

# LONG-GAP ESOPHAGEAL ATRESIA: GASTRIC TRANSPOSITION OR ESOPHAGEAL LENGTHENING WITH DELAYED PRIMARY ANASTOMOSIS? A SYSTEMATIC REVIEW

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## **ABSTRACT**

**PURPOSE:** This study aims to evaluate different surgical approaches to long-gap esophageal atresia (LGEA) with or without tracheoesophageal fistula (TEF) is unclear.

**METHODS:** A systematic literature review was done comparing gastric transposition versus esophageal lengthening with delayed primary anastomosis in infants with LGEA+/-TEF. The primary outcome was time to full oral feeds. Secondary outcomes were time to full enteric feeds, need for further surgery, growth, mortality, and postoperative adverse events.

**RESULTS:** No comparative studies were found, so the literature was re-reviewed to identify non-comparative studies. Four hundred thirty-eight articles were identified and screened, and 18 met the inclusion criteria. All were case series. Forty-three infants underwent gastric transposition, and 106 had esophageal lengthening with delayed primary anastomosis.

One study on gastric transposition reported time to full oral feeds, and one study in each group reported growth. Time to full enteric feeds was reported in one study in each group. Thirty percent of

infants had further surgery following gastric transposition, including hiatus hernia repair (5/43, 12%) and esophageal dilation (7/43, 16%). Following esophageal lengthening, 62/106 (58%) had anti-reflux surgery, 58/106 (55%) esophageal dilatation and 11/106 (10%) esophageal stricture resection.

Anastomotic complications occurred in 13/43 (30%), gastrointestinal in 16/43 (37%), respiratory in 17/43 (40%), and nerve injury in 2/43 (5%) of the gastric transposition group. In the esophageal lengthening group, anastomotic complications occurred in 68/106 (64%), gastrointestinal in 62/106 (58%), respiratory in 6/106 (6%), and none sustained nerve injury. Each group had one death due to a cause not directly related to the surgical procedure.

**CONCLUSIONS:** This systematic review highlights the morbidity associated with both surgical procedures and the variety in reporting outcomes.

**Key words:** Long-gap esophageal atresia; Tracheo-esophageal fistula; Gastric transposition; Esophageal lengthening; Delayed primary anastomosis

## INTRODUCTION

Esophageal atresia (EA) is a rare congenital abnormality and affects approximately 1:3,500 live births [1], and it can be associated with other congenital anomalies and, in particular, tracheoesophageal fistula (TEF).

In some cases, the proximal and distal ends of the esophagus are distant, rendering primary anastomosis technically very difficult. These cases are referred to as long-gap esophageal atresia (LGEA), and their management is not standardized among pediatric surgeons. In particular, there are various surgical techniques for correcting LGEA with or without TEF, and each carries different risks and outcomes. When esophageal anastomosis cannot be achieved as either a primary or delayed procedure, some form of esophageal replacement or lengthening is necessary. Esophageal replacement techniques involve substituting the esophagus with a different part of the gastrointestinal tract. These include interposition of either the colon or jejunum and gastric transposition. In contrast, esophageal lengthening techniques consist of elongating the native esophagus without replacing it with other organs.

There are few comparisons of these techniques, and therefore it can be difficult to counsel parents about the choice of the procedure due to the lack of research evidence. This uncertainty represents a burden to parents who are asked to give informed consent for a procedure for which scarce evidence is available. In a survey conducted by the International Pediatric Endosurgery Group (IPEG) among surgeons from 31 countries, 66% favored gastric transposition as a method of esophageal replacement for long gap esophageal atresia [2]. This is probably because this form of replacement has many advantages which include a single anastomosis compared to other methods.

The aim of this systematic review was to compare the outcomes of gastric transposition and esophageal lengthening with delayed primary anastomosis.

## METHODS

A pre-defined protocol was developed prior to performing this systematic review and registered on the Prospero International Prospective Register of Systematic Reviews (Registration Number: 42016037006).

### Literature Search Strategy

All publications from 1<sup>st</sup> January 2000 to 1<sup>st</sup> January 2020 reporting gastric transposition and/or esophageal lengthening with delayed primary anastomosis for the management of LGEA with or without tracheo-esophageal fistula were identified using the electronic databases MEDLINE, EMBASE and Cochrane Central Register of Controlled Trials. The following terms (free text and MeSH) were used for the search using the "OR" operation within columns and the "AND" operation within/between columns (Table 1). References were managed using EndNote Referencing Software.

Population	Intervention	Comparator/Outcome
<ul style="list-style-type: none"> <li>- Esophageal atresia</li> <li>- Esophag* and atresia</li> <li>- Oesophagi* and atresia</li> <li>- Esophageal or oesophageal</li> <li>- Atresia</li> <li>- Tracheoesopahgeal fistula</li> <li>- Esophageal fistula</li> <li>- Trache* and fistula*</li> <li>- Esophagotrache* and fistula</li> <li>- Oesophagotrache* and fistula</li> <li>- Long gap* or gap length</li> </ul>	<ul style="list-style-type: none"> <li>- Transposition or interposition*</li> <li>- Lengthen* or elongat* or Foker* or Kimura*</li> <li>- Traction</li> <li>- Sutures</li> <li>- Suture technique</li> <li>- Traction* or sutur*</li> <li>- Anastomosis, surgical</li> <li>- Anastom*</li> </ul>	<p><i>Search not restricted on the basis of comparator or outcome as these were assessed at screening stage</i></p>

**Table 1** Key words and MeSH headings used in the literature search

### **Inclusion Criteria**

Articles were considered for inclusion if they were published in the English language between 1<sup>st</sup> January 2000 and 1<sup>st</sup> January 2020. We initially intended to include only comparative studies in any language, that is, those that directly compared outcomes of both gastric transposition and esophageal lengthening with delayed primary anastomosis. However, since no comparative studies were identified, we included non-comparative studies that reported outcomes of either gastric transposition or esophageal lengthening with delayed primary anastomosis.

### **Exclusion Criteria**

Articles published before 1<sup>st</sup> January 2000, not in English, and reporting outcomes of different surgical procedures were excluded. This is with the aim of focusing on the most recent published literature. In addition, single-case reports and articles that reported either surgical technique in populations that were not exclusively LGEA were excluded. Finally, articles that included cases in which a previous attempt at any esophageal anastomosis prior to gastric transposition or esophageal lengthening with delayed anastomosis were also excluded. This is with the aim of achieving a homogenous patient population.

### **Primary Outcome Measures**

The primary outcome of this systematic review was the time taken from surgery to full oral feeds.

### **Secondary Outcome Measures**

Secondary outcomes included time taken from surgery to full enteric feeds, whether patients needed further surgical intervention following esophageal anastomosis, growth (centile), mortality and adverse events including but not limited to anastomotic complications (stenosis/stricture, leak, others), gastrointestinal complications (gastro-esophageal reflux, dysphagia, esophagitis, hiatus hernia, others), respiratory complications (chest infection, pneumothorax, tracheomalacia, others) and (recurrent laryngeal) nerve injury.

### **Study Assessment and Data Extraction**

Titles and abstracts of the identified articles were assessed by three independent reviewers (ON, RM, and YEG). Whenever the abstract was not available or not clear, the full article text was obtained and examined. Any possible conflict between the three reviewers was resolved by a third reviewer (NH). Data from the included articles were extracted by a single investigator (ON), and where data were available, they were checked by NH or YEG. Data were collected using a pre-designed data extraction form containing information about the study and patients' characteristics, primary and secondary outcomes as well as postoperative complications. Where a postoperative complication was not documented, it was assumed not to have occurred except for mortality, which was only assumed to be zero if stated as such. Any unclear information related to data or outcomes was addressed by contacting the corresponding author. Replies from the authors were received in most instances.

### **Statistical Analysis**

Given the absence of comparative studies, it was decided that a meta-analysis would not be performed. All data from included studies are reported descriptively and using appropriate summary statistics.

### **RESULTS**

Using the pre-defined search strategy, 554 articles were identified. Of those, 206 articles were removed as duplicates. Following the title and abstract assessment, 260 articles were excluded as not meeting the inclusion criteria, and the full texts of 88 articles were evaluated for eligibility. After having carefully assessed those 88 articles, 66 were excluded as they did not meet the above-stated inclusion criteria, leaving 22 which were eligible for inclusion (Figure 1).

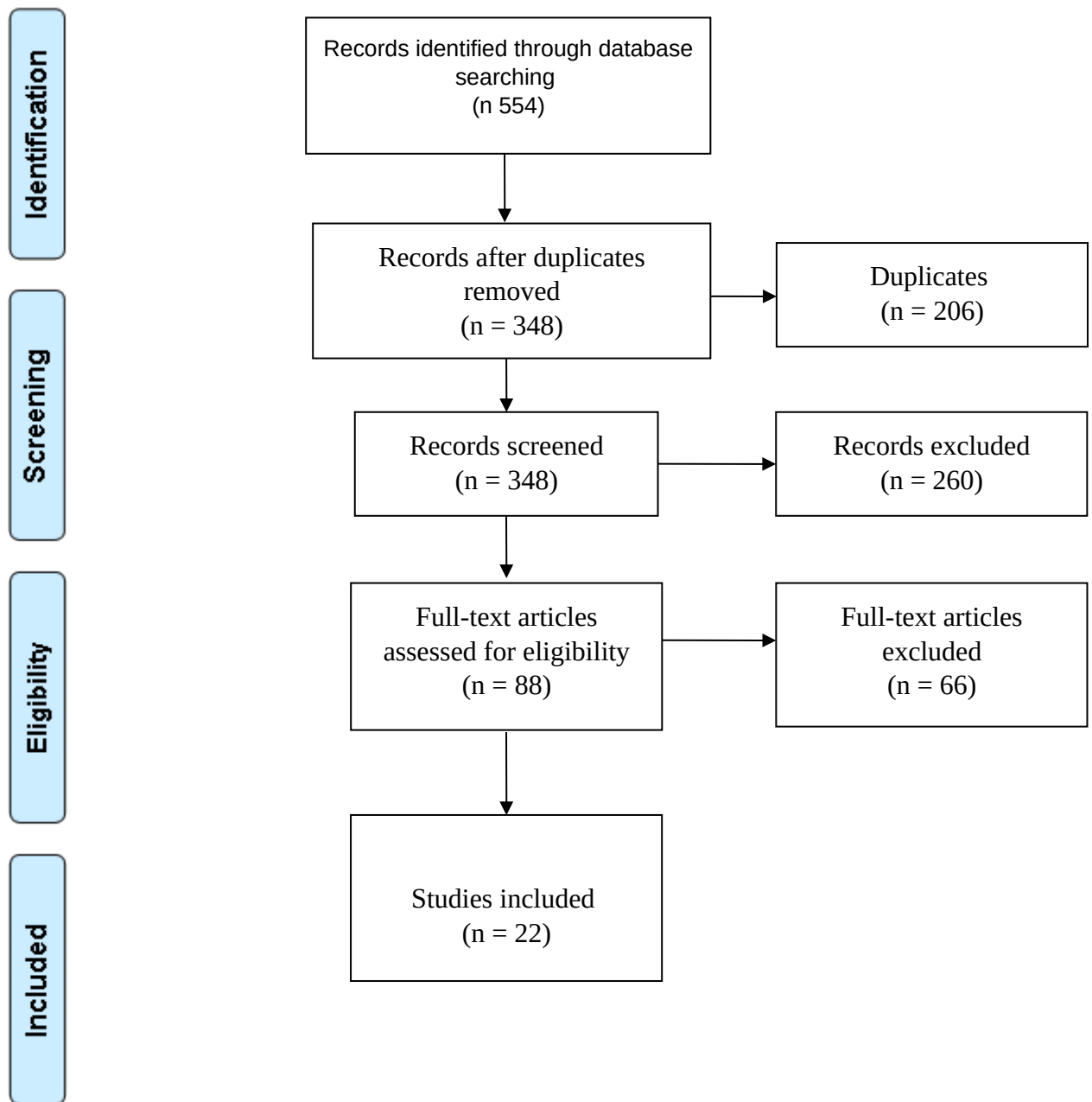


Fig 1 PRISMA flow chart of article selection

### **Characteristics of included studies**

The 22 articles that met the inclusion criteria were all case series. No comparative studies were identified. The region of origin of included studies was North America in seven, Europe in eight, five in Asia, one from South America, and one from Australia. They were all studies undertaken between 1985 and 2018 and published between 2001 and 2018. Seventeen were single-center studies, whereas five were multi-center.

These studies reported 57 patients who underwent gastric transposition and 129 who had esophageal lengthening with delayed primary anastomosis. Most studies included less than 20 patients.

There was a lack of consistency in the measurement of the gap length between the two esophageal ends. This distance was defined using different units of measurement, namely centimeters, vertebral bodies, and vertebral units, and it was therefore unclear how the authors had defined 'long-gap esophageal atresia' (Table 2). In studies reporting esophageal lengthening, the technique used for lengthening was traction alone in 10 studies and traction and bougienage in two.

Author	Publication year	Study period	Country	Number of cases (N)	Single/multi-center	Gap length definition	Surgical technique
<b>Kimura</b>	2001	1986 - 2001	USA	12	Single-center	VB	OL
<b>Al-Qahtani</b>	2003	NR	Canada	3	Single-center	Cm	OL
<b>Skarsgard</b>	2004	NR	Canada	2	Single-center	Cm	OL
<b>Hunter</b>	2009	1987 - 2007	USA	2	Single-center	VB	GT
<b>Stanwell</b>	2010	NR	UK	5	Single-center	VB	GT
<b>Schneider</b>	2011	2007 - 2008	France	4	Single-center	VB	OL
<b>Sharma</b>	2011	1998 - 2009	India	6	Single-center	NR	GT
<b>Van der Zee</b>	2011	2007 - 2009	The Netherlands	2	Single-center	NR	OL
<b>Bairdain</b>	2013	2005 - 2012	USA	7	Multi-center	VB	OL
<b>Miyano</b>	2013	2005 - 2012	Japan	4	Single-center	VB	OL
<b>Parilli</b>	2013	2011 - 2013	Venezuela	10	Single-center	NR	GT
<b>Sroka</b>	2013	2007 - 2010	EU centers	15	Multi-center	Cm	OL

<b>Ng</b>	2014	2003 - 2012	UK	11	Single-center	NR	GT
<b>Bairdain</b>	2015	2005 - 2014	USA	27	Single-center	Cm	OL
<b>Gallo</b>	2015	1985 - 2006	The Netherlands	9	Multi-center	NR	GT
<b>Mochizuki</b>	2015	1990 - 2011	Japan	16	Multi-center	VU	OL
		2010 - 2014					
<b>Van der Zee</b>	2015	2007 - 2014	The Netherlands	8	Single-center	VB	OL
<b>Bobanga</b>	2016	2004 - 2014	USA	4	Single-center	VB	OL
<b>Bogusz</b>	2018	2015 - 2018	Poland	4	Multi-center	NR	OL
<b>Sun</b>	2017	2015 - 2017	China	12	Single-center	VB	OL
<b>Wanaguru</b>	2017	2007 - 2016	Australia	9	Single-center	VB/Cm	OL
<b>Zeng</b>	2017	2008 - 2015	China	14	Single-center	Cm	GT

**Table 2** Characteristics of included studies

NR: not reported; VB: vertebral body; VU: vertebral unit; Cm: centimeters; NPA: no primary anastomosis - inability to perform primary anastomosis; GT: gastric transposition; OL: esophageal lengthening

### **Primary Outcome**

The primary outcome of time to full oral feed was not reported by any study describing gastric transposition.

In the group of patients who underwent esophageal lengthening procedure with delayed primary anastomosis, only one article reported the mean time to full oral feeds, which was 76 and 686 days, in two groups of patients during different study periods [3]. Data from a second article was obtained by contacting the author. In this study, the mean time to full oral feed was 42 (SD 35) months [4]. In another study, the mean was 22 days [5].

### **Secondary Outcomes**

#### Time to full enteric feeds

Only one study reported the time to full oral and, therefore, enteric feeds in the three patients that had esophageal elongation. This was 10, 21, and 35 days, respectively [5].

#### Need for further surgical intervention

Further surgery post gastric transposition procedure was reported in 5/6 studies and was undertaken in a total of 17/43 patients. In one study, 6/9 (67%) patients underwent further surgery, which consisted of anastomotic leak repair (1/9), abdominal wound dehiscence repair (1/9), surgery for delayed gastric emptying (1/9), repair of iatrogenic perforation during endoscopy (1/9) and repair of duodenal perforation caused by placement of a feeding tube (1/9). In addition, 5/9 (55%) patients had anastomotic dilatation due to stenosis. One patient had a proximal tracheo-esophageal fistula which was not initially identified and required ligation [6].

In a second study, 5 of the 11 (45%) patients who had a laparoscopic gastric transposition required further surgical procedures which were hiatus hernia repair (3/11), esophageal stricture dilatations (2/11), pyloroplasty (1/11) and pyloric dilatation (1/11) for gastric outlet obstruction. Some patients had more than one problem requiring surgical intervention [7]. In the third study, of five patients who underwent laparoscopic-assisted gastric pull-up, two (40%) patients required hiatus hernia repair [8]. In the last study, 4/14 (29%) patients developed postoperative anastomotic stricture and required dilatation [9]. (Table 3).

All twelve studies describing esophageal lengthening reported further surgery. Most of the patients (96/129) who had esophageal lengthening had further surgery after restoration of esophageal continuity. The most common surgical procedures were anti-reflux surgery in 62/129 (48%), esophageal dilatations in 76/129 (59%) and stricture resection in 11/129(9%) patients. Some patients underwent multiple procedures (Table 4).

### Growth

Growth (centile) was formally reported in only one study describing gastric transposition. In that article, the authors reported the incidence of height and weight  $<-2$  SD below the mean for age and median BMI (body mass index) at the final follow-up. 2/9 children had height/age  $<-2$  SD, 4/9 had weight/age  $<-2$  SD and median BMI was 15 (range 14-19) [6]. One study simply stated that all patients gained weight appropriately [10]. Another study mentioned that 11/14 patients had a body weight and height comparable to their peers, whereas 1/14 had a lower body weight [9] (Table 3). One mentioned that no growth retardation was found in the series of patients [11]. None of the studies on esophageal lengthening reported growth apart from one article, which indicated a weight centile range from  $<3^{\text{rd}}$  to  $39^{\text{th}}$  at the final follow-up following the procedure [4] (Table 4).

### Mortality

All studies except four reported this outcome. One patient in the gastric transposition group died due to cardiorespiratory failure [12], whereas in another study one died of severe pneumonia with concurrent pyopneumothorax and respiratory failure and another due to anastomotic fistula [9] (Table 3). In the esophageal lengthening group of patients, one death occurred due to respiratory failure in a child with chronic respiratory problems triggered by an iatrogenic perforation of the esophagus at birth [4] (Table 4).

<b>Author</b>	<b>Year</b>	<b>Further surgery n/N (%)</b>	<b>Time to FEF* Mean (SD)</b>	<b>Growth</b>	<b>Mortality</b>
<b>Hunter</b>	2009	NR	NR	see text	0/2 (0%)
<b>Stanwell</b>	2010	2/5 (40%)	NR	NR	0/5 (0%)
<b>Sharma</b>	2011	0/6 (0%)	NR	NR	0/6 (0%)
<b>Parilli</b>	2013	0/10 (0%)	NR	NR	1/10 (10%)
<b>Ng</b>	2014	5/11 (45%)	NR	NR	0/11 (0%)
<b>Gallo</b>	2015	6/9 (67%)	NR	see text	0/9 (0%)
<b>Zeng</b>	2017	4/14 (29%)	NR	see text	2/14 (14%)

**Table 3** Gastric transposition – Secondary outcomes

<b>Author</b>	<b>Year</b>	<b>Further surgery n/N (%)</b>	<b>Time to FEF* Mean (SD)</b>	<b>Growth</b>	<b>Mortality</b>
<b>Kimura</b>	2001	12/12 (100%)	NR	NR	0/11 <sup>†</sup> (0%)
<b>Al-Qahtani</b>	2003	2/3 (67%)	NR	NR	0/3 (0%)
<b>Skarsgard</b>	2004	1/2 (50%)	NR	NR	0/2 (0%)
<b>Schneider</b>	2011	2/4 (50%)	NR	NR	0/4 (0%)
<b>Van der Zee</b>	2011	2/2 (100%)	NR	NR	0/2 (0%)
<b>Bairdain</b>	2013	7/7 (100%)	NR	NR	NR

<b>Miyano</b>	2013	4/4 (100%)	NR	NR	0/4 (0%)
<b>Sroka</b>	2013	10/15 (67%)	NR	NR	0/15 (0%)
<b>Bairdain</b>	2015	17/27 (63%)	NR	NR	0/27 (0%)
<b>Mochizuki</b>	2015	12/16 (75%)	NR	NR	NR
<b>Van der Zee</b>	2015	7/8 (87%)	NR	NR	0/8 (0%)
<b>Bobanga</b>	2016	3/4 (75%)	NR	see text	1/4 (25%)
<b>Bogusz</b>	2018	1/4 (25%)	22 days <sup>#</sup>	NR	NR
<b>Sun</b>	2017	7/12 (58%)	NR	NR	NR
<b>Wanaguru</b>	2017	9/9 (100%)	NR	NR	NR

**Table 4** Esophageal lengthening – Secondary outcomes

NR: not reported; \*FEF: full enteric feeds; <sup>†</sup>One patient lost at follow-up; <sup>#</sup>3/4 cases

Adverse events following esophageal anastomosis

*Gastric transposition (Table 5)*

Following gastric transposition, 9/57 (16%) patients developed anastomotic stricture/stenosis whereas 7/57 (12%) had an anastomotic leak and 1/57 (2%) had both. Of those patients who were affected by gastrointestinal complications, 11/57 (19%) developed gastro-esophageal reflux disease (GERD), 2/57 (4%) had gastric outlet obstruction, 5/57 (9%) patients developed hiatus hernia, and 1/57 (2%) had hospital epidemic viral gastroenteritis. Also, 1/57 (2%) patients had colonic perforation, and 2/57 (4%) had jejunostomy-associated morbidity. Other complications included delayed gastric emptying 1/57 (2%), abdominal wound dehiscence 1/57 (2%), duodenal perforation during feeding tube placement 1/57 (2%), iatrogenic perforation of graft during endoscopy 1/57 (2%) and dysphagia 1/57 (2%). Multiple gastrointestinal complications sometimes occurred in the same patient.

Respiratory complications included 5/57 (9%) pneumothorax, 12/57 (21%) pneumonia, 3/57 (5%) pleural effusion, 1/57 (2%) pulmonary oedema and 3/57 (5%) others (not specified by the authors). Two patients sustained a nerve injury. One of those two developed right-sided Horner's syndrome [6, 7].

<b>Author</b>	<b>Year</b>	<b>Anastomotic complications n/N (%)</b>	<b>Gastrointestinal complications n/N (%)</b>	<b>Respiratory complications n/N (%)</b>	<b>Nerve injury n/N (%)</b>
<b>Hunter</b>	2009	1/2 (50%)	0/2 (0%)	0/2 (0%)	0/2 (0%)
<b>Stanwell</b>	2010	0/5 (0%)	3/5 (60%)	2/5 (40%)	0/5 (0%)
<b>Sharma</b>	2011	0/6 (0%)	0/6 (0%)	0/6 (0%)	0/6 (0%)
<b>Parilli</b>	2013	4/10 (40%)	3/10 (30%)	5/10 (50%)	0/10 (0%)
<b>Ng</b>	2014	2/11 (18%)	4/11 (36%)	3/11 (27%)	1/11 (9%)
<b>Gallo</b>	2015	6/9 (67%)	6/9 (67%)	7/9 (78%)	1/9 (11%)
<b>Zeng</b>	2017	5/14 (36%)	7/14 (50%)	7/14 (50%)	0/14 (0%)

**Table 5** Gastric transposition – Adverse events post esophageal anastomosis

Esophageal lengthening (Table 6)

Patients who underwent esophageal lengthening techniques were also affected by different postoperative complications. In seven studies, all patients had anastomotic complications [4, 13-18]. In total 75/129 (58%) patients had esophageal anastomotic stricture/stenosis, 22/129 (17%) had an anastomotic leak, 18/129 (14%) had an anastomotic leak and stenosis, 4/129 (3%) sustained esophageal rupture/perforation during dilatation, 1/129 (1%) developed an anastomotic leak and sinus, and 1/129 (1%) an anastomotic diverticulum.

Regarding gastrointestinal problems, in one study, all patients (n=4) developed those complications [19], whereas in three studies, no gastrointestinal adverse events were reported [5, 11, 14]. In total, 58/129 (45%) patients were affected by GERD, 2/129 (2%) by dysphagia, 1/129 (1%) by occlusive syndrome, 1/129 (1%) by gastroenteritis, 2/129 (2%) had a hiatus hernia, 3/129 (2%) eosinophilic esophagitis and of those three, one patient also had associated hiatus hernia as well as Barrett's esophagus.

Finally, among the respiratory adverse events, 4/129 (3%) patients developed chylothorax, 1/129 (1%) had pleura effusion, 1/129 (1%) had bronchiolitis, 6/129 (5%) had pneumonia, 2/129 (2%) had severe tracheomalacia and one had both pneumonia as well as tracheomalacia (1%) in the postoperative period. None of the patients who underwent esophageal lengthening with delayed primary anastomosis were reported as having an intraoperative nerve injury.

<b>Author</b>	<b>Year</b>	<b>Type of lengthening</b>	<b>Anastomotic complications n/N (%)</b>	<b>Gastrointestinal complications n/N (%)</b>	<b>Respiratory complications n/N (%)</b>	<b>Nerve injury n/N (%)</b>
<b>Kimura</b>	2001	Traction	12/12 (100%)	11/12 (92%)	1/12 (8%)	0/12 (0%)
<b>Al-Qahtani</b>	2003	Traction	3/3 (100%)	2/3 (67%)	0/3 (0%)	0/3 (0%)
<b>Skarsgard</b>	2004	Traction	1/2 (50%)	1/2 (50%)	0/2 (0%)	0/2 (0%)
<b>Schneider</b>	2011	Gastroplasty	1/4 (25%)	4/4 (100%)	1/4 (25%)	0/4 (0%)
<b>Van der Zee</b>	2011	Traction	2/2 (100%)	1/2 (50%)	1/2 (50%)	0/2 (0%)
<b>Bairdain</b>	2013	Traction	7/7 (100%)	4/7 (57%)	0/7 (0%)	0/7 (0%)

<b>Miyano</b>	2013	Traction	4/4 (100%)	0/4 (0%)	0/4 (0%)	0/4 (0%)
<b>Sroka</b>	2013	Traction	10/15 (67%)	1/15 (7%)	0/15 (0%)	0/15 (0%)
<b>Bairdain</b>	2015	Traction	24/27 (89%)	17/27 (63%)	0/27 (0%)	0/27 (0%)
<b>Mochizuki</b>	2015	Traction and/or Bougienage	12/16 (75%)	11/16 (69%)	2/16 (12%)	0/16 (0%)
<b>Van der Zee</b>	2015	Traction	7/8 (87%)	7/8 (87%)	2/8 (25%)	0/8 (0%)
<b>Bobanga</b>	2016	Traction	4/4 (100%)	3/4 (75%)	1/4 (25%)	0/4 (0%)
<b>Bogusz</b>	2018	Traction	2/4 (50%)	0/4 (0%)	0/4 (0%)	0/4 (0%)
<b>Sun</b>	2017	Bougienage	7/12 (58%)	0/12 (0%)	6/12 (50%)	0/12 (0%)
<b>Wanaguru</b>	2017	Traction	9/9 (100%)	3/9 (33%)	5/9 (44%)	0/9 (0%)

**Table 6** Esophageal lengthening – Adverse events post esophageal anastomosis

## DISCUSSION

This systematic review has identified and included contemporary studies reporting gastric transposition or esophageal lengthening with delayed primary anastomosis for LGEA in an attempt to synthesize data on which to base surgical practice and inform parental counselling. Our initial focus was on patient-centric outcomes, which we believed to be of importance to families, including time to full oral and enteral feeds, growth outcomes and mortality. With the exception of mortality, these were infrequently reported, with our primary outcome (time to full oral feeds) being reported in just one study on esophageal lengthening and no study of gastric transposition. Secondary outcomes and, in particular, surgical complications and postoperative morbidity were reported more frequently.

Overall, this review confirms knowledge that will be all too clear to pediatric surgeons managing infants with LGEA – that this is a challenging group of infants to treat. Following either surgical procedure, infants born with LGEA with or without tracheoesophageal fistula are at significant risk of developing postoperative anastomotic, gastrointestinal and respiratory complications, which at times may necessitate further surgery and certainly justify long-term follow-up. Encouragingly, however, mortality reported here was very low and lower than population-based mortality estimates of infants with all types of EA [20]. This observation must be interpreted with caution, however, as the possibility of publication bias remains high.

Anastomotic leakage is known to be a particular problem with esophageal anastomosis under tension and following esophagogastric anastomosis in the neck. This systematic review showed a leakage rate of 16% (7/43) with gastric transposition and 33% (35/106) with esophageal lengthening and delayed primary anastomosis. This incidence of anastomotic leakage is notably higher than that in series of non-long-gap esophageal atresia in which primary anastomosis can be achieved [18]. Reducing anastomotic leak rate remains a surgical challenge with these techniques. Additionally, anastomotic stenosis/stricture occurred in 12% (5/43) in the gastric transposition group and 50% (53/106) in the esophageal lengthening group. This incidence of anastomotic stricture following esophageal lengthening with delayed primary anastomosis is not necessarily surprising but is certainly higher than most reported series of primary esophageal anastomosis. The need for recurrent anastomotic dilatation places a significant burden on children, families and healthcare providers [21].

GER is recognized to be common following EA repair with a recent study reporting that 55% of infants with type C EA/TEF had GER at 1 year of age [22]. A similarly high incidence of GER (56%) following esophageal lengthening procedure and delayed primary anastomosis is unsurprising given the tension placed on the esophagus and the inevitable strain on the anti-reflux mechanisms at the gastro-esophageal junction. Almost all patients in this review with GOR were treated with a surgical anti-reflux procedure.

This review provides useful information on other gastrointestinal complications in this population. Of particular note is the relatively high incidence of hiatus hernia following gastric transposition (5/43 = 12%), a complication which occurred exclusively in patients who had undergone a laparoscopic-assisted procedure. The

higher rate of hiatus hernia following laparoscopic-assisted gastric transposition has been proposed to be due to fewer postoperative adhesions following minimal invasive surgery by some authors [7]. However, in a different study of 10 patients whom all underwent laparoscopic-assisted gastric transposition for LGEA, none developed a hiatus hernia [12].

Respiratory complications may be under-reported in series reporting EA repair. The anatomical location of the transposed stomach or esophageal anastomosis that is prone to complications may clearly have respiratory consequences. Perhaps unsurprisingly, the risk of respiratory complications does appear to be slightly higher following gastric transposition.

Recurrent laryngeal nerve injury is a recognized complication following EA repair due to the course of the nerve in close proximity to the esophagus and trachea [23]. A cervical approach to the esophagus as during creation of a cervical esophagostomy, gastric transposition or repair of H-type TEF likely carries the highest risk. In this systematic review, there were only two patients (5%) among those who underwent gastric transposition reported to have an intra-operative nerve injury although it is unclear whether any formal assessment was taken of this group of patients.

### **Limitations of this Systematic Review**

There are a number of challenges in interpreting data within this review. The first relates to the definition of 'long-gap' esophageal atresia. There is a clear lack of consensus regarding how 'long-gap' should be measured (Table 2), which likely results in variation in the precise patient population between studies. LGEA is a diagnosis that is open to a certain subjectivity despite efforts of some experts to create standardized definitions (e.g. > 2cm (2 vertebral bodies) [24],  $\geq 3$  vertebral bodies [25], gap length of  $\geq 4$  vertebral units [26]). A reliable and reproducible objective definition of LGEA would aid study comparisons in the future.

Further limitations of this systematic review are that there were no comparative studies that met the inclusion criteria and that all the included studies were retrospective case series, which are considered to be at a low level in the hierarchy of evidence [27]. There was a notable lack of standardization in outcome reporting; important outcomes were frequently not reported at all, and outcomes were frequently not defined and were measured at non-standardized time points. Nonetheless, we believe our methodology has resulted in data that represent the best available evidence on the outcomes of these procedures for this patient population at the current time.

## **CONCLUSIONS**

The surgical management of esophageal atresia with or without tracheoesophageal fistula represents a technical and clinical challenge for pediatric surgeons. This systematic review provides useful evidence concerning the anastomotic complications, need for further surgical intervention and longer-term morbidity related to two common operative techniques. In particular, it highlights the high postoperative morbidity associated with esophageal lengthening with delayed primary anastomosis. However, the literature supporting the choice of surgical approach to these infants is scarce and, in particular, lacks high-quality, adequately powered comparative research studies to influence current clinical practice and create new clinical evidence.

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