Journal of Pediatric Surgery 55 (2020) 1866–1871

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Neonatal Conditions

Outcomes in the giant omphalocele population: A single center comprehensive experience☆,☆☆,★

Heather R. Nolan [1,*], Monica L. Wagner, Todd Jenkins, Foong-Yen Lim

Cincinnati Children's Hospital Medical Center, Division of Pediatric General and Thoracic Surgery, Cincinnati, OH, USA

ARTICLE INFO

Article history:
Received 10 July 2019
Received in revised form 13 April 2020
Accepted 26 April 2020

Key words:
Giant omphalocele
Abdominal wall defect
Staged omphalocele closure
Delayed omphalocele closure

ABSTRACT

Background/Purpose: Morbidity and mortality in the giant omphalocele population is complicated by large abdominal wall defects, physiologic aberrancies, and congenital anomalies.
We hypothesized different anomalies and treatment types would affect outcomes.
Methods: A 2009–2018 retrospective chart review of giant omphaloceles was performed.
Exclusions included cloacal exstrophy, transfer after 3 weeks, surgery prior to transfer, conjoined twins, or not yet achieving fascial closure. Thirty-five patients met criteria and mortality and operative morbidity categorized them into favorable ($n = 20$) or unfavorable ($n = 15$) outcomes. Odds ratios analyzed potential predictors. Survivors were stratified into staged ($n = 11$), delayed ($n = 8$), and primary closure ($n = 6$) for subgroup analysis.
Results: Unfavorable outcomes were associated with other major congenital anomalies, sac rupture, and major cardiac anomalies, but had significantly lower odds with increasing gestational age ($p = 0.03$) and birth weight ($p < 0.001$). In survivors, the primary group was younger at repair ($p < 0.001$) and had shorter length of stay (hospital $p = 0.02$, neonatal intensive care unit $p = 0.005$). There was no significant difference for sepsis, ventilator days, return to the operating room, or ventral hernia.
Conclusions: Predictions of overall outcomes in the giant omphalocele population require analysis of multiple variables. Our findings demonstrated increased odds of unfavorable outcomes in major cardiac anomalies, pulmonary hypertension, genetic diagnosis, other major anomalies, polyhydramnios, postnatal sac rupture, increasing omphalocele sac diameter, lower O/E TLV, lower gestational age at birth, lower birth weight, and repair other than primary. In those surviving to repair, surgical outcomes analyses demonstrated an earlier age of repair and a shorter length of stay for those patients able to be closed primarily; however further research is necessary to determine overall superiority between operative treatment types.
Level of Evidence: Level III.

An omphalocele is a congenital defect of the abdominal wall that occurs in one in 3000 to 10,000 live births [1]. Small omphaloceles are able to have their contents easily reduced into the abdominal cavity with primary closure of the fascial defect. In the giant omphalocele population, management is much more complex as the discrepancy between sac contents and the decreased abdominal domain leads to significant increases in compartment pressures and subsequent cardiopulmonary compromise with attempts at reduction. While some patients are able to be repaired primarily, other techniques have been developed to mitigate this process and typically fall into two broad categories: staged and delayed. In staged closure the contents of the sac are compressed over time while in delayed closure the sac is treated topically to allow for escharization and growth with little to no manipulation of sac contents. While both options have demonstrated safety and feasibility in the literature, treatment type is only a portion of the decision making that goes into surgical management of the giant omphalocele.

The other complicating factor in this unique group of patients is the high propensity for other congenital or genetic findings such as trisomies, heart defects, and intestinal atresias [1–6] that often require stabilization and treatment prior to attempting operative repair of the abdominal wall. Determining how aggressive to be in offering surgery

☆ Declarations of Interest: None.

☆☆ Submission Declaration/Funding Source: This work was completed in partial fulfillment of the Master of Science degree in Clinical and Translational Research in the Division of Epidemiology, University of Cincinnati College of Medicine. This publication was supported by an Institutional Clinical and Translational Science Award, NIH/NCATS 1UL1TR001425. Its contents are solely the responsibility of the authors and do not necessarily represent the official views of the NIH. The funding source had no involvement in study design; in the collection, analysis and interpretation of data; in the writing of the report; nor in the decision to submit the article for publication.

★ Potential Conflicts of Interest: The authors have no conflicts of interest relevant to this article to disclose.

* Corresponding author at: Cincinnati Children's Hospital Medical Center, Division of Pediatric General and Thoracic Surgery, 3333 Burnet Avenue, MLC 2023, Cincinnati, Ohio 45229. Tel.: +1 513 803 9226; fax: +1 513 636 7657.
E-mail address: hnolan2@jhmi.edu (H.R. Nolan).
[1] New address as of 8/1/2019: Johns Hopkins All Children's Hospital, Division of Pediatric Surgery, 601 5th Street South, Ste. 611, St. Petersburg, FL 33701.

https://doi.org/10.1016/j.jpedsurg.2020.04.019
0022-3468/

is therefore difficult as the surgeon must consider the inherent anomalies that will affect overall outcome in addition to the risks of surgical intervention itself. This conundrum is noted in the literature but little guidance is available on how to view these patients as a whole, with most articles focusing on individualized modifiers. We hypothesized different anomalies and treatment types would affect outcomes in varying magnitudes. Therefore, our aim was to evaluate both patient and surgical factors and their impact on overall outcomes.

1. Materials and methods

1.1. Approach

A retrospective chart review was performed on all patients with omphalocele from June 2009 to December of 2018 at a single academic children's hospital (IRB2018–8418). One hundred thirteen patients were identified and 35 met criteria for further analysis. Patients were excluded if the omphalocele did not meet the definition of giant (n = 23) or the patient had cloacal exstrophy (n = 30), was transferred >3 weeks of age (n = 15, mean 1.7 years, range 0.06–7 years), received surgical intervention from another hospital prior to transfer (n = 5), was a conjoined twin (n = 2), or survived but did not achieve final fascial closure (n = 3). Of note, there was crossover within these categories with some patients meeting multiple exclusion criteria. The most pertinent exclusion was used for the aforementioned values. Patients were categorized into outcome groups of favorable or unfavorable based on need for ECMO (Extracorporeal Membrane Oxygenation), mortality, and surgical complications. Those that survived to repair were further stratified into treatment groups of staged, delayed, or primary closure. Thirteen pediatric surgeons experienced in omphalocele/abdominal wall operations performed all the repairs in this study, ranging from one to 10 patients. Surgeons were not exclusive to the type of repair performed. Operative technique was at the discretion of the primary surgeon and was not standardized. Prenatal and postnatal data were collected.

1.2. Definitions

The definition of giant omphalocele varies in the literature and can be as simple as inability to achieve primary closure or liver in the omphalocele sac to more objective findings defined by defect size, commonly >5 cm, or sac dimensions [2,3,7–10]. For our study we defined the following criteria:

- Giant omphalocele: greater than or equal to 50% of the liver in the herniated contents or a defect or sac diameter of >5 cm by prenatal or postnatal imaging.
- Staged closure: placement of a device to the abdominal wall that allowed for serial reduction and included silastic/Bentec silos (Bentec Medical, Woodland, California), mesh silos, external DuoDerm (ConvaTec, Bridgewater, New Jersey) silos, or Schuster technique.
- Delayed closure: topical treatment.
- Final fascial closure: closure of the fascia by primary repair or with supplemental material with or without skin closure.
- Unfavorable outcome: those patients who died, required ECMO, had an omphalocele wound infection requiring revision, or returned to the operating room within 30 days for an omphalocele related procedure beyond simple dressing/wound vac changes. All others were categorized as favorable outcomes.
- Anomalies: Major anomalies included anorectal malformations, Pentalogy of Cantrell/congenital diaphragmatic hernia, tracheoesophageal fistula, and central nervous system anomalies (lissencephaly, colpocephaly, hypoxemic ischemic encephalopathy, Dandy-Walker). Minor anomalies included diagnoses that were identified but were not anticipated to have a significant effect on survival or outcomes such as patent foramen ovale or musculoskeletal defects.
- Wound infection: either culture positive or documented purulence.
- Sepsis: positive blood cultures or antibiotic treatment for greater than or equal to 5 days for sepsis rule-out and not for prophylaxis.
- Omphalocele sac diameter: dimensions measured by the greatest diameter on postnatal imaging closest to birth, or if none was available the latest gestation prenatal imaging as long as it was within 2 weeks of birth.

1.3. Statistical analyses

Continuous variables are presented as means with standard deviations or medians with first and third quartiles. Group comparisons for these variables were made using t-tests or Wilcoxon Rank-Sum tests. Categorical data are presented as percentages and frequencies, with Fisher's exact tests used for group comparisons. Separate exact logistical regression models were used to evaluate predictors of procedure (staged or delayed) and outcome (favorable or unfavorable). Modeling results are presented as odds ratios with 95% confidence intervals. Statistical associations were considered significant if the p value was <0.05. Few data were missing in this cohort, with the primary outcome of interest available for all 35 patients. Therefore, techniques to address missing data were not incorporated into the analyses. All analyses were conducted using SAS v9.4.

2. Results

2.1. Overall patient population

Thirty-five patients met criteria for analysis. Seventeen were males (17/35, 49%) and 18 were females (18/35, 51%). All patients were diagnosed prenatally with omphalocele and all but two patients (2/35, 6%) were evaluated at our corresponding fetal center. All patients had prenatal ultrasound imaging and all but one also had fetal MRI (Magnetic Resonance Imaging). Four patients (4/35, 11%) were delivered at our institution with 31 patients (31/35, 89%) delivered at an outside facility but transferred by day of life two. Three patients were delivered vaginally (3/35, 9%).

2.2. Demographics by favorable and unfavorable outcome

Table 1
Patient demographics by outcome.

	Favorable outcome (n = 20)	Unfavorable outcome (n = 15)	p-Value
Gender			0.50
Male	55% (11)	40% (6)	
Female	45% (9)	60% (9)	
Birth weight (kg)	**3.27 (2.29–6.73)**	**2.36 (1.35–3.45)**	**0.002**
Gestational age at birth			**0.04**
Early preterm <35 weeks	0 (0)	27% (4)	
Preterm 35–37 weeks	35% (7)	13% (2)	
Term ≥37 weeks	65% (13)	60% (9)	
Birth Hospital			0.62
Inborn	15% (3)	7% (1)	
Outborn	85% (17)	93% (14)	
Delivery Method			0.56
Vaginal	5% (1)	13% (2)	
C-section	95% (19)	87% (13)	
O/E TLV			0.37
≤ 50%	17% (2)	36% (4)	
>50%	83% (10)	64% (7)	
Omphalocele sac diameter (cm)	8.8 (5.1–13)	9.3 (5.4–18.2)	0.50

Values expressed as means (range), percentage of group (count);
*Includes initial hospitalization and hospitalization for repair.

Table 2
Predictors of unfavorable outcome.

	Crude		
	OR	95% CI	p-value
O/E TLV	0.99	0.96, 1.01	0.32
Polyhydramnios	1.16	0.21, 6.13	1.00
Gestational age at birth (weeks)	**0.60**	**0.35, 0.95**	**0.03**
Birth weight (kg)*	**0.05**	**0.005, 0.33**	**<0.001**
Omphalocele sac diameter (cm)	1.11	0.82, 1.52	0.53
Postnatal sac rupture	3.16	0.38, 40.47	0.40
Treatment			0.26
Staged	2.96	0.22, 176.88	
Delayed	5.92	0.49, 337.09	
Primary	<REF>		
Major cardiac anomalies	3.16	0.38, 40.47	0.40
Pulmonary hypertension	1.60	0.34, 7.87	0.73
Genetic diagnosis	1.09	0.17, 6.45	1.00
Other major anomalies	4.36	0.83, 27.16	0.09

O/E TLV, observed to expected total lung volume.
<REF> indicates use as the standard for statistical comparison.
* Weight was only term retained as significant in final adjusted model.

Patients were categorized into favorable outcome or unfavorable outcome (Table 1). With regard to baseline characteristics there was no significant difference between gender, inborn/outborn status, delivery method, prenatal O/E TLV (observed to expected total lung volume), or omphalocele sac diameter ($p > 0.05$). Birth weight was significantly lower in the unfavorable outcome group (2.36 kg (0.60)) compared to the favorable outcome group (3.27 kg (0.91)) ($p = 0.002$) and gestational age at birth was also significantly lower in the unfavorable outcome group (early preterm 4/15, 27%; preterm 2/15, 13%; term 9/15, 60%) compared to the favorable outcome group (early preterm n = 0, preterm 7/20, 35%; term 13/20, 65%) ($p = 0.04$).

2.3. Predictors of unfavorable outcomes

Characteristics that could potentially predict favorable or unfavorable outcome status were assessed (Table 2). Crude analysis indicated the odds of having an unfavorable outcome were increased if the patient had polyhydramnios, postnatal sac rupture, major cardiac anomalies, pulmonary hypertension, genetic diagnosis, and other major anomalies. Requiring a repair type other than primary was also predictive of an unfavorable outcome. None of these were statistically significant. Conversely, higher O/E TLV, older gestational age at birth, and increased birth weight were all protective against unfavorable outcomes. Specifically, there was a significantly lower odds of an unfavorable outcome with older gestational age at birth (OR: 0.60; 95% CI: 0.35, 0.95; $p = 0.03$) and higher birth weight (OR: 0.05; 95% CI: 0.005, 0.33; $p < 0.001$). In the adjusted analyses, only birth weight maintained significance. A descriptive table of individual patient characteristics and outcomes allows for visualization of variables across the multiple cohorts (Table 3).

2.4. Survivors: Surgical outcomes

Of the 35 evaluated patients, six were treated with initial primary closure within 7 days (6/35, 17%) and 16 were treated with delayed closure (16/35, 46%). Thirteen patients underwent staged closure (13/35, 37%) but of these patients, only one initially began as staged closure (1/13, 8%) while the remaining 12 were converted from a delayed closure type (12/13, 92%). As the delayed and primary groups did not require reduction or silo/mesh placement, the median number of trips to the operating room before fascial closure, none was significantly different compared to the staged group, four (Q1 0, Q3 7; $p = 0.005$). At post-hoc analysis there remained a significant difference between staged and delayed as well as staged and primary group types ($p < 0.05$).

In those that survived, repair based demographics (Table 4) and outcomes (Table 5) were evaluated. There was no significant difference in patient demographics except for mean birth weight which was lower in the staged repair group (staged 2.66 kg; 1.78, 3.32; delayed 3.68 kg; 2.84, 6.73; primary 3.31 kg; 2.56, 3.83; $p = 0.013$). When evaluating outcomes, age at final fascial closure varied between groups. The youngest group was primary repair (0.14 weeks; 0, 0.14) followed by staged repair (6.1 weeks; 3.0, 29), and then delayed repair (16 weeks; 12, 24.9) ($p < 0.001$). At post-hoc analysis there remained a significant difference in timing of final fascial closure between primary versus staged and primary versus delayed ($p < 0.05$). The type of final fascial closure was significantly different between groups with primary fascial closure obtained in 28% (3/11) of the staged group, 71% (5/7) of the delayed group, and 100% (6/6) of the primary group ($p = 0.01$). As expected, the difference between primary and staged as well as primary and delayed remained significant on post-hoc analysis ($p < 0.05$). NICU and hospital length of stay were also significantly different between groups (staged 123 hospital days; 71, 208; 106 NICU days; 71, 162; delayed 155 hospital days; 68, 237; 155 NICU days; 68, 176; primary 15 hospital days; 13, 39; 15 NICU days, 13, 39; hospital $p = 0.02$; NICU $p = 0.005$) and remained significant for the primary group on post-hoc analysis ($p < 0.05$). The other remaining outcomes showed no significant statistical difference between groups including wound infection, sepsis, days on the ventilator, trips to the OR after fascial closure, concomitant procedures at fascial closure, postoperative ventral hernia, or favorable/unfavorable outcome categorization. Concomitant procedures at fascial closure included gastrostomy tube placement, Ladd's procedure, Meckel's diverticulectomy, diaphragmatic hernia repair, cholecystectomy, appendectomy, Nissen fundoplication, colostomy closure, wound vacuum dressing, circumcision, bowel resection, vitelline duct resection, mucous fistula creation, partial splenorrhaphy, omentectomy, urachal cyst excision, and pulmonary sequestration excision.

3. Discussion

3.1. Favorable versus unfavorable outcomes

The giant omphalocele patient is often more complex than just their associated abdominal wall defect with other anomalies reported to occur in approximately 30–80% of patients [1–3,6,11]. This correlates with our results in which 69% (11/35) had other findings of major cardiac anomalies, pulmonary hypertension, genetic diagnosis, or other major anomalies. The complexity afforded from these other anomalies can range from minor to severe with mortality reported between 17 and 80% depending on anomaly [1,3,6,11,12]. Identifying how these anomalies will predict outcomes is a crucial component to appropriate omphalocele management and not only dictates the lability and status of the infant but also is a major determinant in operative timing. While several studies note the added morbidity from concomitant anomalies, few try to categorize and objectively quantify their effect on patient status [3,6]. Classifying major and minor anomalies into a single category can be misleading and incongruent with patient outcomes. In our study we stratified the anomalies into subcategories and used those in our predictive model. We specifically identified categories with significant impact on mortality that would justify separate analyses such as major cardiac anomalies, pulmonary hypertension, and genetic diagnoses. Other major anomalies were also included but were notably rare such as anorectal malformation and tracheoesophageal fistula. We purposefully excluded minor anomalies such as hypospadias or patent ductus arteriosus in our analysis so as not to confound the "other anomalies" category.

In our data, we found an increased risk of an unfavorable outcome in major cardiac anomalies, pulmonary hypertension, genetic diagnosis, and other major anomalies with the largest increase in odds associated with other major anomalies and major cardiac anomalies. Besides anomalies, there are other factors that can help predict outcome. In

Table 3
Individual patient characteristics summary chart.

	Gestational age at birth (weeks)	Weight (kg)	Omphalocele sac diameter (cm)	Sac rupture	Major cardiac anomaly	PHTN	Genetic dx	Other anomaly	Initial tx	Final tx	Age at closure (days)	Outcome	Details
1	39 4/7	3.69	9.7						D	D	232	F	
2	38 3/7	3.45	9.3		X			X	D	D		U	Death at 89 days, code event
3	34 1/7	1.41	18.2	X		X	X		D	S		U	Death at 33 days, code event
4	38 0/7	2.57	9.3	X		X			D	S	8	F	
5	33 1/7	1.35	5.4				X	X	D	D		U	Death at 92 days, home hospice
6	37 2/7	2.5	9.1			X		X	D	D		U	Death at 16 days, after ECMO decannulation
7	37 0/7	2.95	10.3					X	D	D		U	Death at 4 days, withdrawal of care
8	37 1/7	2.46	8.4						D	S	43	UO	Wound infection, necrotic liver. Additional trips to OR: 4
9	38 0/7	2.74	11.2	X					D	S	1337	UO	ARDS, wound infection/ischemic skin, multiple revisions/mesh exchanges. Additional trips to OR: 17
10	37 6/7	2.96	7.7			X			D	S	47	F	
11	38 3/7	2.5	9						D	S	21	F	
12	35 3/7	1.93	8.7			X		X	D	D		U	Death at 28 days, withdrawal of care
13	37 0/7	2.13	8.2			X			D	D	71	U	Death at 211 days, ECMO with attempted repeat ECMO but unable to cannulate
14	33 5/7	1.78	7.8	X					S	S	203	UO	Wound and mesh infection, mesh removed, healing by secondary intention. Additional trips to OR: 6
15	37 6/7	2.9	9.1						D	S	24	F	
16	37 6/7	2.98	10.3			X		X	D	D		U	Death at 31 days, withdrawal of care
17	35 5/7	2.29	8.4			X			D	S	322	F	
18	38 3/7	2.96	8.6						D	D	174	F	
19	36 3/7	2.68	6						D	S	61	F	
20	37 4/7	3.55	9.8		X			X	D	D	105	F	
21	39 0/7	2.84	8.4		X	X		X	D	D	112	F	
22	37 2/7	2.84	8.3						D	D	161	F	
23	38 2/7	2.5	8.3	X	X	X		X	D	S		U	Death at 16 days, ECMO arterial clot, ECMO withdrawal
24	36 3/7	3.17	9.1			X	X	X	D	D	84	F	
25	35 6/7	2.75	9.6		X				D	D		U	Death at 163 days, ECMO, withdrawal of care
26	38 3/7	3.32	11			X			D	S	42	F	
27	37 3/7	3.32	5.1			X	X		na	P	1	F	
28	33 3/7	2.56	*				X	X	na	P	1	UO	NEC within 2 weeks of closure, bowel resection, ostomy, and subsequent wound infection. Additional trips to OR: 2
29	40	3.6	6.6					X	na	P	1	F	
30	36 3/7	3.83	5.6				X		na	P	0	F	
31	36	3.1	11				X		D	S	12	F	
32	37	1.87	5.9		X	X	X		D	D	9	U	Death at 64 days, severe PHTN/PS, desaturations/shunting despite maximal medical intervention, withdrawal of care
33	35	3.1	9.9						na	P	2	F	
34	38	6.73	13				X		D	D	58	F	
35	36 1/7	3.46	9.7	X					na	P	0	F	

*Unable to measure with existing imaging; dx, diagnosis; tx, treatment; D, delayed; S, staged; P, primary; F, favorable; U, unfavorable; UO, unfavorable-omphalocele related; ECMO, extracorporeal membrane oxygenation; ARDS, acute respiratory distress syndrome; NEC, necrotizing enterocolitis; PHTN, pulmonary hypertension; PS, pulmonary valve stenosis.

our study specifically, we saw an increased odds of unfavorable outcome in polyhydramnios, postnatal sac rupture, increasing omphalocele sac diameter, lower O/E TLV, lower gestational age at birth, and lower birth weight. We also noted that treatment other than primary repair increased the odds of unfavorable outcomes. While the power of our study is insufficient to draw definitive conclusions, it suggests that these factors influence overall outcomes and should be appropriately considered when determining surgical interventions.

3.1.1. Surgical interventions: evolution of closure

Choosing the appropriate surgical management of giant omphalocele abdominal defects is of great debate. An early technique described by Gross involved leaving the sac intact and providing coverage with mobilized skin flaps with the ensuing ventral hernia repaired later in life [13]. This technique has largely been abandoned in favor of others, with two common strategies employed in the modern era if primary closure is unable to be achieved [2]. The first is a staged closure which involves application of synthetic material to the fascial edges to allow for gradual return of the omphalocele contents over time. These serial reductions often require procedural sedation or operative anesthesia. At the final stage, the fascia is closed either primarily or with a synthetic material bridge. In our study we also utilized a DuoDerm silo used similarly for serial reduction but applied to the skin instead of the fascia. The other commonly employed alternative is a nonoperative approach that involves application of a topical treatment that promotes escharization and epithelialization of the sac. Also referred to as delayed closure or "paint and wait," this technique allows deferral of repair with the procedure performed on an elective basis.

3.1.2. Surgical interventions: staged closure

Proponents of staged closure cite that prompt and aggressive surgical management reconstructs the natural anatomic configuration early in life and allows for subsequent pulmonary and diaphragmatic rehabilitation [3,11]. In addition, abdominal compartment pressure is not as

Table 4
Patient demographics by repair type (survivors).

	Staged (n = 11)	Delayed (n = 7)	Primary (n = 6)	p-Value
Gender				0.38
Male	36.4% (4)	71.4% (5)	66.7% (4)	
Female	63.6% (7)	28.6% (2)	33.3% (2)	
Birth weight (kg)	**2.66 (1.78, 3.32)**	**3.68 (2.84, 6.73)**	**3.31 (2.56, 3.83)**	**0.013**
Gestational age at birth				0.40
Early preterm <35 weeks	9.1% (1)	0 (0)	16.7% (1)	
Preterm 35–37 weeks	27.3% (3)	14.3% (1)	50.0% (3)	
Term ≥37 weeks	63.6% (7)	85.7% (6)	33.3% (2)	
Birth hospital				0.42
Inborn	9.1% (1)	28.6% (2)	0 (0)	
Outborn	90.9% (10)	71.4% (5)	100% (6)	
Delivery method				0.054
Vaginal	0 (0)	0 (0)	33.3% (2)	
C-section	100% (11)	100% (7)	66.7% (4)	
O/E TLV				0.54
≤ 50%	25.0% (2)	0 (0)	0 (0)	
>50%	75.0% (6)	100% (6)	100% (1)	
Omphalocele sac diameter (cm)	9.0 (6, 11.2)	9.6 (8.3, 13)	7.4 (5.1, 9.9)	0.37

Values expressed as means (range), percentage of group (count).

dramatically increased as with primary repair [2]. Compared to delayed closure, staged closure avoids the complications of long-term wound care, prolonged hospital stay, and potential damage or rupture of the sac. Conversely, staged closure has been associated with a high risk of infection, loss of fascial margin integrity, exposure to multiple rounds of anesthetic or doses of sedation, and is reported to delay enteral feeding [1,2,8,10–12,14–17].

3.1.3. Surgical interventions: delayed closure

In delayed closure, the infant is allowed to stabilize and treatment of associated anomalies may take place. The sac is preserved and operative intervention postponed, removing the consequences of early anesthesia including the concern that early anesthetic exposure can worsen neurodevelopmental outcomes [18]. Delayed closure also has the added benefit of elective fascial closure with no time constraints as seen with staged closure nor the need to remove the synthetic elements used to achieve reduction [16]. While staged closure provides less intra-abdominal pressure than primary, delayed closure affords no increase in pressure in the initial nonoperative time frame. Opponents cite the downfalls of delayed repair including the systemic effects of topical treatments, prolonged wound care, and inability for early diagnosis of gastrointestinal anomalies such as atresia or rotational defects [1,2,5,7,9,10,12,17,19].

3.1.4. Surgical interventions: staged versus delayed closure

In our study, we found the majority of patients were initially treated with the delayed management strategy. Interestingly, 12 patients (34.3%) were converted from a delayed to a staged treatment. Four were converted for sac rupture and one required abdominal exploration for a bile duct kink. The remaining seven patients were deemed stable enough to undergo serial reductions, with two converted to fascial mesh silos and five converted to external DuoDerm silos. Our experience demonstrates that while conversion can often be necessary to control sac rupture, an elective conversion based on patient stability is also feasible and does not necessarily require violating the integrity of the sac. The confounders of this hybrid technique must be further studied.

Our findings did not demonstrate any significant difference in outcomes between the staged and delayed group.

3.1.5. Surgical interventions: primary closure

In group analyses, patients deemed suitable candidates for primary repair had a shorter length of stay and were significantly younger at final fascial closure. This correlates with the existing literature as the ability to achieve primary closure is a surrogate marker for patient stability and amenable abdominal wall anatomy.

Table 5
Repair based outcomes (survivors).

	Staged (n = 11)	Delayed (n = 7)	Primary (n = 6)	p-Value
Wound infection	36% (4)	0 (0)	17% (1)	0.21
Sepsis	55% (6)	14% (1)	17% (1)	0.21
Time on ventilator (days)	17 (4, 28)	8 (0, 17)	1.5 (0, 2)	0.09
Trips to OR after fascial closure	0 (0, 4)	0 (0, 0)	0	0.23
Age at final fascial closure (weeks)	**6.1 (3.0, 29)**	**16 (12,24.9)**	**0.14 (0, 0.14)***	**<0.001**
Type of final fascial closure				**0.01**
Primary	28% (3)	71% (5)	100% (6)*	
Synthetic	72% (8)	29% (2)	0	
Concomitant procedures at final fascial closure	64% (7)	71% (5)	67% (4)	1.00
Postoperative ventral hernia	9% (1)	0 (0)	0	1.00
Total hospital length of stay (days)	**123 (71, 208)**	**155 (68, 237)**	**15 (13, 39)***	**0.02**
Total NICU length of stay (days)	**106 (71, 162)**	**155 (68, 176)**	**15 (13, 39)***	**0.005**
Outcome				0.33
Favorable	73% (8)	100% (7)	83% (5)	
Unfavorable	27% (3)	0 (0)	17% (1)	

Values expressed as percentage of group (count) or median (Q1, Q3).
* Significant difference between group means for primary vs staged and primary vs delayed (post-hoc analysis, $p < 0.05$).

3.2. Surgical decision making

In the existing literature, both staged and delayed closure have been demonstrated as feasible, but little data exists to determine superiority; and, although potential risks of both procedures are hypothesized, there is little evidence that directly compares these risks among groups while accounting for concomitant congenital anomalies. Surgical decision making must therefore revolve around patient stability and the benefits and risks of going to the operating room for staged or definitive repair. Understanding the concurrent risks of other anomalies is critical in this process and includes not only morbidity and mortality but also an appreciation for prioritizing anomaly interventions prior to omphalocele repair. Our data provides stratification of this patient cohort into favorable and unfavorable outcomes. Our findings highlight factors the surgeon should weigh prior to determining treatment strategy. Furthermore, our series description and analysis of surgical outcomes begins to shed light on the impact of surgical repair type and will hopefully guide strategies for future considerations.

3.3. Limitations

This study is inherently limited in the fact that it is a retrospective chart review. To control for confounders, multiple comorbidities were analyzed and described; however, minor nuances of day to day care were difficult to capture. Furthermore, while omphalocele alone might be a frequently encountered defect in pediatric hospitals, patients whose anatomy defines them as giant omphaloceles are exceedingly more rare. As such, it is difficult to attain the appropriate sample size to achieve adequate statistical power. This becomes even more complicated, as evidenced by our findings, when comparing outcomes of treatment approaches as many patients will not survive to final fascial closure and depending on anomaly do not inherently have the equivalent ability to achieve outcome variables.

3.4. Next steps

To overcome the limitations of our study and those found in the literature, a prospective multi-center randomized controlled trial is needed. Giant omphalocele patients must be identified and their associated anomalies categorized to appropriately define the population. Overall outcomes must be assessed including mortality rates in patients with multiple comorbidities. Ultimately, of those that survive to repair, the goal would be to directly compare primary, staged, and delayed surgical options with one another. A comparative long-term study that follows these patients through to definitive surgery will allow us to address complications associated with each repair type as well as cumulative incidence and exposure to risk factors such as anesthesia time, sedative use, ventilator requirements, and time off of enteral feeding.

4. Conclusions

Giant omphalocele patient management is often complicated by congenital anomalies that have the potential to negatively affect patient and surgical outcomes. Our study highlights the effect of these interactions and correlates subcategorization of anomalies with the potential to more accurately predict outcomes and inform management strategies. Our findings demonstrated increased odds of unfavorable outcomes in major cardiac anomalies, pulmonary hypertension, genetic diagnosis, other major anomalies, polyhydramnios, postnatal sac rupture, increasing omphalocele sac diameter, lower O/E TLV, lower gestational age at birth, lower birth weight, and repair other than primary. Utilizing this data, the physician and family will be more informed of prognosis and risks based on how each anomaly type alters predictive odds. In those that survived to repair, there was no difference in the majority of surgical outcomes indicating a need for future prospective studies to appropriately categorize patients and define variations in management and surgical intervention that can mitigate morbidity and mortality.

Acknowledgements

We would like to thank Misty Troutt for assistance with research design and database management. We would also like to acknowledge that this work was completed in partial fulfillment of the Master of Science degree in Clinical and Translational Research in the Division of Epidemiology, University of Cincinnati College of Medicine for author Heather R. Nolan, MD. Study data were collected and managed using REDCap electronic data capture tools hosted at Cincinnati Children's Hospital [20]. REDCap (Research Electronic Data Capture) is a secure, web-based application designed to support data capture for research studies, providing 1) an intuitive interface for validated data entry; 2) audit trails for tracking data manipulation and export procedures; 3) automated export procedures for seamless data downloads to common statistical packages; and 4) procedures for importing data from external sources.

References

[1] McNair C, Hawes J, Urquhart H. Caring for the newborn with an omphalocele. Neonatal Netw. 2006;25(5):319–27.
[2] Bauman B, Stephens D, Gershone H, et al. Management of giant omphaloceles: a systematic review of methods of staged surgical vs. nonoperative delayed closure. J Pediatr Surg. 2016;51(10):1725–30.
[3] Akinkuotu AC, Sheikh F, Olutoye OO, et al. Giant omphaloceles: surgical management and perinatal outcomes. J Surg Res. 2015;198(2):388–92.
[4] Cohen-Overbeek TE, Tong WH, Hatzmann TR, et al. Omphalocele: comparison of outcome following prenatal or postnatal diagnosis. Ultrasound Obstet Gynecol. 2010;36(6):687–92.
[5] Kouame BD, Odehouri Koudou TH, Yaokreh JB, et al. Outcomes of conservative treatment of giant omphaloceles with dissodic 2% aqueous eosin: 15 years' experience. Afr J Paediatr Surg. 2014;11(2):170–3.
[6] Saxena AK, Raicevic M. Predictors of mortality in neonates with giant omphaloceles. Minerva Pediatr. 2018;70(3):289–95.
[7] Pandey V, Gangopadhyay AN, Gupta DK, et al. Non-operative management of giant omphalocele with topical povidone-iodine and powdered antibiotic combination: early experience from a tertiary Centre. Pediatr Surg Int. 2014;30(4):407–11.
[8] Whitehouse JS, Gourlay DM, Masonbrink AR, et al. Conservative management of giant omphalocele with topical povidone-iodine and its effect on thyroid function. J Pediatr Surg. 2010;45(6):1192–7.
[9] Ein SH, Langer JC. Delayed management of giant omphalocele using silver sulfadiazine cream: an 18-year experience. J Pediatr Surg. 2012;47(3):494–500.
[10] Jiang W, Zhang J, Lv X, et al. Use of small intestinal submucosal and acellular dermal matrix grafts in giant omphaloceles in neonates and a rabbit abdominal wall defect model. J Pediatr Surg. 2016;51(3):368–73.
[11] Roux N, Jakubowicz D, Salomon L, et al. Early surgical management for giant omphalocele: results and prognostic factors. J Pediatr Surg. 2018;53(10):1908–13.
[12] Nuchtern JG, Baxter R, Hatch Jr EI. Nonoperative initial management versus silon chimney for treatment of giant omphalocele. J Pediatr Surg. 1995;30(6):771–6.
[13] Gross RE. A new method for surgical treatment of large omphaloceles. Surgery. 1948;24(2):277–92.
[14] Canty TG, Collins DL. Primary fascial closure in infants with gastroschisis and omphalocele: a superior approach. J Pediatr Surg. 1983;18(6):707–12.
[15] van Eijck FC, de Blaauw I, Bleichrodt RP, et al. Closure of giant omphaloceles by the abdominal wall component separation technique in infants. J Pediatr Surg. 2008;43(1):246–50.
[16] Hatch Jr EI, Baxter R. Surgical options in the management of large omphaloceles. Am J Surg. 1987;153(5):449–52.
[17] Lee SL, Beyer TD, Kim SS, et al. Initial nonoperative management and delayed closure for treatment of giant omphaloceles. J Pediatr Surg. 2006;41(11):1846–9.
[18] Snow HA, Choi JM, Cheng MW, et al. Irrigation versus suction alone during laparoscopic appendectomy; a randomized controlled equivalence trial. Int J Surg. 2016;28:91–6.
[19] Pacilli M, Spitz L, Kiely EM, et al. Staged repair of giant omphalocele in the neonatal period. J Pediatr Surg. 2005;40(5):785–8.
[20] Harris PA, Taylor R, Thielke R, et al. Research electronic data capture (REDCap)–a metadata-driven methodology and workflow process for providing translational research informatics support. J Biomed Inform. 2009;42(2):377–81.