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# Determinants of outcomes in patients with simple gastroschisis

Fouad Youssef, Jean-Martin Laberge, Pramod Puligandla, Sherif Emil *
The Canadian Pediatric Surgery Network (CAPSNet)

*The Division of Pediatric General and Thoracic Surgery, The Montreal Children's Hospital, McGill University Health Centre, Montreal, Quebec, Canada*

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ABSTRACT

*Purpose:* We analyzed the determinants of outcomes in simple gastroschisis (GS) not complicated by intestinal atresia, perforation, or necrosis.
*Methods:* All simple GS patients enrolled in a national prospective registry from 2005 to 2013 were studied. Patients below the median for total parenteral nutrition (TPN) duration (26 days) and hospital stay (34 days) were compared to those above. Univariate and multivariate logistic and linear regression analyses were employed using maternal, patient, postnatal, and treatment variables.
*Results:* Of 700 patients with simple GS, representing 76.8% of all GS patients, 690 (98.6%) survived. TPN was used in 352 (51.6%) and 330 (48.4%) patients for ≤26 and >26 days, respectively. Hospital stay for 356 (51.9%) and 330 (48.1%) infants was ≤34 and >34 days, respectively. Univariate analysis revealed significant differences in several patient, treatment, and postnatal factors. On multivariate analysis, prenatal sonographic bowel dilation, older age at closure, necrotizing enterocolitis, longer mechanical ventilation, and central-line associated blood stream infection (CLABSI) were independently associated with longer TPN duration and hospital stay, with CLABSI being the strongest predictor.
*Conclusions:* Prenatal bowel dilation is associated with increased morbidity in simple GS. CLABSI is the strongest predictor of outcomes. Bowel matting is not an independent risk factor.
*Level of evidence:* 2c.



Gastroschisis (GS) is a congenital anomaly with increasing incidence over the last few decades [1,2]. Although the survival rate for newborns with GS is high, morbidity is still considerable [2]. The role of several potential determinants of outcomes has been assessed in neonates with GS. The most important determinant has been consistently found to be the presence or absence of intestinal complications, namely atresia, necrosis, and perforation. Patients with these complications are classified as complex GS, and have consistently worse outcomes than those without these complications, classified as simple GS [3,4]. Unfortunately, the presence of intestinal complications is a patient-determined factor, amenable to limited manipulation [4,5]. Modifiable treatment factors, such as mode of delivery and method of abdominal closure, have also been studied, but not consistently found to affect outcomes [6,7].

In the absence of intestinal complications, it is not clear why some simple GS patients have worse outcomes than others, with longer bowel dysfunction, typically resulting in a longer hospital stay [6,7]. Candidates for outcome determinants in these patients include gestational age, delivery mode, age at closure, closure method, the degree of bowel matting, necrotizing enterocolitis (NEC), cardiac anomalies, and lung hypoplasia [8,9]. However, risk stratification has focused mostly on predicting mortality, and has typically included both simple and complex gastroschisis [8,9]. This included the gastroschisis prognostic score, or GPS, created using the Canadian Pediatric Surgery Network (CAPSNet) database [9,10].

The goal of our study was to identify factors that influence outcomes in patients with simple GS, using the most recent iteration of the CAPSNet database. We also specifically investigated whether the severity of bowel matting independently predicts increased morbidity.

## 1. Methods

### 1.1. Study population

CAPSNet is a prospectively collected database of all patients with GS and congenital diaphragmatic hernia born in Canada [10]. GS patients entered into the database between 2005 and 2013 formed the base cohort. Patients with necrosis, perforation or confirmed atresia were excluded from the analysis.

### 1.2. Outcomes

The two primary outcomes were duration of TPN and length of hospital stay. Both of these outcomes had a non-normal distribution

* Corresponding author at: Division of Pediatric General and Thoracic Surgery, The Montreal Children's Hospital, 1001 Decarie Boulevard, Room B04.2028, Montreal, Quebec H4A 3J1, Canada. Tel.: +1 514 412 4497; fax: +1 514 412 4289.
*E-mail address:* sherif.emil@mcgill.ca (S. Emil).

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skewed to the left. The median of each outcome was utilized to create categorical variables for analysis, and in fact resulted in two groups with widely divergent outcomes. The duration of TPN was therefore analyzed as a dichotomous variable using the median duration, 26 days, as a cutoff, as well as a continuous variable. Likewise, the length of hospital stay was analyzed as a dichotomous variable using median stay, 34 days, as a cutoff, as well as a continuous variable. The primary outcomes analysis included only survivors to discharge.

NEC was studied both as a secondary outcome, as well as a potential determinant of primary outcomes.

### 1.3. Independent variables

The independent variables analyzed were classified as maternal variables, patient variables, treatment variables, and postnatal complications. Maternal variables included maternal age, ethnicity (Caucasian, first nations, others), smoking, alcohol consumption, illicit drug use, and delivery mode. Patient variables included gender, gestational age, gestational weight, Apgar score at 1 min, Apgar score at 5 min, the incidence of bowel dilation on the last prenatal ultrasound that reported this information, the degree of bowel matting (none, mild, or severe), and the presence of a cardiac anomaly. Treatment factors included transfer status (inborn or outborn), success of attempted closure, age at closure, hospital GS volume per year [(low, <3), (medium, 3–9), (high, >9)], duration of mechanical ventilation, and the year of admission (2005–2009 vs. 2010–2014). Postnatal complications included the incidence of central line-associated blood stream infection (CLABSI) and the incidence of NEC.

### 1.4. Analysis of the effect of bowel matting

To further assess the effect of bowel matting, a univariate analysis was performed comparing patients with no or mild mating to those with severe matting.

### 1.5. Statistical analyses

Thresholds of TPN duration and hospital stay were set at the median for each, 26 days and 34 days, respectively. Infants in study were categorized by their TPN duration, hospital stay, NEC, or severe bowel matting. Maternal, patient, treatment, and complication data were compared between groups. Frequency (percentage), mean (standard deviation) or median (inter quintile range) were reported. Significance across groups was assessed by Pearson's chi-square test for categorical variables, and ANOVA or Wilcoxon rank test for continuous variables.

Multivariate logistic analyses were applied for TPN duration and hospital stay to explore associated factors. Odds ratios and 95% confidence intervals (CI) were estimated. General linear regression was used to assess the TPN duration and hospital stay as continuous outcomes, and coefficient (95% CI) was estimated. The use of both logistic regression and linear regression analyses optimized the detection of any potential independent outcome determinants. All analyses were conducted using SAS v.9.2 (SAS Institute Inc., Cary, NC) with significance level 0.05.

### 1.6. Study approval

The study underwent scientific review and approval by the CAPSNet steering committee. Institutional approval was obtained from the Pediatric Research Ethics Board of the McGill University Health Centre (15–144-MUHC).

## 2. Results

### 2.1. Study cohort

During the period of study, a total of 912 patients with GS were prospectively enrolled in the CAPSNet database, with complete data to discharge. Of those, 700 met the inclusion criteria for simple GS, representing 76.8% of all GS patients. 690 (98.6%) patients survived to discharge. Average duration of TPN and hospital stay for the non-survivors was 33.9 ± 50.8, and 36.3 ± 53.3, respectively. Among the 690 survivors, data for TPN duration and hospital stay were available for 682 (98.8%) and 686 (99.4%), respectively. Duration of TPN was 35.1 ± 33.0 days, with a median of 26 days. Hospital stay was 47.0 ± 46.3 days, with a median of 34 days. Twenty-six patients (3.8%) developed NEC. Mechanical ventilation was employed in 653 (94.6%) of patients, for an average of 6.3 ± 5.5 days. The first enteral feed was started at 15.2 ± 11.8 days. Comorbidities at discharge included cholestatic liver disease in 124 (18.0%), gastroesophageal reflux disease in 148 (21.4%), and intestinal failure in 17 (2.5%). Discharge feeding status was full oral feeding in 457 (66.2%), some component of tube feedings in 129 (18.7%), some component of TPN in 86 (12.5%), and unknown in 18 (2.6%).

### 2.2. Primary outcomes: univariate analyses

The univariate analyses of primary outcomes as dichotomous variables are shown in Table 1. 352 (51.6%) patients at or below the median for TPN duration were on TPN for 18.9 ± 4.9 days, and 330 (48.4%) above the median were on TPN for 52.5 ± 40.6 days. 356 (51.9%) patients at or below the median for hospital stay had a stay of 24.3 ± 6.5 days, and 330 (48.1%) above the median had a hospital stay of 71.5 ± 57.1 days. None of the maternal variables had a significant effect on outcomes in univariate analysis. There were several patient, treatment, and complication variables significantly associated with worse outcomes, as highlighted in italics in Table 1.

### 2.3. Primary outcomes: multivariate logistic regression analyses

The multivariate logistic regression analyses of primary outcomes as dichotomous variables are shown in Table 2. Essentially the same variables were found to be independent predictors of both TPN duration and hospital stay. Sonographic bowel dilatation emerged as an independent predictor of morbidity. Severe bowel matting was not an independent predictor of morbidity. Interestingly, moderate versus large hospital volume appeared to confer a small outcome advantage. The complications of CLABSI and NEC had the greatest effects on morbidity.

### 2.4. Primary outcomes: multivariate linear regression analyses

The multivariate linear regression analyses of primary outcomes as continuous variables showed the following variables to be associated with a longer TPN duration: sonographic bowel dilation [5.01 (0.81–9.21), $p = 0.02$], severe bowel matting [6.62 (0.08–13.2), $p < 0.01$], longer ventilation period [1.27 (0.94–1.64), $p < 0.01$], CLABSI [23.7 (17.7–29.8), $p < 0.01$], and NEC [27.5 (17.3–37.8), $p < 0.01$]. The same analysis revealed that the following variables were associated with longer hospital stay: lower gestational age [−2.93 (−4.62 – −1.25), $p < 0.01$], longer ventilation days [2.04 (1.49–2.59), $p < 0.01$], CLABSI [41.5 (32.8–50.2), $p < 0.01$], and NEC [21.7 (6.25–37.1), $p < 0.01$].

### 2.5. Secondary outcome

The univariate analysis of NEC as a secondary outcome is shown in Table 3. Outborn status, CLABSI, and admission after 2009 were significantly associated with NEC. All three variables persisted as independent predictors of NEC on multivariate logistic regression: outborn status [7.01 (3.05–16.10), $p < 0.01$], CLABSI [3.11 (1.24–7.83), $p = 0.04$], and admission after 2009 [3.12 (1.25–7.76), $p = 0.01$]. Severe matting was not associated with an increased risk of NEC.