Journal of Pediatric Surgery 51 (2016) 1725–1730

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

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

Review Articles

Management of giant omphaloceles: A systematic review of methods of staged surgical vs. nonoperative delayed closure☆

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ARTICLE INFO

Article history:
Received 5 January 2016
Received in revised form 6 June 2016
Accepted 15 July 2016

Key words:
Giant omphalocele
Silvadene
Betadine
Staged surgical closure
Nonoperative delayed closure
Neonatal surgery

ABSTRACT

Purpose: Despite the numerous methods of closure for giant omphaloceles, uncertainty persists regarding the most effective option. Our purpose was to review the literature to clarify the current methods being used and to determine superiority of either staged surgical procedures or nonoperative delayed closure in order to recommend a standard of care for the management of the giant omphalocele.

Methods: Our initial database search resulted in 378 articles. After de-duplication and review, we requested 32 articles relevant to our topic that partially met our inclusion criteria. We found that 14 articles met our criteria; these 14 studies were included in our analysis. 10 studies met the inclusion criteria for nonoperative delayed closure, and 4 studies met the inclusion criteria for staged surgical management.

Results: Numerous methods for managing giant omphaloceles have been described. Many studies use topical therapy secondarily to failed surgical management. Primary nonoperative delayed management had a cumulative mortality of 21.8% vs. 23.4% in the staged surgical group. Time to initiation of full enteric feedings was lower in the nonoperative delayed group at 14.6 days vs 23.5 days.

Conclusion: Despite advances in medical and surgical therapies, giant omphaloceles are still associated with a high mortality rate and numerous morbidities. In our analysis, we found that nonoperative delayed management with silver therapy was associated with lower mortality and shorter duration to full enteric feeding. We recommend that nonoperative delayed management be utilized as the primary therapy for the newborn with a giant omphalocele.

An omphalocele, a congenital abdominal wall defect of the umbilical ring, occurs in about 1 in 4000 to 6000 live births [1–3]. It is characterized by eviscerated abdominal contents covered by a 3-part membrane: amnion externally, peritoneum internally, and mesenchyme or Wharton's jelly in between [2,4]. The underlying cause is an abdominal wall folding defect in utero [5]. Normally, the lateral and craniocaudal abdominal folds close in utero at 5 weeks of gestation; however, arrested folding processes can leave the abdominal viscera outside the abdominal cavity, resulting in failure of the abdominal cavity to expand during gestation [6]. The defect is caused by failure of *lateral* abdominal wall folds, but *cephalic* and *caudal* folding defects may also occur, and are associated with a worse prognosis [4,7,8].

Clinically, omphaloceles are categorized as small, giant, or ruptured [9]. Giant omphaloceles are rarer and have a larger abdominal wall defect. Moreover, 37% to 67% of giant omphaloceles are associated with additional congenital anomalies [5,10].

Historically, giant omphaloceles have been defined by various criteria, including the diameter of their sac, the diameter of the abdominal wall defect, the inability to primarily close the abdominal wall defect, a tissue defect >5 cm, liver-containing herniation of viscera, and volume disproportion between the abdominal viscera and abdominal cavity [2,11]. Most surgeons define them as 5 cm or larger in diameter, although a consensus definition has not been reached [3].

The mortality rate of infants with small omphaloceles ranges from 13% to 25%, but it is even higher for infants with giant omphaloceles because of the larger size of the tissue defect, the increased visceroabdominal disproportion [1,10], and the higher frequency of associated anomalies (such as Beckwith–Wiedemann syndrome, pulmonary hypoplasia, congenital cardiac defects, trisomy 13–15, trisomy 16–18, and pentalogy of Cantrell [5,12]). Other prognostic factors for these infants include rupture of the sac, perinatal respiratory distress, younger gestational age, and their lower live birth rate [2].

Two distinct strategies for managing giant omphaloceles are (1) staged surgical closure, defined as abdominal tissue closure after

☆ Conflicts of interest: None.

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http://dx.doi.org/10.1016/j.jpedsurg.2016.07.006
0022-3468/

multiple operations, and (2) nonoperative delayed closure, defined as abdominal tissue closure by epithelialization of the sac [13]. Both strategies allow for a more controlled reduction of the omphalocele without life-threatening cardiopulmonary complications. Yet both leave the viscera exposed to the environment, increasing the infant's risk of gram-positive as well as gram-negative infections [1,2].

Nonoperative delayed closure most commonly involves application of a topical medication directly onto the omphalocele membrane, in an effort to promote formation of eschar, followed by granulation and neoepithelialization; then, the next step traditionally is interval repair of the remaining ventral hernia [14].

During nonoperative delayed closure, a variety of topical medications have been employed to promote neoepithelialization of the omphalocele sac and to help mitigate the infectious risk before complete neoepithelialization. Such medications have included silver sulfadiazine (Silvadene), povidone–iodine (Betadine), a 70% alcohol solution, a 2% merbromin (Mercurochrome) solution, and silver nitrate.

For staged surgical closure, multiple methods are being utilized including placement of Silastic silos, intraabdominal tissue expanders, synthetic interposition mesh, component separation, and skin flap creation. All of these closure methods, as a staged surgical closure method, must be followed up by a subsequent operation to close the abdominal wall fascia.

Controversy continues regarding the relative efficacy of the various methods of staged surgical vs. nonoperative delayed closure; no standard of care exists [15]. Retrospective reviews and case series have described numerous methods of nonoperative delayed closure, but have not compared their relative efficacies.

1. Methods

We performed a systematic review of the literature for the various methods of staged surgical vs. nonoperative delayed closure of giant omphaloceles. This systematic review adheres to the Preferred Reporting Items for Systematic Reviews and Meta-Anyalyses (PRISMA) statement. Our outline included analyses and reporting as noted by IOM Standards, and the Cochrane Collaboration [16,17].

Our purpose was to review the existing therapies available to treat the giant omphalocele and to determine superiority of either staged surgical procedures or nonoperative delayed closure in order to recommend a standard of care for the management of the giant omphalocele.

1.1. Selection criteria

In our review, we included studies meeting the following criteria: (a) patients: age = < 4 weeks with a giant omphalocele defined as a fascial defect or a sac > 5 cm that contains liver tissue and that is not amenable to primary fascial closure; (b) interventions: studies on primary conservative management of GO including topical management or negative pressure wound therapy with minimum of three patients all receiving the same therapy continued until closure or complete neoepithelelization; (c) comparator: studies on the operative management of interposition mesh or silo; and (d) outcome: length of stay (total duration of hospital stay from birth to initial discharge), time to full feeds, and mortality.

We excluded (a) case studies with <3 patients; (b) studies which used a combination of conservative and surgical management; and (c) studies without at least one outcome related to length of stay, time to full feedings, and mortality.

1.2. Search strategy

We performed a comprehensive literature search with the assistance of an experienced medical librarian using multiple databases, and varied algorithms. Databases included OVID Medline, EMBASE, Cochrane's Systematic Reviews, Web of Science and Scopus. The search strategy included: exploded MeSH, (Medical Subject Heading) database specific controlled vocabulary, keyword, keyword truncation, and combined keyword. To maximize capturing relevant citations, both indexed and in-process citations were part of the search strategy. Terms used included: (a) hernia, umbilical; (b) omphalocele; and (c) giant. In order to define an initial comprehensive list of treatment options, no limits were placed on treatment terminology. Searches were not restricted by year or language and included citations through April 8th, 2016. The only limiter placed on the search strategy was “human.” This included indexed and nonindexed citations. Key specialty associations in surgery and pediatrics were individually searched for relevant guidelines, protocols, and opinion statements or any documented references on the subject. Presentation of the results included abstracts to aid in the critical review process.

1.3. Data abstraction and quality assessment

Our initial search of these databases resulted in 387 articles. After deduplification and review, we requested 32 of these articles relevant to our topic based on our inclusion and exclusion criteria. We found that 14 articles met our criteria; these 14 studies were included in our analysis. 10 studies met the inclusion criteria for nonoperative delayed closure, and 4 studies met the inclusion criteria for staged surgical management. In Tables 2 and 3 we calculated the mean values with standard deviation of the data presented in the studies listed in Table 1. Mortality was calculated as the sum value of all patients included within each category (surgical vs nonsurgical). We followed the levels of evidence and grades of recommendations used by the National Guideline Clearninghouse [18].

2. Results

For nonoperative delayed closure, our review demonstrated use of the 5 different techniques (silver-based, iodine-based, manuka honey, 2% aqueous eosin, and negative pressure wound therapy). For staged surgical closure, our review encompassed 3 different methods (Proline silo, Silastic silo, and Interposition mesh). Table 1 lists the study organized by technique and the data reported including length of stay, time to initiation of full feeds, and mortality.

We identified 4 studies utilizing Silvadene that met our inclusion criteria. There were two mortalities in the study by Lee et al. [1] and one mortality in the study by Ein and Langer [2]. Table 2 lists the range and mean with standard deviation of reported data on LOS, time to full feeds and mortality. The length of hospital stay ranged from 20 to 78 days (one study did not report data), and the time to initiation of full feeds ranged from 6 to 8 days (2 studies did not report data). In the study by Lee et al. [1], the median time to the initiation of a full diet was 8 days; to hospital discharge, 20 days; and to definitive fascial closure, 14 months.

We reviewed 3 studies that used Betadine (Table 1) [2,3,9]. In all 3 studies, tissue closure was performed at 6 to 12 months of age. Importantly, no thyroid dysfunction occurred. The range of hospital LOS was 14–34 days (Table 2). The time to enteral feeding was given in only 2 of the studies; their range was 8.5 to 33 days.

In addition, our search identified two alternative methods that used topical medication other than Betadine or Silvadene, namely, dissodic 2% aqueous eosin [19] and manuka honey [20]. Like the other topical medications, dissodic 2% aqueous eosin has antimicrobial properties through its active ingredient, disodium eosin, which also promotes rapid epithelialization [17]. In their 15-year retrospective study, Kouame et al. [19] reported a mean hospital LOS of 21 days; of note, they also reported a 25% mortality rate from sepsis or from functional intestinal obstruction related to sac infection. In their 4 year study with 5 patients, Nicoara et al. [20] reported a 66 day median hospital stay and 13 day median time to initiation of full feedings after treatment of the sac with manuka honey.