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Journal of Pediatric Surgery

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Immediate versus silo closure for gastroschisis: Results of a large multicenter study ☆



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ARTICLE INFO

Article history: Received 12 April 2019 Received in revised form 7 August 2019 Accepted 13 August 2019

Key words: Gastroschisis Immediate closure Silo Ventral hernia

ABSTRACT

Background/Purpose: The optimal method to repair gastroschisis defects continues to be debated. The two primary methods are immediate closure (IC) or silo placement (SP). The purpose of this study was to compare outcomes between each approach using a multicenter retrospective analysis. We hypothesized that patients undergoing SP for ≤5 days would have largely equivalent outcomes compared to IC patients.

Methods: Gastroschisis patient data were collected over a 7-year period. The cohort was separated into IC and SP groups. The SP group was further stratified based on time to closure (≤5 days, 6–10 days, >10 days). Characteristics and outcomes were compared between groups. Multivariate logistic regression was also performed.

Results: 566 neonates with gastroschisis were identified including 224 patients in the IC group and 337 patients in the SP group. Among SP patients, 130 were closed within 5 days, 140 in 6–10 days, and 57 in >10 days. There were no significant differences in mortality, sepsis, readmission, or days to full enteral feeds between IC patients and SP patients who had a silo ≤5 days. IC patients had a significantly higher incidence of ventral hernias. Multivariate analysis revealed time to closure as a significant independent predictor of length of stay, ventilator duration, time to full enteral feeds, and TPN duration.

Conclusions: Our data show largely equivalent outcomes between patients who undergo immediate closure and those who have silos ≤5 days. We propose that closure within 5 days avoids many of the risks commonly attributed to delay in closure.

Level of evidence: Level II retrospective study.

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Gastroschisis is the most common congenital abdominal wall abnormality and is increasing in incidence [1,2]. Advances in both neonatal intensive care and surgical techniques have led to a dramatic increase in survival and reduction in morbidity over the past few decades; however, substantial issues remain including delayed tolerance of enteral feeding, prolonged ventilator requirement, and increased intensive care unit length of stay as well as cost [3–5].

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The method of closure in gastroschisis remains a somewhat contentious topic of discussion. Immediate closure was the primary method until the early 1990's when the advent of the spring-loaded silo occurred and had rapid adoption [6–8]. Proponents of immediate closure argue that the technique leads to shorter hospital stays and fewer complications, with some centers planning elective preterm delivery to facilitate immediate primary closure [9]. Those who prefer the use of silos argue that they offer the ability to reduce abdominal wall tension by gradual visceral reduction and potentially allow earlier tolerance of enteral feeding [10]. Much of the data supporting each approach is based on relatively small, single-center studies. Better understanding of the outcomes associated with each approach is necessary to guide clinical decision making. The purpose of this study was to compare outcomes between these two gastroschisis management approaches using a large, contemporary, multicenter database analysis.

[★] Disclosures: The Abdominal Wall Defects database was established with the help of an internal grant funded by the Children's Miracle Network. The authors otherwise have no competing interests to disclose.

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1. Methods

1.1. Study design

A retrospective observational study was conducted at 8 United States medical centers. The study was approved by the Institutional Review Board at each institution prior to initiation. Live-born neonates born between January 2005 and January 2013 with a diagnosis of gastroschisis were included. Cases of gastroschisis were identified using the ICD-9-CM code 756.7, followed by clinical chart review to confirm the diagnosis. A total of 36 surgeons participated in gastroschisis cases between the 8 study sites. Data were collected using an encrypted, proprietary database that was stored at the primary investigator's site.

1.2. Variables and outcomes

Maternal data were collected including maternal age, maternal conditions, and maternal alcohol or smoking or illicit drug use. Delivery location (inborn or outborn) and route of delivery (caesarean section or vaginal) as well as the reason for planned or emergency caesarean section were recorded. Inborn patients were defined as those who were delivered at one of the study sites, and outborn patients were defined as those delivered elsewhere and subsequently transferred.

Neonatal data including sex, race/ethnicity, gestational age, birth weight, and Apgar scores at 1 and 5 min were also collected. Additional data regarding severity of disease were collected, including atresia, sepsis, and short bowel syndrome. Sepsis was defined as the occurrence of a systemic inflammatory response syndrome requiring antibiotics, resucitation, and culture. Short bowel syndrome was defined as intestinal malabsorption related to resection. Line infections were defined as bacteremia with positive cultures from removed central venous lines. Information about silo placement, silo size, duration of silo, and time to definitive closure was also recorded. Variables pertinent to and detailing the neonatal hospital course were included in the study as well as outcome related data and morbidity / mortality.

Patients were stratified into silo closure (SC) or immediate closure (IC) groups depending on whether a silo was used initially or not. Further stratification of the patients receiving silos was performed based on duration of silo placement, with SC patients sorted into ≤ 5 days, 6-10 days, or > 10 day silo duration groups. At the 8 study sites, the same surgeons operated on patients from different time-to-closure groups.

The primary outcome compared between groups was survival to hospital discharge. Secondary outcomes included length of stay (LOS), duration of total parenteral nutrition (TPN), duration of mechanical ventilation, time to full enteral feeds, and incidence of ventral hernias. LOS was recorded as the number of inpatient days during the initial hospitalization and did not factor in additional days from readmissions. Ventral hernias were defined as clinically diagnosed abdominal wall defects present after gastroschisis closure and/or silo removal.

1.3. Statistical analysis

Data are presented as frequency and percentage for categorical variables and median and range for continuous variables. Fischer's exact test was used to compare categorical variables, and Mann–Whitney U test was used to compare non-parametric continuous variables. Students T test was used for parametric continuous data. Missing variables were labeled as unknown and excluded from analysis. All significance tests are two-sided, with a p-value less than 0.05 considered statistically significant. Univariate and multivariate logistic regression analyses were performed to evaluate the effect of possible confounders on outcome variables. Covariates considered included silo duration, the presence of complex gastroschisis, gestational age at delivery, and Apgar score at 5 min. Complex gastroschisis was defined as the presence of intestinal atresia, perforation, or volvulus [11,12]. Statistical analysis was

performed using Prism GraphPad (La Jolla, CA) and SAS version 9.4 (Cary, NC).

2. Results

2.1. Patient demographics, baseline characteristics, and management

Five-hundred and sixty-six patients from eight academic centers were enrolled in the study, of whom 224 underwent immediate closure and 337 had a silo placed with delayed closure. Five patients were excluded from the study, 3 for death within the first two hours of life and 2 for incomplete recording of closure technique. The majority of patients were male (54%) with a median gestational age of 36 weeks and median birth weight of 2390 g (Table 1). There was a higher proportion of males in the silo placement group than the immediate closure group. Otherwise there were no significant differences between the groups in baseline characteristics or markers of severity of disease, including designation as complex gastroschisis.

2.2. Outcomes

Overall mortality was low, with 95% of patients surviving to hospital discharge (Table 2). Eighty-six percent of patients required intubation at birth with a 5 day median duration of mechanical ventilation. The median time to full tolerance of enteral feeds was 26 days. Sepsis occurred in 19% of patients over the course of their hospitalization. Cholestasis was noted in 14% of neonates in the study.

Among the 337 patients who had a silo placed, 130 had it for ≤ 5 days prior to closure, 140 for 6–10 days, and 57 for > 10 days. Outcomes were compared between the immediate closure group and the three groups of varying silo duration (Table 2). There were no significant differences between immediate closure and ≤ 5 day silo groups in terms of mortality, sepsis, hospital length of stay, time to tolerance of full enteral feeds, or readmission. Patients who had a silo ≤ 5 days had a significantly longer duration of mechanical ventilation than those who underwent immediate closure (median 5 vs. 3 days, p=0.0059). However, patients who underwent immediate closure had significantly higher risk of ventral hernias than those who had a silo ≤ 5 days (12% vs. 3%, p=0.0032).

2.3. Univariate and multivariate logistic regression

Univariate logistic regression was performed to evaluate the effect of various explanatory variables on outcomes including mortality, length of stay, ventilator duration, time to full enteral feeds, and sepsis (Table 3). Silo duration was not a significant univariate predictor of mortality, but was a significant predictor of length of stay, ventilator duration, and time to full enteral feeds.

Multivariate logistic regression was performed to evaluate the effect of potential confounders in prediction of outcomes including mortality, length of stay, ventilator duration, time to full feeds, duration of TPN, and sepsis (Table 4). Explanatory variables that were included in multivariate analysis were time to closure, the presence of complex gastroschisis, gestational age at delivery, and Apgar score at 5 min. Birth weight and Apgar score at 1 min were excluded from multivariate analysis owing to high correlation with gestational age and Apgar score at 5 min, respectively. Multivariate analysis revealed that time to closure was a significant independent predictor of length of stay, ventilator duration, time to full enteral feeds, and TPN duration.

An additional multivariate analysis was performed evaluating outcomes only between patients who received immediate closure and those with silo duration ≤ 5 days (Table 5). There was no significant independent effect between immediate and ≤ 5 day closure in terms of time to full enteral feeds, TPN duration, or sepsis. Immediate vs. ≤ 5 day closure was a significant independent predictor of ventilator duration and the occurrence of ventral hernia between these two groups, with the IC group having fewer ventilator days but more ventral hernias.

Table 1Patient demographics, baseline characteristics, and initial management.

Characteristics	Overall $(n = 566)$	Immediate Closure ($n = 224$)	Silo Closure ($n = 337$)	p-value	
Gestational age in weeks, median (range)	36 (28-40)	36 (29–40)	36 (28–40)	0.1960	
Birth weight in grams, median (range)	2390 (770-4340)	2365 (770-4020)	2410 (1100-5622)	0.9897	
Male, n (%)	307 (54)	105 (47)	198 (59)	0.0073*	
Race, n (%)					
Asian	4(1)	2(1)	1 (0)	0.5667	
Black or African American	75 (13)	27 (12)	46 (13)	0.6106	
Hispanic or Latino	54 (10)	26 (12)	35 (10)	0.6790	
White, non-Hispanic	325 (57)	126 (56)	198 (59)	0.6007	
More than one race	15 (3)	7 (3)	8 (2)	0.6024	
Unknown	104 (18)	46 (21)	58 (17)	0.3209	
Maternal age in years, median (range)	21 (13-48)	21 (14–42)	21 (13–48)	0.6739	
Maternal Substance Use, n (%)	, ,	, ,	, ,		
Tobacco	206 (36)	78 (35)	126 (37)	0.5909	
Alcohol	149 (26)	58 (26)	89 (26)	0.9221	
Illicit drug	26 (5)	10 (5)	16 (5)	>0.9999	
Delivery Method, n (%)	, ,	, ,	, ,		
Emergent C-section	115 (20)	37 (17)	78 (23)	0.0692	
Planned C-section	168 (30)	72 (32)	94 (28)	0.2995	
Vaginal	179 (32)	67 (30)	112 (33)	0.4595	
Unknown	104 (18)	48 (21)	53 (16)	0.0929	
Apgar score, median (range)					
At 1 min	8 (1-9)	8 (1-9)	8 (1-9)	0.3241	
At 5 min	9 (1–10)	9 (1–10)	9 (1-10)	0.3031	
Prenatal gastroschisis diagnosis, n (%)	383 (68)	145 (65)	236 (70)	0.1970	
Gastrointestinal comorbidities, n (%)	77 (14)	` '	,		
Atresia	42 (7)	19 (8)	23 (7)	0.5136	
Perforation	20 (4)	7 (3)	12 (4)	>0.9999	
Volvulus	4(1)	2(1)	2(1)	0.6532	
More than one	11 (2)	5 (2)	6(2)	0.7602	

^{*} Denotes p-value less than 0.05.

3. Discussion

This large, multicenter, retrospective observational study demonstrated generally equivalent outcomes between gastroschisis patients who underwent immediate closure and those who had a silo placed for less than or equal to 5 days. There was no significant difference between these groups in terms of mortality or time to tolerance of full enteral feeds, suggesting that short-term silo placement is a reasonable approach. Additionally, multivariate analysis revealed that silo duration is not a significant independent predictor of time to full enteral feeds or TPN duration between patients who underwent immediate closure or those who had a silo for ≤5 days. While the time to closure was a strong predictor of outcome, our data suggest that patients who require a silo longer than 5 days may represent a subset of patients with a higher 'disease severity', and therefore may not be appropriate to compare to those patients that underwent immediate closure. Patients undergoing immediate closure (as well as the silo group closed within 5 days) likely represent a select group that are 'favorable' at the outset. We speculate that those patients who achieve closure within 5 days of silo placement have less severe disease and therefore have favorable outcomes.

Previous reports have shown that early initiation and tolerance of enteral feeding are associated with improved outcomes in patients with gastroschisis [10]. Some centers have adopted planned preterm delivery of neonates with gastroschisis to facilitate immediate closure in hopes of promoting earlier tolerance of feeding, reduced duration of TPN, and shorter hospital length of stay [13,14]. A prospective randomized controlled trial of elective preterm delivery of neonates with gastroschisis did not demonstrate improved outcomes for neonates who underwent elective preterm delivery, and although there was a trend toward reduced time to full enteral feeding and hospital LOS in the elective preterm delivery group, the study was underpowered and these differences did not reach statistical significance [15]. In the current study, we noted a progressive increase in the duration of parenteral nutrition required as well as time to full feeds with longer silo placement. This has been shown in multiple previous studies as well, but without a large enough number of patients to show differences between

Table 2Clinical outcomes between immediate closure and silo placement groups stratified by time to closure.

Outcomes	Overall (n=566)	Immediate (n=224)	Silo \leq 5 Days (n=130)	Silo 6-10 Days (n=140)	Silo > 10 Days (n=57)	p-value (Immediate vs. Silo ≤ 5 Days)	p-value (Immediate vs. Silo >10 days)
Sepsis, n (%)	107 (19)	44 (20)	18 (14)	29 (21)	14 (25)	0.1927	0.4636
Line infection, n (%)	32 (6)	11 (5)	10 (8)	9 (6)	2 (4)	0.3512	>0.9999
Cholestasis, n (%)	78 (14)	30 (13)	11 (8)	28 (20)	8 (14)	0.1732	0.8320
Short bowel syndrome, n (%)	39 (7)	20 (9)	5 (4)	5 (4)	5 (9)	0.0860	>0.9999
Days to full enteral nutrition, median (range), $n=147$	26 (1–536)	22 (1–142)	23 (6–106)	31 (13–536)	70.5 (26–229)	0.2275	0.0001*
TPN days, median (range), n = 365	27 (1-1718)	26.5 (2-1718)	24 (4-138)	31 (1-334)	34 (1-229)	0.7142	0.0095*
Need for mechanical ventilation, n (%)	486 (86)	188 (84)	116 (89)	121 (86)	51 (89)	0.2056	0.4052
Ventilator days, median (range), n = 430	5 (1-194)	3 (1-42)	5 (1-138)	9 (1-108)	13.5 (1-194)	0.0059*	<0.0001*
Ventral hernia, n (%)	49 (9)	27 (12)	4(3)	9 (6)	7 (12)	0.0032*	>0.9999
Hospital LOS in days, median (range), n=433	37 (1-306)	34 (1-221)	34 (14-920)	45 (5-197)	62 (1-306)	0.7641	<0.0001*
Readmission, n (%)	100 (18)	39 (17)	16 (12)	29 (20)	16 (28)	0.2257	0.0912
Survival, n (%)	536 (95)	214 (96)	126 (97)	135 (96)	54 (95)	0.5857	0.7310

^{*} Denotes p-value less than 0.05.

Table 3Univariate logistic regression predicting mortality, length of stay, ventilator duration, time to full enteral feeds, and sepsis.

Variable	Odds Ratio	95% Confidence Interval	Wald Chi-Square	p-value
Outcome: Mortality				
Time to closure (categorical; immediate, ≤5 days, 6–10 days, ≥10 days)	0.991	0.656-1.498	0.0018	0.9662
Silo duration (continuous; n days)	1.025	0.959-1.096	0.5217	0.4701
Complex gastroschisis (atresia, perforation, or volvulus)	3.15	1.240-8.004	5.8149	0.0159*
Birth weight	0.998	0.997-0.999	12.6497	0.0004*
Gestational age at delivery	0.697	0.571-0.852	12.4425	0.0004*
Male gender	1.245	0.523-2.964	0.2461	0.6198
Apgar score at 1 min	0.849	0.721-0.999	3.9057	0.0481*
Apgar score at 5 min	0.766	0.628-0.935	6.8761	0.0087*
Outcome: Length of Stay (days)				
Time to closure (categorical; immediate, ≤5 days, 6–10 days, ≥10 days)	0.619	0.534-0.718	40.5386	< 0.0001*
Silo duration (continuous; n days)	0.874	0.834-0.916	31.3982	< 0.0001*
Complex gastroschisis (atresia, perforation, or volvulus)	0.127	0.080-0.202	76.2249	< 0.0001*
Birth weight	1.001	1.000-1.001	16.3427	<0.0001*
Gestational age at delivery	1.277	1.170-1.394	29.9162	<0.0001*
Male gender	0.881	0.656–1.183	0.7075	0.4003
Apgar score at 1 min	1.007	0.941–1.077	0.039	0.8434
Apgar score at 5 min	1.028	0.926–1.141	0.2622	0.6086
Outcome: Ventilator Duration	11020	0.020 111 11	0,2022	0.0000
Time to closure (categorical; immediate, ≤5 days, 6–10 days, ≥10 days)	0.393	0.328-0.470	103.5527	< 0.0001*
Silo duration (continuous; n days)	0.842	0.795-0.891	34,9500	<0.0001*
Complex gastroschisis (atresia, perforation, or volvulus)	0.517	0.314-0.851	6.7191	0.0095*
Birth weight	1.000	1.000–1.001	1.6414	0.2001
Gestational age at delivery	1.236	1.124–1.359	19.1500	<0.0001*
Male gender	0.874	0.626–1.220	0.6228	0.4300
Apgar score at 1 min	1.055	0.979–1.137	1.9523	0.1623
Apgar score at 5 min	1.051	0.942-1.172	0.7985	0.3715
Outcome: Time to Full Enteral Feeds (days)	1.051	0.3 12 1.172	0.7303	0.5715
Time to closure (categorical; immediate, ≤5 days, 6–10 days, ≥10 days)	0.417	0.299-0.581	26.6737	<0.0001*
Silo duration (continuous; n days)	0.812	0.735-0.897	16.6785	<0.0001
Complex gastroschisis (atresia, perforation, or volvulus)	0.04	0.014-0.118	34.4202	<0.0001
Birth weight	1.001	1.000-1.001	3.2948	0.0695
Gestational age at delivery	1.128	0.974–1.306	2.5982	0.1070
Male gender	0.844	0.480-1.484	0.3486	0.5549
Apgar score at 1 min	0.971	0.845-1.116	0.1743	0.6764
Apgar score at 5 min	1.005	0.815-1.239	0.0024	0.9612
Outcome: Sepsis	1.005	0.815-1.255	0.0024	0.3012
Time to closure (categorical; immediate, ≤5 days, 6–10 days, ≥10 days)	1.145	0.930-1.409	1.6263	0.2022
Silo duration (continuous; n days)	1.014	0.999-1.029	3.4757	0.0623
Complex gastroschisis (atresia, perforation, or volvulus)	3.824	2.203-6.637	22.7243	<0.0023
Birth weight	0.999	0.999-1.000	10.3363	0.0013*
Gestational age at delivery	0.779	0.690-0.881	15.8583	<0.0013*
Male gender	1.080	0.698-1.671	0.1199	< 0.0001* 0.7291
· ·	0.999	0.698-1.671	0.1199	0.7291
Apgar score at 1 min	0.999		3.7446	0.9763
Apgar score at 5 min	0.874	0.763-1.002	5./440	0.053

^{*} Denotes p-value less than 0.05.

groups clustered by days [7,16]. Here we found no significant difference between the immediate closure and short duration silo groups in terms of time to full enteral feeds, duration of TPN, or hospital length of stay. Although our patients who underwent silo placement did require a slightly longer duration of mechanical ventilation, there was no association with sepsis or longer length of stay. Future prospective work is required to determine the reasons for prolonged mechanical ventilation in these patients and if this is associated with pulmonary complications. More recent practice may reflect a progressive reduction in intubation and ventilation for gastroschisis undergoing silo placement as neonatal units become more familiar. When examining our dataset for changes in ventilator use over time, however, we found no significant difference between patients managed before or after 2008 in terms of requirement for mechanical ventilation or duration of mechanical ventilation.

Ventral hernias are a well-known complication following gastroschisis repair [17,18]. However, very few studies have compared incidence of ventral hernia based on whether the patient received immediate or silo closure. In this report we noted that patients who underwent immediate closure had a higher incidence of ventral hernias than those who had silos placed for a short duration. The hernia rate increased with longer duration of silo and was equivalent to the immediate group when the silo was present for greater than 10 days. The reason for this observed difference is unclear, but may be related to higher

abdominal wall tension and fascial stress in immediate closure patients than those who have a short duration silo placed with staged closure in which abdominal domain has increased. Silo placement may also facilitate fluid management with reduced bowel edema and less tension at the time of definitive fascial closure.

Our overall understanding of gastroschisis and the factors involved with increased morbidity has evolved over the past few decades, allowing refinements in risk stratification of the condition. We now accept that neonates with atresia or any bowel compromise represent a 'complex' variant of the condition and have a much higher burden of complications compared to 'simple' cases. Similarly, the CAPSNetderived gastroschisis prognosis score (GPS), which attempts to take into account the degree of inflammation, matting and bowel thickening, has started to stratify the condition even better [19]. Our data suggest that patients who are unable to be closed safely by 5 days also may face a worse prognosis, and therefore represent a higher risk group of neonates. At the very least, continued inclusion of these cases when comparing silo vs. immediate closure may not be appropriate when assessing outcomes. We have used these data to help counseling parents and set appropriate expectations based on risk category.

Our study has several limitations which require discussion. Given that this was a retrospective study, the variables collected were limited to those that could be found from medical record review. We did not

 Table 4

 Multivariate logistic regression predicting mortality, length of stay, ventilator duration, time to full feeds, TPN duration, and sepsis.

Variable	Adjusted Odds Ratio	95% Confidence Interval	Adjusted Wald Chi-Square	p-value
Outcome: Mortality				
Time to closure (categorical; immediate, ≤5 days, 6–10 days, ≥10 days)	1.080	0.700-1.666	0.1202	0.7288
Complex gastroschisis (atresia, perforation, or volvulus)	1.959	0.692-5.545	1.6061	0.2050
Gestational age at delivery	0.721	0.581-0.894	8.9187	0.0028*
Apgar score at 5 min	0.810	0.651-1.007	3.6090	0.0575
Outcome: Length of Stay (days)				
Time to closure (categorical; immediate, ≤5 days, 6–10 days, ≥10 days)	0.602	0.514-0.706	39.2243	<0.0001*
Complex gastroschisis (atresia, perforation, or volvulus)	0.146	0.091-0.245	56.4856	<0.0001*
Gestational age at delivery	1.196	1.091-1.312	14.4219	0.0001*
Apgar score at 5 min	1.002	0.900-1.116	0.0017	0.9672
Outcome: Ventilator Duration (days)				
Time to closure (categorical; immediate, ≤5 days, 6–10 days, ≥10 days)	0.365	0.301-0.443	103.7504	<0.0001*
Complex gastroschisis	0.587	0.344-1.001	3.8306	0.0503
Gestational age at delivery	1.200	1.084-1.328	12.4105	0.0004*
Apgar score at 5 min	1.071	0.957-1.199	1.4431	0.2296
Outcome: Time to Full Enteral Feeds (days)				
Time to closure (categorical; immediate, ≤5 days, 6–10 days, ≥10 days)	0.432	0.300-0.621	20.4537	<0.0001*
Complex gastroschisis	0.042	0.014-0.129	30.6283	<0.0001*
Gestational age at delivery	1.129	0.965-1.322	2.2930	0.1300
Apgar score at 5 min	0.977	0.785-1.216	0.0445	0.8329
Outcome: TPN Duration (days)				
Time to closure (categorical; immediate, ≤5 days, 6–10 days, ≥10 days)	0.730	0.600-0.887	10.0480	0.0015*
Complex gastroschisis	0.138	0.077-0.247	44.7090	<0.0001*
Gestational age at delivery	1.197	1.074-1.335	10.4663	0.0012*
Apgar score at 5 min	1.042	0.920-1.180	0.4151	0.5194
Outcome: Sepsis				
Time to closure (categorical; immediate, ≤5 days, 6–10 days, ≥10 days)	1.123	0.884-1.425	0.9050	0.3414
Complex gastroschisis	3.705	2.004-6.851	17.4380	<0.0001*
Gestational age at delivery	0.793	0.691-0.909	11.0477	0.0009*
Apgar score at 5 min	0.871	0.753-1.007	3.4811	0.0621

^{*} Denotes p-value less than 0.05.

collect data regarding surgeon intention to treat as a determinant of time-to-closure group or whether patients with longer duration silo placements had previously undergone repeated failed attempts at closure. Additionally, there was no effort to standardize practice across the 8 study sites, with the retrospective study capturing a diverse gastroschisis management practices between institutions. Despite likely practice variations between centers in this study, our data regarding the association between silo duration and outcomes are strong, suggesting again that patients requiring longer silo duration likely have a higher

degree of disease severity. We did not collect data on the details of the closure technique, and as such the patients in the immediate closure group may have had a higher incidence of sutureless repair which is prone to a higher umbilical hernia rate [20]. Although we noted significant differences between time-to-closure groups in terms of duration of mechanical ventilation, data regarding reasons for endotracheal intubation and prolonged ventilation are not available, limiting these conclusions. Also, the study was performed at tertiary referral centers for neonatology and pediatric surgery, and it is unclear if equivalent

 Table 5

 Multivariate logistic regression between immediate and silo duration ≤5 days predicting time to full enteral feeds, ventilator duration, TPN duration, recurrent ventral hernia, and sepsis.

Variable	Adjusted Odds Ratio	Adjusted 95% Confidence Interval	Adjusted Wald Chi-Square	p-value
Outcome: Time to Full Enteral Feeds (days)				
Time to closure (categorical; immediate or ≤5 days)	0.720	0.332-1.563	0.6890	0.4065
Complex gastroschisis (atresia, perforation, or volvulus)	0.066	0.016-0.274	14.0287	0.0002*
Gestational age at delivery	1.006	0.819-1.234	0.0030	0.9565
Apgar score at 5 min	1.067	0.837-1.360	0.2731	0.6012
Outcome: Ventilator Duration (days)				
Time to closure (categorical; immediate or ≤5 days)	0.501	0.313-0.802	8.2788	0.0040*
Complex gastroschisis (atresia, perforation, or volvulus)	1.050	0.515-2.140	0.0179	0.8936
Gestational age at delivery	1.171	1.032-1.330	5.9437	0.0148*
Apgar score at 5 min	1.035	0.900-1.189	0.2305	0.6312
Outcome: TPN Duration (days)				
Time to closure (categorical; immediate or ≤5 days)	0.910	0.557-1.485	0.1433	0.7050
Complex gastroschisis (atresia, perforation, or volvulus)	0.165	0.078-0.350	22.0243	< 0.0001*
Gestational age at delivery	1.192	1.041-1.364	6.4820	0.0109*
Apgar score at 5 min	1.120	0.955-1.314	1.9454	0.1631
Outcome: Ventral Hernia				
Time to closure (categorical; immediate or ≤5 days)	3.434	1.111-10.612	4.5947	0.0321
Complex gastroschisis (atresia, perforation, or volvulus)	2.483	0.519-11.869	1.2984	0.2545
Gestational age at delivery	1.140	0.888-1.463	1.0503	0.3054
Apgar score at 5 min	0.771	0.507-1.171	1.4915	0.2220
Outcome: Sepsis				
Time to closure (categorical; immediate or ≤5 days)	0.939	0.473-1.865	0.0326	0.8566
Complex gastroschisis (atresia, perforation, or volvulus)	3.009	1.315-6.886	6.8009	0.0091*
Gestational age at delivery	0.724	0.606-0.864	12.8167	0.0003*
Apgar score at 5 min	0.940	0.778-1.134	0.4211	0.5164

outcomes could be expected at dissimilar institutions. Despite these limitations, the study is strengthened by the quality of standardized variable collection for a large number of patients enrolled from eight institutions, which may help to generalize the results.

4. Conclusions

To our knowledge, this is the largest multicenter retrospective study of neonates with gastroschisis comparing outcomes by time to closure as well as immediate vs. stratified silo closure techniques. Our study is unique in demonstrating largely equivalent outcomes between patients who underwent immediate closure and those who had a silo less than 5 days, and in fact reduced ventral hernias among those patients. These data suggest that immediate closure may not always be required, and elective preterm delivery may not be necessary. We also suggest that future studies comparing immediate with silo closure for gastroschisis should exclude the longer duration patients from analysis. The patients requiring silo for a longer period of time should be studied further as a high risk group. Further prospective data collection is necessary to confirm these findings.

Funding

The Abdominal Wall Defects database was established with the help of an internal grant funded by the Children's Miracle Network. The authors otherwise have no competing interests to disclose.

References

- Sekabira J, Hadley GP. Gastroschisis: a third world perspective. Pediatr Surg Int 2009;25(4):327–9.
- [2] Stoll C, Alembik Y, Dott B, et al. Omphalocele and gastroschisis and associated malformations. Am | Med Genet A 2008;146A(10):1280-5.

- [3] Bradnock TJ, Marven S, Owen A, et al. Gastroschisis: one year outcomes from national cohort study. BMJ 2011;343:d6749.
- [4] Holland AJ, Walker K, Badawi N. Gastroschisis: an update. Pediatr Surg Int 2010;26 (9):871–8.
- [5] Lap CC, Brizot ML, Pistorius LR, et al. Outcome of isolated gastroschisis; an international study, systematic review and meta-analysis. Early Hum Dev 2016;103: 209–18
- [6] Charlesworth P, Akinnola I, Hammerton C, et al. Preformed silos versus traditional abdominal wall closure in gastroschisis: 163 infants at a single institution. Eur J Pediatr Surg 2014;24(1):88–93.
- [7] Lobo JD, Kim AC, Davis RP, et al. No free ride? The hidden costs of delayed operative management using a spring-loaded silo for gastroschisis. J Pediatr Surg 2010;45(7):
- [8] Schlatter M, Norris K, Uitvlugt N, et al. Improved outcomes in the treatment of gastroschisis using a preformed silo and delayed repair approach. J Pediatr Surg 2003;38(3):459-64 [discussion -64].
- [9] Glasmeyer P, Grande C, Margarit J, et al. Gastroschisis. Preterm elective cesarean and immediate primary closure: our experience Cir Pediatr 2012;25(1):12–5.
- [10] Harris J, Poirier J, Selip D, et al. Early closure of gastroschisis after silo placement correlates with earlier enteral feeding. J Neonatal Surg 2015;4(3):28.
- [11] Arnold MA, Chang DC, Nabaweesi R, et al. Risk stratification of 4344 patients with gastroschisis into simple and complex categories. J Pediatr Surg 2007;42(9):1520–5.
- [12] Molik KA, Gingalewski CA, West KW, et al. Gastroschisis: a plea for risk categorization. J Pediatr Surg 2001;36(1):51–5.
- [13] Landisch RM, Yin Z, Christensen M, et al. Outcomes of gastroschisis early delivery: A systematic review and meta-analysis. J Pediatr Surg 2017;52(12):1962–71.
- [14] Moir CR, Ramsey PS, Ogburn PL, et al. A prospective trial of elective preterm delivery
- for fetal gastroschisis. Am J Perinatol 2004;21(5):289–94. [15] Logghe HL, Mason GC, Thornton JG, et al. A randomized controlled trial of elective
- preterm delivery of fetuses with gastroschisis. J Pediatr Surg 2005;40(11):1726–31.

 [16] Kunz SN, Tieder JS, Whitlock K, et al. Primary fascial closure versus staged closure
- with silo in patients with gastroschisis: a meta-analysis. J Pediatr Surg 2013;48(4): 845–57.
- [17] Harris EL, Minutillo C, Hart S, et al. The long term physical consequences of gastroschisis. J Pediatr Surg 2014;49(10):1466–70.
- [18] Tullie LG, Bough GM, Shalaby A, et al. Umbilical hernia following gastroschisis closure: a common event. Pediatr Surg Int 2016;32(8):811–4.
- [19] Puligandla PS, Baird R, Skarsgard ED, et al. Canadian Pediatric Surgery N. Outcome prediction in gastroschisis — the gastroschisis prognostic score (GPS) revisited. J Pediatr Surg 2017;52(5):718–21.
- [20] Witt RG, Zobel M, Padilla B, et al. Evaluation of clinical outcomes of sutureless vs sutured closure techniques in gastroschisis repair. JAMA Surg 2019;154(1):33–9.