Use of Paralysis in Silo-Assisted Closure of Gastroschisis

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Objective To examine the association between pre-closure neuromuscular paralysis and time to final surgical closure for infants with gastroschisis undergoing silo reduction.

Study design This study was an exploratory review of observational variables obtained from the Canadian Pediatric Surgery Network database. The focus was on the subset of infants with gastroschisis undergoing silo reduction between May 2005 and March 2009. Of the 186 infants, paralysis use could be ascertained for 167 infants (79 received pre-closure paralysis and 88 received none). Groups were compared by using statistical tests, with relationships explored using regression analysis.

Results Infants receiving paralysis took longer to achieve closure by an average of 3 days (8 versus 5 days; $P < .001$) and had greater mean number of ventilation days (12 versus 7 days; $P < .001$). The relationship between paralysis and days to closure remained after adjusting for other variables.

Conclusions In infants with gastroschisis undergoing silo reduction, use of paralysis was associated with longer time to closure. Pre-closure paralysis should be carefully weighed in this population. *(J Pediatr 2012;161:125-8)*.

Gastroschisis is a major congenital anomaly characterized by a full-thickness defect of the anterior abdominal wall leading to variable viscera herniation. Depending on the size of the defect, volume of extruded viscera, and condition of the bowel, it may be mechanically unfeasible to restore the exposed viscera into the abdomen in a single-step primary closure. In this case, a staged silo secondary reduction over the course of days may allow for progressive return of the bowel to the abdominal cavity while avoiding abdominal compartment syndrome.

The use of paralytics is thought to facilitate "forced" reduction and primary closure of gastroschisis. The evidence, however, predates the availability of "pre-formed" silos and is not necessarily associated with a reduction in length of hospital stay or parenteral nutrition duration.[1-4] Thus, the usefulness of paralysis for contemporary silo reduction is unclear. Current practices range from no sedation, to limited sedation, to deep sedation, and, finally, to combined sedation-paralysis.[5-11]

Uncertainty exists about the short- and long-term risks of the routine use of muscle relaxation in gastroschisis.[12-20] The aim of our study was to determine whether pre-closure use of paralysis (compared with no paralysis) was associated with a shorter time to final surgical closure in infants with gastroschisis treated with a silo to facilitate visceral reduction.

Methods

This study was an exploratory database review of observational variables obtained from the Canadian Pediatric Surgery Network (CAPSNet) multicenter national surgical database. CAPSNet collects standardized data on every case of gastroschisis evaluated in the 16 perinatal referral centers in Canada.[21,22] CAPSNet, and its process of case ascertainment and data abstraction, has been described in detail elsewhere.[23] Data collection at individual sites was sanctioned by each center's institutional ethics review board and conformed to provincial privacy protection laws.

This study focused on the subset of live-born infants with gastroschisis undergoing a silo reduction between May 2005 and March 2009.

Standard perinatal demographic variables included sex, birth weight, gestational age, age at admission to hospital, and out/inborn status. Proven bowel atresia, necrosis, or both were also noted. Illness severity was appraised by using the Score for Acute Neonatal Physiology, version II (SNAP-II). SNAP-II is a physiological index of illness severity measured within 12 hours of neonatal intensive care unit admission.[24] This index has been shown to predict both mortality and survival outcomes in gastroschisis.[25]

The primary outcome measure was days to abdominal wall closure. Secondary outcomes included mortality (in hospital), length of hospital stay, mechanical

CAPSNet	Canadian Pediatric Surgery Network
SNAP-II	Score for Acute Neonatal Physiology, version II

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ventilation days (total in hospital), days to first enteral feed, days on parenteral nutrition, development of necrotizing enterocolitis (Bell's stage 2 or higher), culture-confirmed bacteremia, bowel obstruction requiring operation, abdominal compartment syndrome (requiring opening of the abdomen), abdominal fascial or silo dehiscence, and surgical site infection (culture-proven with associated signs of site inflammation).

Study patients were classified in two groups: silo reduction with paralysis before closure and silo reduction without paralysis before closure. Because CAPSNet does not differentiate reasons for paralysis use, pre-closure paralysis was defined as use of depolarizing or non-depolarizing muscle relaxant medications (succinylcholine, pancuronium, or rocuronium) before the day of definitive operative abdominal closure. Paralysis use on the day of operative closure was not included, because this paralysis use may have been for the purpose of operative anesthesia. Within these groups, patients were substratified according to the timing of silo placement: silo placed before attempt of operative closure or silo placed after attempt of primary operative closure. Timing of silo placement was used as a proxy variable for indication of silo placement.

Statistical Analysis

Data for each group were described as means and SDs for continuous variables and as frequency and percentage for categorical variables. *t* tests (or Mann-Whitney tests) and χ^2 tests (or Fisher exact tests) were used for group comparisons. A *P* value <.05 was considered to be statistically significant. Kaplan-Meier curves displayed time to closure by paralysis use. Cox proportional hazards regression techniques assessed paralysis use differences in time to closure by using a robust variance estimator to adjust for correlation within hospital site.[26,27] Variables were entered in a multivariable model when statistically significant at the 0.2 level and removed, with backward elimination when not statistically significant at the 0.05 level, to arrive at the final model. The final model was assessed for adequacy of the proportional hazards assumption and fit (eg, deviance, score residuals).[27] SPSS software for Windows, version 17 (SPSS Inc, Chicago, Illinois) and S-PLUS software version 8.0 for Windows (TIBCO Software Inc, Palo Alto, California) were used for analysis.

Results

Of the 186 infants with gastroschisis undergoing silo reduction, 19 had missing information, so paralysis use could be ascertained for 167 patients (79 received pre-closure paralysis and 88 received none). The characteristics of the two groups are shown in Table I. With risk variable comparisons, no significant differences between groups were revealed.

Outcome measures are shown in Table II. Infants receiving pre-closure paralysis took longer to achieve surgical closure ($P < .001$; Figure). Ventilation days were also higher in the paralysis group. Paralysis use did not differ after substratifying by timing of silo placement.

Table I. Characteristics of the study population

	Pre-closure paralysis	No pre-closure paralysis	*P* value
Birth weight, g	2587 ± 490 n = 77	2524 ± 503 n = 86	.423
Gestational age, weeks	36.4 ± 1.6 n = 79	36.0 ± 1.8 n = 86	.218
Age at admission, days	0.11 ± 0.32 n = 79	0.12 ± 0.32 n = 85	.941
Outborn (%)	50/79 (63.3)	44/88 (50.0)	.084
Male (%)	42/79 (53.2)	45/86 (52.3)	.914
SNAP-II*	8.6 ± 11.5 n = 78	5.4 ± 11.6 n = 85	.071
Presence of bowel atresia (%)	5/79 (6.3)	4/88 (4.5)	.737
Presence of bowel necrosis (%)	1/79 (1.3)	3/88 (1.1)	1.000

Expressed as mean ± SD or proportion (%).
Differing "n" or ratio denominator reflects missing data points.
*SNAP-II calculated within 12 hours of admission.

Paralysis use, birth weight, gestational age, age at admission, out/inborn status, sex, timing of silo placement, SNAP-II, presence of atresia, and presence of necrosis were variables assessed with the time to abdominal closure analysis. On the basis of a *P* value <.2, paralysis use, timing of silo placement, SNAP-II, and presence of atresia were entered in the multivariable model. After backward elimination, paralysis use and SNAP-II remained. There was no evidence of a statistically significant interaction of paralysis use and SNAP-II. Thus, SNAP-II and paralysis use variables were found to be independent and not necessarily linked to each other.

The hazard ratio for use of paralysis as a factor related to time to closure was calculated as 0.423 (Table III). This means that after controlling for other variables, patients receiving pre-closure paralysis who had not yet progressed

Table II. Outcome measures by groups

	Pre-closure paralysis	No pre-closure paralysis	*P* value
Primary outcome			
Days to closure	8.1 ± 6.7 n = 79	4.9 ± 2.2 n = 86	<.001
Secondary outcomes			
Mortality	2/79 (2.5)	2/85 (2.4)	1.000
Length of stay, days	52.5 ± 37.3 n = 79	59.5 ± 47.2 n = 86	.288
Mechanical ventilation, days	12.4 ± 7.0 n = 79	6.5 ± 6.2 n = 85	<.001
Days to first enteral feed	19.3 ± 10.7 n = 77	17.6 ± 11.7 n = 83	.353
Days on parenteral nutrition	42.1 ± 29.7 n = 79	44.0 ± 31.6 n = 84	.687
Necrotizing enterocolitis (%)	1/79 (1.3)	3/88 (3.4)	.623
Culture confirmed bacteremia (%)	10/79 (12.7)	19/88 (21.6)	.128
Abdominal compartment syndrome (%)	5/79 (6.3)	1/88 (1.1)	.102
Bowel obstruction (%)	8/79 (10.1)	7/88 (8.0)	.624
Abdominal fascial/silo dehiscence (%)	8/79 (10.1)	5/88 (5.7)	.284
Surgical site infection (%)	16/79 (20.3)	18/88 (20.5)	.974

Expressed as mean ± SD or proportion (%).
Differing "n" or ratio denominator reflects missing data points.