Primary Fascial Closure versus Staged Closure with Silo in Patients with Gastroschisis: A Meta-Analysis

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Abstract

Background/Purpose—Gastroschisis is the most common congenital abdominal wall defect. Despite advances in the surgical closure of gastroschisis, consensus is lacking as to which method results in the best patient outcomes. The purpose of this meta-analysis was to compare short-term outcomes associated with primary fascial closure and staged repair with a silo in patients with gastroschisis.

Methods—We reviewed Medline citations, as well as the Cochrane Database of Systematic Reviews, between January 1, 1996 and June 1, 2012. Articles were identified using the search term "gastroschisis" and [("treatment outcome" or "prognosis") or randomized controlled trials]. Case reports, reviews, letters, abstracts only, non-English abstracts, and studies that did not address at least one of the outcomes of interest were excluded from the meta-analysis. Two independent reviewers identified relevant articles for final inclusion. A standard data collection

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form created by the authors was used to extract study information, including study design, patient characteristics, and reported patient outcomes. The data were analyzed using standard meta-analytic techniques.

Results—Twenty studies were included in the meta-analysis. In the five studies that selected closure method randomly or as a temporal shift in practice, silo was associated with better outcomes, with a significant reduction in ventilator days ($p<0.0001$), time to first feed ($p=0.04$), and infection rates ($p=0.03$). When all studies were included, primary closure was associated with improved outcomes.

Conclusions—Silo closure is associated with better clinical outcomes in the studies with the least selection bias. Larger prospective studies are needed to definitively determine the best closure technique.

Keywords

Gastroschisis; abdominal wall defects; primary fascial closure; spring-loaded silo; surgical silo

Gastroschisis is the most common abdominal wall defect in the newborn, and incidence is increasing worldwide, affecting 4–5/10,000 newborns (1, 2). Survival has dramatically improved to greater than 90% over the past 6 decades, due to improved techniques to close the abdominal wall defect and advances in neonatal care (3, 4, 5). Despite these advances, post-surgical care for gastroschisis remains challenging, and gastroschisis is the congenital defect with the longest ICU length of stay (LOS)(6). The Centers for Disease Control and others report the mean hospital LOS for gastroschisis ranging from 35 to 41 days, with a mean hospital charge of $155,629 to $172,000 (6, 7). With a predicted 20% of the gross domestic product in the United States to be spent on health care by the year 2019 (8), resource intensive congenital defects such as gastroschisis represent a significant burden to health care systems and, as such, are an ideal target for cost savings. Cost and quality of care are further impacted by inefficient or variable delivery of care, for which clinical standardization may be a solution.

Variation in the management of gastroschisis, including closure/coverage techniques, continues to be a crucial factor in both short- and long-term outcomes of infants with gastroschisis (9). Three surgical techniques have been described: primary fascial closure, staged repair with a silo, and most recently, "umbilical turban" or plastic closure. In 1943, the first successful primary fascial closure of an abdominal wall defect was reported (10, 11). Historically, patients failing primary closure received a custom-made silo sewn to the abdominal fascia, which enabled gradual reduction of the bowel into the abdomen.

By the mid-1970s, preformed silos were introduced, and by 1995 featured a spring-loading mechanism that inserts beneath the fascia, providing an alternate method of temporary closure (10, 12, 13). Spring loaded silos (SLS) or preformed silos have been used as both a salvage technique in patients failing primary closure or as an initial therapy to provide intestinal coverage with definitive closure at a later time. Placement of a SLS was welcomed as an alternative to a silo sutured to the fascia, as it can be placed at the bedside rather than in the OR, and requires minimal sedation, without the need for endotracheal intubation.

Placement of a SLS has the theoretical benefit of allowing the bowel edema to resolve, allowing partial reduction of the intestine and reduced intra-abdominal pressures at the time of definitive fascial closure (12, 14). It is postulated that reduction of bowel in the setting of reduced intra-abdominal pressures improves splanchnic perfusion resulting in faster return of bowel function and reduced rates of infection and necrotizing enterocolitis (NEC) (14, 15, 16).

The umbilical turban is the most recent reported closure technique for gastroschisis (17). In this procedure, the intestinal contents are reduced into the abdomen and the umbilical cord is coiled over the defect and fixed into place with an adhesive dressing. Eventually the defect epithelizes and the umbilical cord desiccates and detaches, occasionally leaving patients with an umbilical hernia.

Multiple studies have attempted to address the impact of these closure methods on clinical outcomes, and none of the methods has emerged as a clearly superior choice. This meta-analysis sought to identify the best closure method for newborns with gastroschisis by comparing hospital outcomes in patients receiving either primary fascial closure or staged repair with a silo.

METHODS

The review was performed according to the PRISMA guidelines (Appendix 1).

Selection of Studies

We reviewed Medline citations between January 1, 1996 and June 1, 2012 and the Cochrane Database of Systematic Reviews database through June 1, 2012. Citations from DynaMed and other reviews were included. The search terms used were "gastroschisis" and [("treatment outcome" or "prognosis") or randomized controlled trials]. Reference lists from selected papers were further used to identify publications of interest. Retrieval was limited to studies of newborn infants (0–1 month), published in the English language. Case reports, reviews, letters, abstracts only, non-English abstracts, and studies that did not address at least one of the outcomes of interest were identified and excluded independently by two reviewers. Studies were also excluded from analysis when continuous outcomes were reported in a non-continuous manner or for which a minimum of number and p-value were not provided. Only studies that directly compared primary fascial closure to delayed closure using a silo (either SLS or sutured silos) were included. Though we had originally anticipated including turban closure in the analysis, too few studies directly compared turban closure to either of the other methods.

Data Extraction

Abstracts for all articles were independently subjected to preliminary review by two investigators (JA, SK) to determine whether inclusion criteria were satisfied. A third reviewer (JT) resolved disagreement between reviewers. Data abstraction was conducted independently by the same two investigators from the studies that met inclusion criteria. A standard data collection form (Appendix 2) created by the authors (JA, JT, SK) was used to extract information about study quality, including overall and per-group sample sizes,

selection of method to close gastroschisis, inclusion of patients receiving surgically sutured silos in the silo group, and inclusion of patients with complicated gastroschisis (atresia, volvulus, or perforation) in the analysis; patient characteristics, including gestational age and birth weight; ascertainment bias; and reported patient outcomes. Extracted data were cross-referenced between reviewers for accuracy. Discrepancies between reviewers were resolved by consensus.

Primary Outcomes

Outcomes of clinical interest were initially devised by the study authors; from this list, outcomes to be included in the analysis were selected based on whether data were reported in at least half of the studies selected, and included the following: total hospital LOS, total days on the ventilator, time to first feed (TFiF), time to full feeds (TFuF), parenteral nutrition duration (PND), infection rates (including sepsis, central line infections, pneumonia, and infections not otherwise specified), rates of necrotizing enterocolitis (NEC), and mortality rates.

Statistical Analysis

The data were analyzed using standard meta-analytic techniques (18). For each study, treatment effects were calculated using a fixed effect model to obtain weighted mean difference and 95% confidence interval for continuous outcomes, and odds ratio and 95% confidence interval for dichotomous outcomes. For studies reporting median and either range or interquartile range, median was entered as an estimate of the mean, and standard deviations were estimated, conservatively, as larger of [(max-median)/2 OR (median-min)/2] for range and as larger of [(Q3 – median)/.675 OR (median – Q1)/0.675] for interquartile range. To assess associations of gestational age and birth weight with estimated treatment effects, Pearson correlations were calculated for weighted mean differences for continuous outcomes and for log-transformed odds ratios for dichotomous outcomes.

In studies comparing primary closure to placement of a silo, rationale for selection of closure method differed and was categorized into three groups: 1) objective, based on randomization or temporal assignment due to shift in practice within the institution, 2) subjective, based on surgeon preference, or 3) silo placement after failed primary closure. To assess potential bias associated with subjective treatment allocation, sensitivity analyses were performed in which pooled estimates of treatment effect were calculated based only on studies that randomized closure method or in which closure method differed due to a temporal shift in practice within an institution. In pre-specified subgroup analyses, we qualitatively compared estimated treatment effects based on the following factors, which represent variation in study design: 1) inclusion of patients receiving surgically sutured silos in the silo group; and 2) inclusion of patients with complicated gastroschisis, including atresia, volvulus, or perforation, in the analysis. Heterogeneity was assessed by the I^2 statistic, which is a measure of the proportion of variance across studies that can be attributed to heterogeneity rather than chance. All meta-analyses were performed using Comprehensive Meta Analysis software (19). The original source for all variables may be found in Appendix 3.

RESULTS

Studies Analyzed

The literature search yielded 365 articles (Figure 1). Reviews, case reports, letters, and abstracts only (n=257) were excluded. After review of the remaining 108 abstracts and/or full text articles by two independent reviewers, studies that did not address gastroschisis repair methods and studies that did not address at least one of the outcomes of interest (n=88) were excluded. Twenty studies met inclusion criteria and were included in the meta-analysis: 1 randomized controlled trial, 3 prospective cohort studies, and 16 retrospective studies (Table 1).

Results of Meta-Analyses

Estimates of weighted mean differences and odds ratios for individual studies are shown in Figures 2 and 3, respectively. In studies with less biased manners of selecting closure method (n=5), silo closure was associated with shorter TFiF, fewer ventilator days, and lower infection rates (Table 2, random/temporal group). Ventilator days were reduced by 2.6 days (95% CI: 1.8–3.4 days; $P<0.001$; $I^2=14\%$); TFiF was decreased by 1.9 days (95% CI: −1.3–5.1 days; $P<0.001$; $I^2=82\%$), and infection rates were reduced by 14% (OR: 0.46; 95% CI: 0.23–0.92; $P=0.03$; $I^2=32\%$). However, when studies judged to be prone to ascertainment bias in their selection of closure technique were included, primary closure was associated with shorter LOS, PND, and ventilator days (Table 2, overall group). In this overall analysis, primary closure and silo closure did not differ for any of the other outcomes studied.

We next stratified the studies by whether the silo group comprised only SLS or included surgically sutured silos and SLS. Of the 8 studies that combined SLS and surgically sutured silos, 4 reported proportions for each type of silo (20, 21, 23, 26). There were 135 patients in the silo groups across these 4 studies, of which 101 (74.8%) were SLS and 34 (15.2%) were surgically placed (data not shown). When surgically placed silos were included in the study group, primary closure was associated with significantly shorter LOS, TFiF, TFuF, PND, and ventilator days. PND was significantly shorter in the primary closure group when only SLS were included in the silo group (Table 2).

Studies were also stratified by whether complicated gastroschisis (for example, gastroschisis associated with bowel atresia or perforation), was included in the analysis. In studies that included patients with complicated gastroschisis, primary closure was associated with significantly shorter LOS, PND, and ventilator days. However, in studies with only uncomplicated gastroschisis patients, primary closure was associated with significantly shorter TFuF and PND (Table 2).

Data for birth weight and gestational age by type of closure were provided for 16 studies, and neither birth weight nor gestational age was strongly associated with study effects (Table 3). However, the following variables were moderately (0.3>r>0.7) associated: birth weight and gestational age with ventilator days and TFiF; gestational age with NEC and mortality; and birth weight with TFuF and PND.

DISCUSSION

This meta-analysis demonstrates that in studies with less selection bias, silo closure is associated with better outcomes for patients with gastroschisis. The results also highlight the importance of assessing bias prior to drawing conclusions, as primary closure appears better when more biased studies are included in the analysis.

In studies based on treatment allocation via randomization or temporal shifts in practice, selection bias was reduced, favoring silo closure with significantly reduced ventilator days, infection, and TFiF. The study by Schlatter appeared to more strongly favor silo closure than the other studies (Figure 2) (12). This effect is most evident when evaluating ventilator days, where other studies in this selection group did not demonstrate a significant difference in ventilator days based on closure method. The authors attribute their improved outcomes with SLS closure to several factors, including avoidance of anesthesia leading to fewer ventilator days, lower intra-abdominal pressures reducing complications, and use of more PICC lines placed later in the SLS group (as opposed to Broviac lines placed on the first day of life with primary closure) leading to fewer infectious complications (12). Of note, the only prospective randomized controlled study did not demonstrate a significant difference in outcomes based on closure method (33). This study had small numbers in each arm (n=27) that were similar in terms of gestational age, weight, sex, Apgar scores, prenatal diagnosis, and mode of delivery.

Selection of the method of closure can clearly bias the conclusions of the study, which is highlighted in studies that compared primary closure to patients receiving a silo after failure of primary closure (Table 1) (15, 25, 28, 34, 35). Patients receiving a silo because primary closure has failed most likely represent a patient population prone to worse clinical outcomes (38). The association of primary closure with better outcomes in this study population may reflect this bias. The impact of this bias was the major contributor to the overall measured benefit of primary closure compared to silo closure.

Studies also favored primary closure when surgeon's preference was used as the closure selection method, with a significant reduction in PND, TFuF, and ventilator days. Through experience, surgeons may have identified which patients have fascial defects more amenable to primary closure; when primary closure is perceived to be likely to fail, surgeons may be more prone to choose closure with SLS prior to attempting primary fascial closure. If such selection bias results in silo placement in patients with bowel wall edema or in infants too small to accommodate primary closure, clinical outcomes for patients receiving a silo may be negatively impacted. The studies by Bradnock et al (23) and Eggink et al (26) feature surgeon preference for selection of closure method and strongly impact the conclusions for this selection subgroup. The Eggink study reported a marked association of primary closure with better outcomes, including significantly shorter TFiF and TFuF, and a trend towards significantly fewer ventilator days in the primary closure group, even when complicated gastroschisis cases were excluded. In keeping with our assumptions, the authors of this study point to selection of a "sicker" population in patients receiving a silo as a possible explanation for better outcomes with primary closure. A similar study by Choi et al compared sutureless ward reduction (turban closure, without initial silo placement) to SLS

placement and found that those patients undergoing sutureless reduction tended to have shorter TFiF, TFuF, PND, and LOS than those undergoing SLS placement (39). Again, these results are likely impacted by the method of selection, which was a combination of surgeon preference and silo after failure of sutureless reduction.

Studies were stratified to assess potential differences based on whether the silo group comprised solely SLS or also included surgically sutured silos. LOS, TFiF, TFuF, PND, and ventilator days were all improved in patients receiving primary closure compared to silo closure when surgically sutured silos were included in the silo group. Placement of a surgically sutured silo indicates a failed primary closure, implying that this cohort of patients is more complex. Thus, the benefit ascribed to primary closure may be incorrectly interpreted.

Similarly, studies were separated by whether patients with complicated gastroschisis were included in the analysis. When complicated gastroschisis patients were included, primary closure was associated with significantly shorter LOS, PND, and ventilator days. Patients who were primarily closed likely represented patients with simple gastroschisis and improved outcomes. In studies that excluded complicated gastroschisis, TFuF and PND were reduced in patients undergoing primary closure; these results were, again, influenced largely by the Bradnock and Eggink studies (23, 26), which feature surgeon preference as the method of closure selection. In addition, patients with complicated gastroschisis have prolonged hospital stays regardless of closure method, as the length of stay in complicated gastroschisis is often based on the patient's intestinal pathology (40).

There are several limitations inherent in this meta-analysis. First, we identified the following three major variations in study design: 1) manner of selection of gastroschisis closure method, 2) inclusion of patients receiving surgically sutured silos in the silo group, and 3) inclusion of patients with complicated gastroschisis (including atresia, volvulus, and perforation). Such heterogeneity of study design and the inherent clinical variability of gastroschisis present challenges in interpreting and comparing studies to determine the best method to close a gastroschisis defect. As detailed previously, criteria for selection of closure method likely introduced selection bias into the closure decision in many studies. Grouping random and temporal methods of closure selection into the same group is imperfect, as outcomes after the adoption of SLS closure compared to controls may be confounded by unrelated advances in neonatal care. Second, definitions of silo closure differ between studies such that some studies include surgical silos in the silo group, while others include only spring-loaded silos. Such misclassification may also be present for other variables in these studies. Third, the current literature in gastroschisis closure methods is relatively small and comprises many retrospective reviews with few prospective or randomized trials. Given the paucity of large, randomized trials, controlling for covariates becomes difficult and one study can have a dominating influence on the outcome results. Fourth, due to the small number of studies, both overall and particularly within certain arms of the meta-analysis, we felt that it was not advisable to further sub-stratify studies into more specific groups (for example, a "gold standard" group with objective method of closure selection, uncomplicated gastroschisis only, and SLS only). Such analyses would enable a

clearer understanding of the complex factors that may be associated with differences in outcomes of gastroschisis closure if more studies with these populations were available.

CONCLUSION

Silo closure is associated with better clinical outcomes in the studies with the least selection bias. This is especially relevant to the group of patients for whom primary closure is not readily achievable but whose presentation is not so complex as to immediately warrant delayed closure; for these patients, the evidence suggests that silo closure may be preferable. This analysis highlights the heterogeneity of the available literature on closure methods for gastroschisis and the impact of study design on reported outcomes. Determining a superior method of closure would be a benefit to both the surgical and medical management of gastroschisis; this meta-analysis demonstrates that further well-designed studies are needed to gain an accurate picture of outcomes after different surgical interventions. The randomized controlled trial registered in January 2012 will be an important step toward answering this important question (41).

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

Abbreviations

LOS	Length of stay
NEC	Necrotizing enterocolitis
PICC	Percutaneously-inserted central catheter
PND	Parenteral nutrition duration
SLS	Spring-loaded silo
TFiF	Time to first feed
TFuF	Time to full feeds

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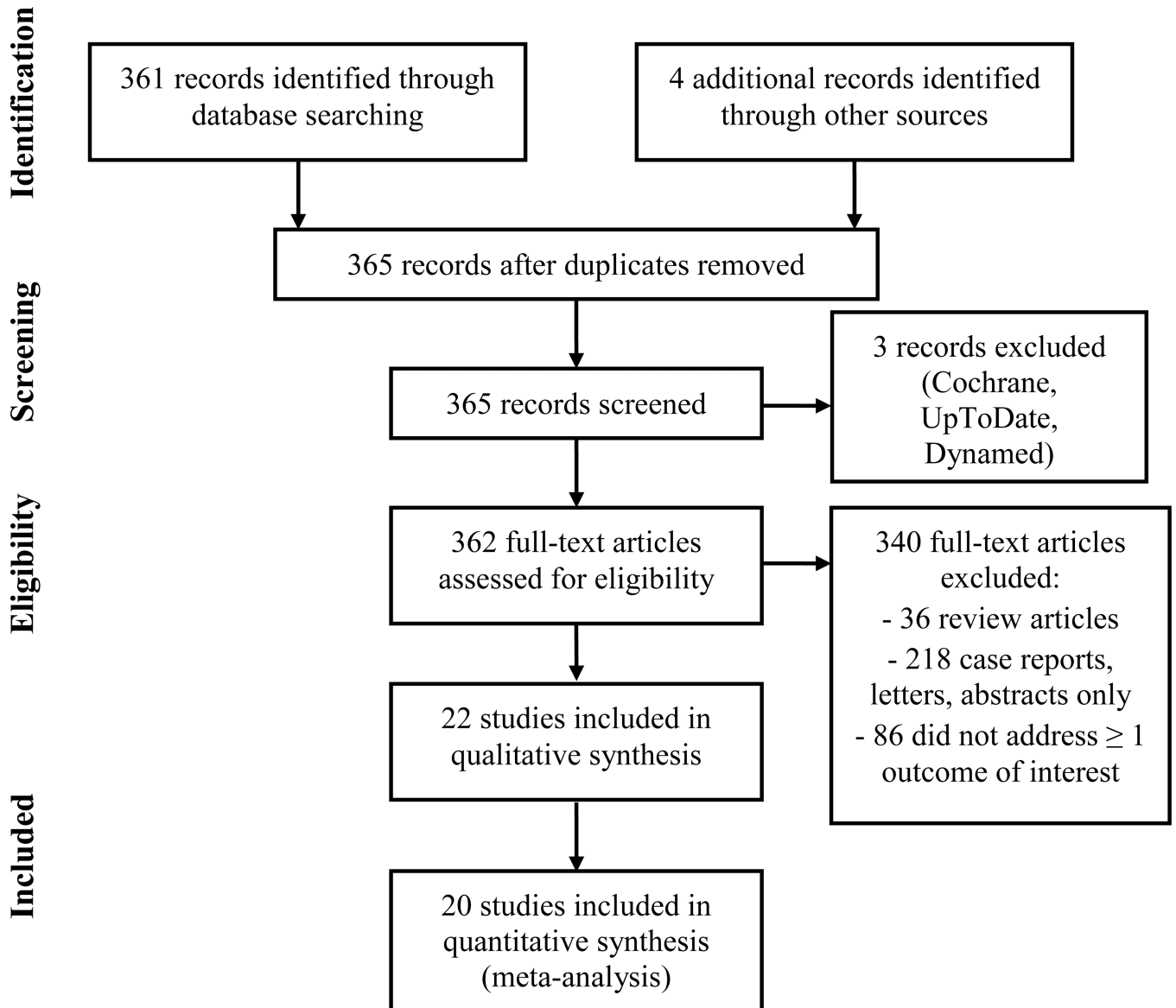
Figure 1.
Details of included and excluded studies.
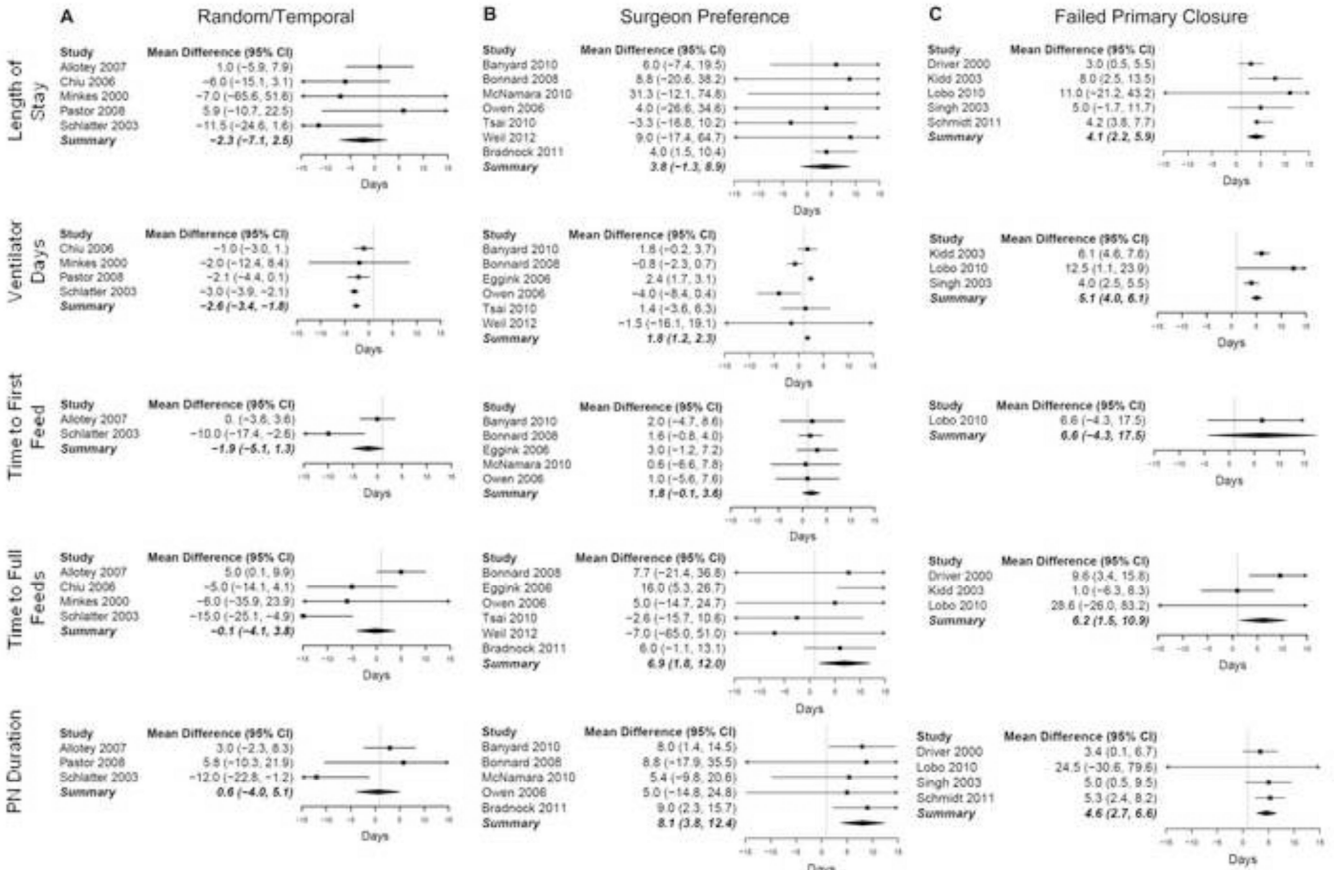
Figure 2.
Forest plots for continuous variables. (A) Mean differences for studies with random or temporal allocation of patients to study group. (B) Mean differences for studies using surgeon preference to assign patients to study group. (C) Mean differences for studies in which silo closure was only used after failure of primary closure. Mean differences falling to the left of the line favor silo closure; those falling to the right of the line favor primary fascial closure.

Figure 3.

Forest plots for dichotomous variables. (A) Odds ratios for studies with random or temporal allocation of patients to study group. (B) Odds ratios for studies using surgeon preference to assign patients to study group. (C) Odds ratios for studies in which silo closure was only used after failure of primary closure. Odds ratios falling to the left of the line favor silo closure; those falling to the right of the line favor primary fascial closure.
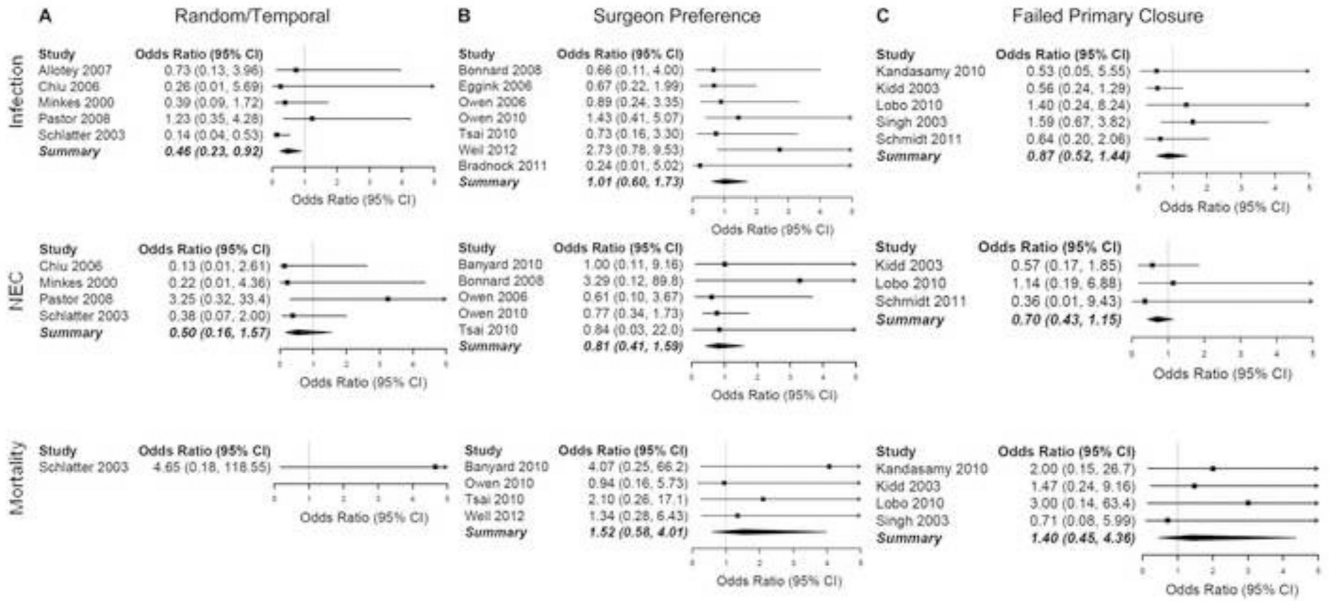
Table 1

Characteristics of included studies.

Study author, year (reference)	Study design	Number of patients Total	Primary	Silo	Outcomes included	Method of closure selection	Silo group contains surgical silos	Data for uncomplicated gastroschisis only
Allotey, 2007 (20)	Retrospective, single-center review	53	40	13	TFiF, TFuF, PND, ventilator days, LOS, infection, NEC, mortality	Temporal	No	Yes
Banyard, 2010 (21)	Retrospective, single-center review	235	188	47	TFiF, PND, ventilator days, LOS, NEC, mortality	Surgeon preference	Yes	No
Bonnard, 2008 (22)	Retrospective, single-center, case-control	22	11	11	TFiF, TFuF, PND, ventilator days, LOS, infection, NEC, mortality	Surgeon preference	Yes	Yes
Bradnock, 2011 (23)	Prospective, multi-center cohort study	219	120	99	TFuF, PND, LOS, infection, NEC	Surgeon preference	No	Yes
Chiu, 2006 (24)	Retrospective, single-center review	48	28	20	TFuF, ventilator days, LOS, infection, NEC, mortality	Temporal	No	No
Driver, 2000 (25)	Retrospective, single-center review	90	72	18	TFuF, PND, LOS	Primary failure	Yes	No
Eggink, 2006 (26)	Retrospective, single-center review	55	21	34	TFiF, TFuF, ventilator days, infection	Surgeon preference	Yes	Yes
Kandasamy, 2010 (27)	Retrospective, single-center review	28	22	6	TFiF, TFuF, PND, ventilator days, LOS, infection, NEC, mortality	Primary failure	Yes	Yes
Kidd, 2003 (15)	Retrospective, single-center review	118	58	60	TFuF, ventilator days, LOS, infection, NEC, mortality	Primary failure	Yes	No
Lobo, 2010 (28)	Retrospective, single-center review	37	10	27	TFiF, TFuF, PND, ventilator days, LOS, infection, NEC, mortality	Primary failure	No	No
McNamara, 2010 (29)	Retrospective, single-center review	14	5	9	TFiF, PND, LOS	Surgeon preference	No	Yes: TFiF, PND No: LOS
Minkes, 2000 (30)	Retrospective, single-center review	43	30	13	TFuF, ventilator days, LOS, NEC	Temporal	No	No

Study author, year (reference)	Study design	Number of patients Total		Outcomes included	Method of closure selection	Silo group contains surgical silos	Data for uncomplicated gastroschisis only
		Primary	Silo				
Owen, 2006 (31)	Retrospective, single-center, case-control	48		TFiF, TFuF, PND, ventilator days, LOS, infection, NEC	Surgeon preference	No	Yes
		27	21				
Owen, 2010 (32)	Prospective cohort study	290		Infection, NEC, mortality	Surgeon preference	No	Yes
		170	120				
Pastor, 2008 (33)	Multicenter randomized controlled trial	54		PND, ventilator days, LOS, infection, NEC, mortality	Random	No	No
		27	27				
Schlatter, 2003 (12)	Retrospective, single-center review	65		TFiF, TFuF, PND, ventilator days, LOS, infection, NEC, mortality	Temporal	No	No
		39	26				
Schmidt, 2011 (34)	Prospective, single-center cohort study	45		TFiF, PND, LOS, infection, NEC	Primary fail	Yes	No
		24	21				
Singh, 2003 (35)	Retrospective, multicenter review	181		PND, ventilator days, LOS, infection, mortality	Primary fail	No	No
		151	30				
Tsai, 2010 (36)	Retrospective, single-center review	44		TFuF, ventilator days, LOS, infection, NEC, mortality	Surgeon preference	Yes	Yes: TFuF, ventilator days, LOS, mortality No: infection, NEC
		32	12				
Weil, 2012 (37)	Retrospective, single-center review	190		TFuF, ventilator days, LOS, infection, mortality	Surgeon preference	No	No
		43	147				

LOS = length of stay; NEC = necrotizing enterocolitis; TFiF = time to first feed; TFuF = time to full feeds; primary fail = silo after failure of primary closure

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Table 2

Meta-analysis results by subgroups and overall analysis.

OUTCOME	Study Group Based on Selection of Closure Method Closure method favored (p-value) (Number of studies)			Study Group Based on Type of Silo Included Closure method favored (p-value) (Number of studies)		Study Group Based on Inclusion of Complicated Gastroschisis Closure method favored (p-value) (Number of studies)		Overall
	Random/Temporal	Surgeon Preference	Failed Primary Closure	Spring-loaded silo only	Spring-loaded and surgical silos	Uncomplicated gastroschisis only	Complicated gastroschisis included	
Length of stay	Silo (p=0.28) (5)	Primary (p=0.17) (7)	**Primary (p=0.0001) (5)**	Primary (p=0.37) (11)	**Primary (p<0.0001) (6)**	Primary (p=0.37) (5)	**Primary (p=0.004) (12)**	**Primary (p=0.004) (17)**
Ventilator days	**Silo (p<0.0001) (4)**	**Primary (p=0.04) (6)**	**Primary (p=0.0001) (3)**	Silo (p=0.51) (8)	**Primary (p<0.0001) (5)**	Primary (p=0.06) (4)	**Primary (p=0.001) (9)**	**Primary (p<0.0001) (13)**
Time to first feed	**Silo (p=0.04) (2)**	Primary (p=0.13) (5)	**Primary (p<0.0001) (2)**	Silo (p=0.42) (5)	**Primary (p=0.002) (4)**	Primary (p=0.16) (5)	Primary (p=0.22) (4)	Primary (p=0.07) (9)
Time to full feeds	Silo (p=0.14) (4)	**Primary (p=0.04) (6)**	**Primary (p=0.03) (3)**	Primary (p=0.66) (8)	**Primary (p=0.007) (5)**	**Primary (p=0.003) (6)**	Silo (p=0.87) (7)	Primary (p=0.06) (13)
Parenteral nutrition duration	Silo (p=0.69) (3)	**Primary (p<0.0001) (5)**	**Primary (p<0.0001) (4)**	**Primary (p=0.005) (8)**	**Primary (p<0.0001) (4)**	**Primary (p=0.003) (5)**	**Primary (p<0.0001) (7)**	**Primary (p<0.0001) (12)**
Infection	**Silo (p=0.03) (5)**	Primary (p=0.96) (7)	Silo (p=0.59) (5)	Silo (p=0.83) (11)	Silo (p=0.06) (6)	Silo (p=0.44) (7)	Silo (p=0.27) (10)	Silo (p=0.18) (17)
Necrotizing enterocolitis	Silo (p=0.24) (4)	Silo (0.54) (5)	Silo (p=0.40) (3)	Silo (p=0.23) (7)	Silo (p=0.47) (5)	Silo (p=0.53) (3)	Silo (p=0.18) (9)	Silo (p=0.16) (12)
Mortality	Primary (p=0.35) (1)	Primary (p=0.40) (4)	Primary (p=0.56) (4)	Primary (p=0.60) (5)	Primary (p=0.22) (4)	Primary (p=0.55) (3)	Primary (p=0.29) (6)	Primary (p=0.23) (9)

Bold text indicates statistically significant result (p<0.05).

Table 3

Associations of study outcomes with gestational age and birth weight.

Outcome	n	Effect Size Measure	Gestational Age (r)	Birth Weight (r)
Length of stay	14	std mean	0.04	−0.02
Ventilator days	11	std mean	−0.43	−0.40
Time to first feed	9	std mean	−0.42	−0.68
Time to full feed	10	std mean	−0.02	−0.38
Parenteral nutrition duration	10	std mean	−0.12	0.50
Infection	12	log(odds)	−0.23	−0.07
Necrotizing enterocolitis	9	log(odds)	−0.39	0.11
Mortality	6	log(odds)	0.49	0.30

r = Pearson's correlation; std mean = standardized (weighted) mean difference; log(odds) = log-transformed odds ratios