Analysis of gap length as a predictor of surgical outcomes in esophageal atresia with distal fistula: a single center experience

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Abstract

Purpose

Long-gap esophageal atresia (LGEA) is still a challenge for pediatric surgery. No consensus exists as to what constitutes a long gap, and few studies have investigated the maximum gap length safely repairable by primary anastomosis. Based on surgical outcomes at a single institution, we aimed to determine the gap length in LGEA with a high risk of complications.

Methods

The medical records of 51, consecutive patients with esophageal atresia (EA) with primary repair in the early neonatal period between 2001 and 2021 were retrospectively reviewed. Three, major complications were found in the surgical outcomes: 1) anastomotic leakage, 2) esophageal stricture requiring dilatation, and 3) GERD requiring fundoplication. The predictive power of the postsurgical complications was assessed using receiver operating characteristic analysis, and the area under the curve (AUC) and the cutoff value with a specificity of > 90% were calculated.

Results

Sixteen patients (31.4%) experienced a complication. The AUC of gap length was0.90 ($p < 0.001$), and the gap length cutoff value was ≥ 2.0 cm for predicting any complication (sensitivity: 62.5%, specificity: 91.4%).

Conclusion

A gap length ≥ 2.0 cm was considered as defining LGEA and was associated with an extremely high complication rate after primary repair.

Introduction

Despite significant progress in the management and improvement of esophageal atresia (EA) outcomes over the last few decades [1], long-gap esophageal atresia (LGEA) presents a challenge to pediatric surgeons, and its optimal method of management is still moot. In addition, the definition of patients with LGEA has varied across studies [2, 3], and there is no consensus on the precise definition of a long gap [4, 5]. A long gap is frequently associated with pure EA without a tracheoesophageal fistula (TEF) (Gross classification type A) or with EA with an upper esophageal pouch TEF (Gross type B) [6]. However, it can occur with almost any type of EA [7] and should therefore not be equated with type A atresia [2]. In studies of LGEA, as many as 50% of the patients with EA had a distal TEF (Gross type C or D) [8]. Although primary anastomosis often fails when the gap is too large, as stated above no consensus exists

as to what constitutes a long gap, and only a few studies have discussed how to determine the maximum gap length which is safe to repair using primary anastomosis [9, 10]. Previous studies have based their definition of LGEA on the number of vertebral bodies (VB) [11–13], length in centimeters [14, 15] or both [16, 17].

Esophageal replacement may be considered if a gap is judged to be too large for a primary anastomosis. Several techniques of esophageal replacement have been developed, including total or partial gastric pull-up, colon or jejunal interposition, and gastric tube reconstruction. Nevertheless, the native esophagus is the most suitable conduit both anatomically and functionally [18] and is commonly accepted to be superior to any reconstruction or replacement [1, 5, 8, 19–21]. A failed attempt to save the esophagus does not preclude replacement [21]; therefore a concerted effort to achieve primary anastomosis should always be attempted first [4, 21]. We aimed herein to define LGEA by determining the gap length with a high risk of complications in primary anastomosis based on surgical outcomes at a single institution.

Methods

Data collection

All patients who underwent early primary esophageal anastomosis in the neonatal period for EA at Tokyo Metropolitan Children's Medical Center between October 2001 and October 2021 and whose information was able to be collected from the medical records were reviewed retrospectively. The exclusion criteria were delayed primary repair in infancy after a gastrostomy in the neonatal period or primary anastomosis via the cervical approach. Also excluded were patients with incomplete medical records. Data on the patients' sex, gestational age, age at primary repair, birth weight, cardiovascular anomalies, VACTER association, CHARGE syndrome, Gross classification, intra-operative gap length, X-ray findings, length of hospital stay (LOS), and complications were collected from the records.

Surgical technique

An open extra-pleural thoracotomy on the right side and single-layer anastomosis using absorbable thread were performed. In patients with a right aortic arch, left side thoracotomy was considered. Extensive dissection of the upper pouch was possible owing to the sufficient submucosal blood supply. Although the lower end of the esophagus was dissected minimally, sufficient mobilization was required if the gap width precluded anastomosis with minimal dissection. If anastomosis was unable to be performed because the gap was unbridgeable, a gradual, intraoperative, mechanical traction of the esophageal ends was used. The gap length between the esophageal segments was measured under direct vision at the time of surgery. In detail, a shortened measuring tape was placed in the surgical field of view, and the length between the horizontal levels of the upper pouch (the natural position without pressing or mobilization) and the distal fistula (before ligation) was measured in centimeters. An extra-pleural chest drain was placed near the anastomosis, and a nasogastric tube was placed to serve as a transanastomotic tube.

Postoperative care and complications

Postoperative ventilation under deep sedation or muscle paralysis was performed in all the cases, and the intubation period was determined by the grade of anastomotic tension. Patients received an esophagography approximately one week after surgery. Anastomotic leakage was diagnosed based on the findings of chest tube drainage, chest X-ray, and esophagography. The surgical outcomes in relation to gap length were analyzed in terms of 1) anastomotic leakage, 2) esophageal stricture requiring dilatation, and 3) gastroesophageal reflux disease (GERD) requiring fundoplication.

Statistics

Statistical analysis was performed using the Statistical Package for the Social Sciences (SPSS) 27.0 (IBM Corp., Armonk, NY, USA). Nominal variables were expressed as a number (%), and Fisher's exact test was used for comparison. Continuous variables were expressed as the median (minimum-maximum), and the Mann-Whitney's U test was used for comparison. The predictive power of the postsurgical complications was assessed using receiver operating characteristic (ROC) analysis; the area under the curve (AUC) and a cutoff value with a specificity of > 90% were calculated. $P < 0.05$ was considered to indicate statistical significance.

Results

Patient characteristics

In total, 64 patients had undergone early or delayed primary esophageal anastomosis for EA. Thirteen patients were excluded; three had insufficient data, nine had delayed primary repair, and one had the cervical approach. Finally, 51 patients were included, all of whom had Gross classification type C, including 30 male and 21 female patients. Primary repair within several days after birth was performed in all the patients. The median gap length was 0.5 (range: 0.0–3.0) cm, and the median birth weight was 2.506 (range: 1.868–3.302) kg.

Complications

Sixteen patients (31.4%) had at least one complication, and 35 had no complication (68.6%). Anastomotic leakage (including partial overlapping), anastomotic stricture, and GERD was observed in seven (13.7%), eight (15.7%), and 12 (23.5%) patients, respectively. The median gap length in patients with and without complications was 2.3 cm (range: 0.5-3.0 cm) and 0 cm (range: 0-2.5 cm) ($p < 0.001$), respectively. No significant difference was observed between the two groups with or without a complication in terms of sex, co-morbidity rate of cardiovascular anomalies, right aorta or aortic arch, VACTER association or CHARGE syndrome while a significant difference was observed in terms of birth weight, gestational age, and gap length. Table 1 shows the patient demographics after stratification by the presence or absence of complications. The median postoperative LOS for EA was 39 days (range: 13–618 days). Forty-seven patients had good esophageal function in terms of oral intake; among these,

39 patients achieved oral feeding during infancy, four patients by age 2 years, and the remaining four patients by age 7 years. Four patients failed to achieve oral feeding. Of these, one patient had an eating disorder associated with mental retardation, one patient had a severe laryngotracheo-esophageal cleft, and only two patients had esophageal dysfunction associated with EA. All these patients received gastrostomy feeding. There were no deaths.

Table 1
Patient demographics after stratification by the presence or absence of complications

	Group with complication(s) **n = 16**	**Group without complications** **n = 35**	***P value***
Sex (Male: Female)	9: 7	21: 14	0.80
Median gestational age (weeks)	38 (33–41)	39 (34–42)	0.07
Median body weight at primary repair (kg)	2.269 (1.868–2.978)	2.616 (1.934–3.302)	0.02
Median age at primary repair (days)	1 (0–6)	1 (0–6)	0.18
Median intra-operative gap length (cm)	2.3 (0.5-3.0)	0 (0-2.5)	< 0.001
Associated anomalies			
VACTER association	4 (25.0%)	5 (14.3%)	0.35
Cardiovascular anomaly			
-Simple	2 (12.5%)	2 (5.7%)	0.40
-Complex	4 (25.0%)	5 (14.3%)	
Right aorta or aortic arch	3 (18.8%)	4 (11.4%)	0.48
CHARGE syndrome	1 (6.3%)	0 (0.0%)	0.14
Anastomotic leakage	7	-	-
Stricture requiring dilatation	8	-	-
GERD requiring fundoplication	12	-	-
Median LOS after surgery (days)	119 (22–618)	29 (13–309)	< 0.001
Median age at establishment of oral intake (years)	1 (0–6), not established: 3	0 (0–4), not established: 1	0.001
LOS: length of hospital stay			
GERD: gastroesophageal reflux disease			

Prediction of postsurgical complications by gap length

Gap length (cm) showed satisfactory performance as a predictor of any of the aforementioned complications (AUC: 0.90; 95% confidence interval [CI]: 0.811–0.983; p < 0.001). Based on a specificity of 90% or higher, the cutoff value was 2.0 cm (sensitivity: 62.5%, specificity: 91.4%) (Fig. 1). Complications occurred in 10 of the 13 patients with a gap of 2.0 cm or more (positive predictive value: 76.9%) (Table 2).

Table 2
Comparison of the complication rate in patients with esophageal atresia with a gap < 2 cm and ≥ 2 cm

Complications	**Gap length < 2 cm** **n = 38**	**Gap length ≥ 2 cm** **n = 13**	***P value***
Any anastomotic complication	6 (15.8%)	10 (76.9%)	< 0.001
-Anastomotic leakage	2 (5.3%)	5 (38.5%)	0.003
-Stricture requiring dilatations	4 (10.5%)	4 (30.8%)	0.08
-GERD requiring fundoplication	4 (10.5%)	8 (61.5%)	< 0.001
Dysphagia present after age 1 year	6 (15.8%)	6 (46.2%)	0.03
Long-term postoperative hospitalization ≥ 60 days	10 (26.3%)	8 (61.5%)	0.02

Discussion

The present study demonstrated that the cut-off value of the gap length at which primary anastomosis can be performed without complications was < 2.0 cm, which had a specificity > 90%. Thus, a long gap may be defined as being 2.0 cm or more in size. Most of the patients had a good, long-term prognosis and improved without oral feeding difficulties over the long term regardless of gap length even when anastomotic leakage occurred. Patients with long-gap will probably require therapeutic intervention for postoperative complications and an extended postoperative management period. Nevertheless, the primary anastomosis was performed successfully in all the EA patients in the present cohort with a gap ≤ 3.0 cm. Therefore, a primary anastomosis should be performed for EA. However, patients with a gap length > 2.0 cm should be carefully managed postoperatively, and informed consent should be obtained before treatment because complications are unavoidable. Additional procedures, such as drain insertion in case of leakage, fundoplication or anastomotic dilatation, might be required.

Several studies have specifically defined a long gap based on personal experience [21] or previous research [17, 19], but as of yet there is no consensus on a standard length for defining LGEA because the definition of a long gap has varied across studies. A long gap is often defined functionally as having a length precluding a primary anastomosis or leading to a failed anastomosis [3]. However, this definition is imprecise because the performance of a primary anastomosis depends heavily on the skill of the surgeon

and other variables [4]. Specifically, Spitz et al. [4] suggested that if a gap is greater than six VB, the chance of saving the esophagus is remote while Friedmacher et al. [8] stated that esophageal replacement was necessary only in a few patients who either had no distal esophageal segment or only a nub of the distal esophageal segment. Additionally, Bagolan et al. [21] reported that nearly all the patients in their study were able to be anastomosed successfully using any of several maneuvers, such as extensive proximal or distal mobilization, dissection of the upper esophageal pouch via a cervical incision, internal traction on both segments or the addition of an upper esophageal flap. In the present study, early primary anastomosis was able to be performed for EA with a gap length of up to 3.0 cm.

Some studies not providing a specific gap length in their definition of LGEA have defined LGEA by the presence of a distal fistula at the carina [6, 22] or the absence of a TEF [23] other than by the failure of anastomosis [1, 24–26].

On the other hand, in studies defining gap length in centimeters, lengths including > 2 cm [9, 10, 27–29], > 2.1 cm [30], ≥ 2.5 cm [15, 19], > 3 cm [31], and ≥ 3.5 cm [32], and ≥ 5 cm [33] were use to define a long gap. Studies using VB defined a long gap as VB ≥ 2 [4, 34], ≥ 3 [21], ≥ 4 [35] or ≥ 5 [36]. Several studies have employed two definitions, namely, VB > 3 cm or > 2 [17, 37]; ≥3 cm or ≥ 5 [16]; or ≥ 3 and/or the inability to perform the primary anastomosis in the first operation [13]. Other articles have included a subset of LGEA dubbed ultra-LGEA, which has a gap length ≥/>3.5 cm [19, 38] or > 6 cm [39]. Al-Shanafey et al. [1] reported that 40% of pediatric surgeons they surveyed defined LGEA as having 3–4 VB, and 24% thought it had no TEF. Baird et al. [2] reported that an audience response system poll revealed that 63% of physicians favored using VB to describe gap length while 10% simply ‘know it when they see it’.

In EA, the gap length between the proximal and distal segments is a measure of the severity of the anatomical defect and is directly related to the degree of technical difficulty of surgery [19, 31]. The longer the gap, the greater the tension if primary end-to-end esophageal anastomosis is carried out [19]; therefore, a long gap is associated with an increased incidence of anastomotic complications, such as leakage, strictures, and GERD [6, 10, 31, 40]. LGEA is challenging for pediatric surgeons. Because the survival of infants with EA has improved markedly, the relationship between gap length and both short and long-term outcomes has begun to attract attention [22, 27, 29]. It has been known for several decades that gap length largely determines the complication rate [27, 28, 38]. When a gap is 2 to 3 cm or more, the complication rate is significantly higher [28, 31, 41]. On the other hand, there are surprisingly few studies reporting a detailed comparison of outcomes based on gap length [9, 10, 27, 29, 31]. Sillen et al. [29] found that LGEA (gap length > 2 cm) was associated with more anastomotic complications than no or moderate gap-EA. Hands et al. [27] reported that postoperative complications, such as anastomotic leakage, wound sepsis, septicemia, pneumothorax, and pneumonia, were significantly more common in patients with LGEA (gap length > 2 cm). In a more recent study dividing patients into three or four groups according to the gap lengths documented during thoracotomy, Brown et al. [31] demonstrated that the incidence of anastomotic complications was highest in the long gap group (> 3 cm) while it was moderate in the intermediate gap group (> 1-≤3 cm). Upadhyaya et al. [10] divided EA patients with TEF into four groups (ultralong: >3.5 cm, long: 2.1–3.5 cm, intermediate: >1-≤2 cm, and short: ≤1 cm) and

found a statistically significant difference in the incidence of esophageal leakage and mortality. Thakkar et al. [9] divided their patients into three groups (long: >2-≦5 cm, intermediate: >1-≦2 cm, and short: ≦1 cm) and found that gap length had no significant correlation with leakage or stricture; however, they observed a significant increase in the need for fundoplication. Orringer et al. [42] found GERD to be more common in patients who required a distal esophageal mobilization of 3 cm or more for the primary anastomosis.

Moreover, no consensus exists on how and when to measure gap length[1, 6, 21]. Intraoperative direct measurement [1, 9, 10, 31] and preoperative radiological measurement [11, 12, 17, 19, 20, 34, 37]) of a gap using VB or in centimeters have been reported. In EA without a distal fistula (type A or B), radiological measurement of gap length is generally performed after creating a gastrostomy. However, there are few reports describing a method of preoperatively assessing gap length in EA with a distal fistula in patients without a gastrostomy [21]. Bagalon et al. [21] reported measuring gaps with a combination of fluoroscopy and bronchoscopy. However, this method is not common. On the other hand, several studies have intraoperatively measured gap length during a thoracotomy [1, 19, 24]. The clinical significance of this method has not been substantiated in some reports because the studies lacked uniformity. Most studies have failed to indicate whether a gap was measured before or after dissection and if it was measured under tension [1]. The present study used direct, uniform, intraoperative measurement of gap length, in which the measurement deviations are negligible, as the most accurate and easiest method to perform [31].

Body weight reportedly affects esophageal strength [43]. Therefore, the impact of gap length on anastomosis may vary depending on the patient's body weight. The present study found a significant difference in body weight at surgery. In low-birth-weight infants weighing less than 2.5 kg, a long gap tended to produce worse outcomes.

Our report has some limitations. The retrospective analysis might have limited the validity of the data. Intraoperative measurements of gap length were reviewed retrospectively, and repeated measurements were not taken as in a prospective study. Therefore, it was not possible to evaluate the reproducibility of this measurement method with statistical reliability. Different surgeons performed the surgery and managed the patients, thereby introducing the possibility of a measurement bias arising from individual variations in experience, etc.

Moreover, the patients who underwent delayed primary repair or esophageal replacement as the primary repair were excluded. Because patients with a gap length > 3 cm were classified as Gross type A or B and underwent delayed primary repair, primary repair of a gap length longer than 3.0 cm was not included. A prospective study of EA should be undertaken using uniform criteria to measure gap length and to compare results from different institutions.

Conclusion

A gap length ≥ 2.0 cm was considered adequate to define LGEA and was associated with a high complication rate after early primary repair. Patients with a gap length ≥ 2.0 cm should be carefully managed postoperatively because complications are unavoidable. However, as the present study was small and retrospective, a prospective study of EA with a larger cohort should be undertaken using uniform criteria for measuring gap length.

Declarations

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Compliance with ethical standards

Conflicts of interest: The authors declare that they have no conflict of interest. Ethical approval: This study was approved by the institutional ethical committee (2021b-1) and was performed in accordance with the ethical standards of the 2000 Declaration of Helsinki. The requirement for informed consent was waived.

Author Contribution

All authors contributed to the study conception and design. Data collection and analysis were performed by M.I.. The first draft of the manuscript was written by M.I. and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Figures

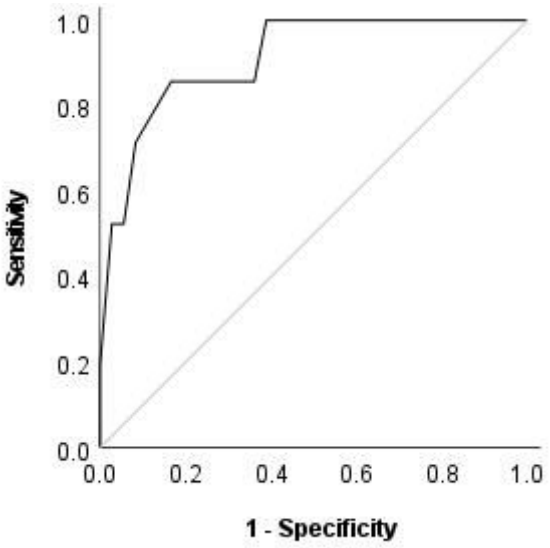

Figure 1

Predictive power of postsurgical complications was assessed using receiver operating characteristic (ROC) analysis; the area under the curve (AUC) and the cutoff value with a specificity of >90% were calculated. Gap length (cm) showed satisfactory performance as a predictor of both complications (95% confidence interval [CI]: 0.811-0.983; AUC: 0.91; p<0.001). Based on a specificity of 90% or higher, the cutoff values were 2.0 cm for both complication (sensitivity: 62.5%, specificity: 91.4%)