also found that time to abdominal wall closure was also independently associated with the time from closure to full enteral feeds.

Prenatal and postnatal gastrointestinal complications were significant predictors of the age at full enteral feeds, as well as duration of TPN and hospital stay in the current study. Other reports have documented similar findings in infants with gastroschisis. A study of 2490 subjects by Lao and colleagues using the Pediatric Health Information Systems Database documented the need for intestinal resection and the development of necrotizing enterocolitis as independent predictors of mortality in infants with gastroschisis. [12] The detrimental effect of gastrointestinal complications is likely related to the need for multiple surgical interventions to restore intestinal continuity, as well as shortened bowel length. In the current study, prenatal maternal complications were independently associated with younger age at full enteral feeds. This favorable outcome may be a marker for adequate prenatal care, as mothers with poor prenatal care would not necessarily have prenatal complications diagnosed. A limitation of the retrospective nature of the present study, prenatal care was not consistently documented in the medical records, and the documentation of prenatal care did not indicate adequacy or consistency of this care.

The present study has several limitations. The retrospective nature of the study limits our analysis to variables included within the medical record. This limited our ability to document, for example, the actual time that the intestine was reduced into the abdominal cavity. We attempted to control for this by using a standardized time of the start of anesthesia for all operative procedures. In addition, selection bias may exist, as we only analyzed subjects from one institution (SLCH), who as a group may not be comparable to infants treated at other institutions.

Conclusion

In conclusion, we have shown that time to surgical evaluation is not predictive of any clinically relevant outcomes of infants with gastroschisis. Time to abdominal wall closure, prenatal gastrointestinal complications, and postnatal gastrointestinal complications were independently predictive of older age at attaining full enteral feeds, longer duration of TPN, and longer hospital stay. The current study shows that any benefit derived from referral to a tertiary care center for delivery is not due a shorter time to surgical evaluation.

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Table 1
Demographics of Infants with Gastroschisis (2001-2010)

Variable		All Patients
Total		118
Demographic	Gender (male %)	60 (51%)
	Race (n, %)	
	Caucasian	92 (78%)
	African American	20 (17%)
	Hispanic	4 (3%)
	Other	2 (1%)
Prenatal History	Prenatal Diagnosis (n, %)	106 (90%)
	Maternal Age (years, mean±SD)	22 ± 4
	Any Prenatal Complication (n, %)	69 (58%)
Birth History	Gestational Age (weeks, mean±SD)	35.9±2.1
	Inborn (n, %)	83 (71%)
	Birthweight (grams, mean±SD)	2412±554
	1 Minute APGAR (median± IQR)	7±2
	5 Minute APGAR (median±IQR)	9±1
	Delivery Method (n, %)	
	Spontaneous Vaginal	51 (43%)
	Induced Vaginal	12 (10%)
	Elective C-Section	19(16%)
	Urgent C-Section	36 (31%)
	Amniotic Fluid (n, %)	
	Clear	35(30%)
	Meconium-Stained	55 (47%)
	Bloody	5 (4%)
Postnatal Course	Any Congenital Anomaly (n, %)	11 (9%)
	Prenatal Gastrointestinal Complication (n, %)	16 (14%)
	Postnatal Gastrointestinal Complication (n, %)	32 (27%)
	Breast Milk Enteral Feeds (n, %)	81 (69%)
Operative Course	Defect Size (n, %)	
	Small (<2.5cm)	37 (31%)
	Medium (2.5-5cm)	73 (62%)
	Large (>5cm)	5 (4%)
	Closure Method (n, %)	
	Immediate Closure	17 (14%)
	Delayed Closure	101 (86%)
	Initial Operative Location (n, %)	
	NICU	88 (75%)

Variable		All Patients
OR		30 (25%)
Times	Transport Time (minutes, median±IQR)	57.5±110
	Stabilization Time (minutes, median±IQR)	65±73
	Closure Time (hours, median±IQR)	129±92
Outcomes	Survival (n, %)	112 (95%)
	Hospital Length of Stay (days, median±IQR)	55±64
	Age at Full Enteral Feeds (days, median±IQR)	44±59
	Total TPN Days (days, median±IQR)	36±42
	TPN At Discharge (n, %)	8 (7%)
	Total Ventilator Days (days, median±IQR)	5±11
	Any Major Complication (n, %)	14 (12%)
	Any Hospital Complication (n, %)	54 (46%)

SD: Standard deviation. IQR: Interquartile range. CM: centimeter. NICU: neonatal intensive care unit. OR: operating room. TPN: Total parental nutrition.

Table 2
Cox Regression Analysis: Independent Predictors of Subject Age at Reaching Full Enteral Feeds and Time from Abdominal Wall Closure to Full Enteral Feeds

Variable	Age at Full Enteral Feeds		Time From Closure to Full Enteral Feeds	
	HR (95%CI)	P-Value	HR (95%CI)	P-Value
Transport Time (per 60 minute increase)	1.07 (0.98, 1.17)	0.15	1.06 (0.87, 1.31)	0.15
Stabilization Time (per 60 minute increase)	1.11 (0.90, 1.36)	0.32	1.07 (0.98,1.16)	0.55
Closure Time (per 12 hour increase)	0.95 (0.92, 0.98)	0.005	0.96 (0.93, 1.00)	0.03
Prenatal GI Complication (Yes vs. No)	0.17 (0.07, 0.44)	0.002	0.19 (0.08,0.48)	0.0005
Postnatal GI Complication (Yes vs. No)	0.16 (0.078, 0.32)	<0.0001	0.17 (0.86, 0.35)	<0.0001
Amniotic Fluid Character (vs. Clear)				
Bloody	0.23 (0.08, 0.72)	0.01	0.24 (0.08, 0.75)	0.0005
Meconium-Stained	0.41 (0.24, 0.71)	0.002	0.41 (0.24, 0.71)	0.001
Maternal Complications (Yes vs. No)	2.30 (1.27, 4.18)	0.006	2.21 (1.22, 3.98)	0.01

HR: Hazard ratio, larger ratio indicated higher likelihood of younger age at or time from abdominal wall closure to full enteral feeds. CI: Confidence interval. GI: Gastrointestinal

Table 3
Linear Regression Analysis: Independent Predictors of TPN Days, Ventilator Days, and Hospital Length of Stay. (A) Continuous Variables.
(B) Categorical Variables

Variable	Outcome					
	TPN Days (per day)		Ventilator Days (per day)		Hospital Length of Stay (per day)	
	β (95% CI)	p	β (95% CI)	p	β (95% CI)	p
Transport Time (per min)	−0.02 (−0.07,0.02)	0.28	−0.002 (−0.008,0.008)	0.67	−0.04 (−0.01,0.02)	0.21
Stabilization Time (per min)	−0.004 (−0.12,0.11)	0.94	0.01 (−0.02,0.03)	0.67	−0.01 (−0.1,0.1)	0.90
Closure Time (per hour)	0.24 (0.03,0.35)	<0.0001	0.06 (0.03,0.08)	<0.0001	0.33 (0.19,0.46)	<0.0001
	β: Strength of association in multivariate model. CI: Confidence Interval. p: p-value					
Variable	Outcome					
	TPN Days		Ventilator Days		Hospital Length of Stay	
	μ(95% CI)	p	μ(95% CI)	p	μ(95% CI)	p
Prenatal GI Complication (Yes vs. No)	12.5 (−15.0, 40.0)	0.37	5.4 (−1.3, 12.1)	0.11	30.7 (−4.2, 65.6)	0.09
Postnatal GI Complication (Yes vs. No)	34.2 (12.6, 43.2)	0.003	0.5 (−4.6, 5.6)	0.84	37.3 (9.9, 64.7)	0.009
Amniotic Fluid Character (vs. Clear)						
Bloody	3.4 (−30.3, 33.7)	0.84	3.7 (−4.5, 11.7)	0.38	−0.23 (−43.2, 42.7)	0.99
Meconium-Stained	12.3 (−4.8, 29.4)	0.16	1.1 (−3.0, 5.2)	0.60	13.5 (−8.5, 35.5)	0.23
Maternal Complications (Yes vs. No)	−13.2 (−29.8, 3.3)	0.12	−0.14 (−4.1, 3.78)	0.94	−7.9 (−29.1, 13.3)	0.47

μ : Mean difference within each category in multivariate model. CI: Confidence Interval. p: p-value