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Predictors of recurrent strictures after oesophageal atresia repair

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KEYWORDS

Oesophageal stricture, Delayed repair, Prematurity, Oesophageal dilatation

ABSTRACT

Background: Anastomotic strictures continue to complicate the outcome after oesophageal atresia (OA) repair. Multiple variables contribute to the development of strictures, and oesophageal dilatations are the mainstay of treatment. We aim to analyse the factors that impact the timing for initiation of oesophageal dilatations, the duration, frequency, and success of the dilatation regimen for OA.

Methods: It was a retrospective review of data (13-year) of children who underwent repair for Gross type C OA (OA with distal tracheo-oesophageal fistula). Delayed anastomosis was performed for long gap OA. Leaks were clinically obvious or identified on contrast swallow. Strictures that were symptomatic underwent oesophageal dilatations.

Results: The data of 72 children were analysed. The stricture rate was 37.5%. Ten had delayed repair, out of which 50% developed strictures compared to 35.5% who had a primary repair (P=0.48). There was no statistical difference in the mean birth weight (BW) and gestational age (GA) of children who developed strictures compared to those with no strictures (2.74kg vs 2.63Kg; P =0.548; 37.4 weeks vs 37.3 weeks; P=0.9). Children that underwent a delayed repair required significantly more dilatation sessions (12 vs 2 median sessions; P =0.001) and had a significantly prolonged duration of treatment (610 vs 63 median days; P = 0.013). There was a significant negative correlation between the GA and BW and the number of dilatation sessions required (P=0.03 and P=0.02, respectively). Linear regression revealed that delayed repair was the most important factor related to the number of dilatation sessions required (p <0.001); this was followed by lower GA or BW (p = 0.0265) and early onset of dilatations (p=0.0471).

Conclusions: The early onset of oesophageal dilatation for oesophageal strictures or when they occur in premature babies or those that have had a delayed repair, it should be anticipated that they would be refractory or recurrent.

INTRODUCTION

The surgical management of oesophageal atresia (OA) without a tracheo-oesophageal fistula (TOF) (Gross Type A), with a proximal fistula (Type B), distal fistula (Type C), or proximal and distal fistulas (Type D) is frequently complicated by anastomotic strictures in 18% to 59% of cases.[1-7] Oesophageal dilatation is the mainstay of treatment with a reported success rate of 70-100% after three median dilatation sessions.[3,6,8,9] Several factors play a role in the aetiology of strictures. These include prematurity and low birth weight; long oesophageal gap length resulting in anastomotic tension, and due to its segmental blood supply vascular compromise to the lower oesophagus from excessive mobilisation; suture type; anastomotic leak; and gastro-oesophageal reflux (GOR).[3-6,10,11] There is limited published data on whether these factors can cause strictures to become recurrent or refractory and therefore difficult to manage.[9] However, it is accepted that the different anatomic variants have different outcomes, with Type A being associated with long oesophageal gap [2] and refractory strictures.[9]

We aim to analyse these factors and determine how they can impact the timing for initiation of oesophageal dilatations, the duration, frequency, and overall success of the dilatation regimen for Type C OA.

METHODS

After obtaining institutional review board approval, a retrospective review of data of all children who underwent repair of Gross Type C oesophageal atresia between October 2004 and December 2017 was performed. Data on demographics, comorbidities, strictures, leaks, and dilatations were obtained for the cohort.

The standard approach to repair was via an extrapleural open right thoracotomy. A trans-anastomotic tube was used routinely, and a chest drain inserted in the majority. Sutures used for anastomosis were mostly 5-0, occasionally 6-0, polyglyconate (Maxon™). Less often 5-0 or 6-0 polydioxanone (PDS), polyglactin 910 (Vicryl®), or polypropylene (Prolene) were used. A contrast swallow was performed around a week post-surgery.

Significant anastomotic leaks were defined as those that presented early with either radiological opacification of the right hemithorax or with saliva draining out of the thoracostomy drain. Small, contained leaks were defined as leaks identified at contrast swallow. Oesophageal strictures were defined as anastomotic narrowing on contrast oesophagram in children that were symptomatic with regurgitation or dysphagia and required management with oesophageal dilatations.

A long gap between the oesophageal ends, when encountered, was documented but its definition is not standardized. However, when gap length was significant, delayed oesophageal anastomosis at a second procedure was performed after assessment for improved gap length. Therefore, children that underwent delayed repair were analysed as somewhat representative of the long gap group.

Children that had died, had an oesophageal traction technique or a primary oesophageal replacement were excluded.

Acid suppression was prescribed to all children, but the duration of use and compliance was not consistently documented and therefore not included in the analysis. Likewise, gastro-oesophageal reflux was not consistently assessed with pH monitoring for the entire cohort and therefore not analysed.

Fisher's Exact test was used to test the association between categorical variables. Student's T-test for comparing means of parametric continuous data and Mann-Whitney U test was used to compare non-parametric data sets. Spearman's Rho test was used for non-parametric correlation analysis. Stepwise linear regression analysis was used to analyse the relationship between dependent variables and independent categorical and continuous variables. Significance was set at $P < 0.05$.

RESULTS

There were 91 children with Gross Type C anomaly. Nineteen children were excluded and data of the remaining 72 children were analysed. The follow-up duration had a range (median) of 2.4 to 148 (80.5) months (Mean 75.3 ±45 months). Their mean (range) birth weight (BW) and gestational age (GA) were 2.67kg (0.98 to 3.86kg) and 37.4weeks (29.6 to 42 weeks), respectively.

Table 1 shows the number of children with associated comorbidities, complications, and further related procedures including anti-reflux surgery. Not shown are the other severe comorbidities encountered in the children that had died during the study period.

Figure 1 summarises the details on anastomotic strictures and leaks encountered in the cohort. The stricture rate was 37.5%. Of the 11 children that developed anastomotic leaks, 54.5% of them developed strictures while 34.4% of the 61 children without leaks developed strictures (P=0.31).

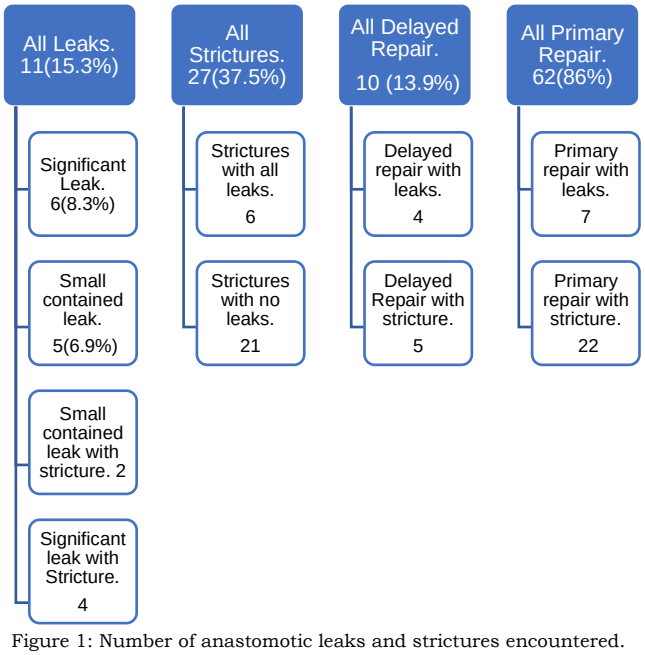

Figure 1: Number of anastomotic leaks and strictures encountered. Total study population =72

There were 10 (13.9%) children who due to long gap length underwent ligation of their fistula and formation of a gastrostomy only. This was then followed by delayed oesophageal anastomosis. The delayed repair was performed post-birth at a median (interquartile range) of 132 days (87 to 178 days). Figure 1 shows that 50% (n=5) of children who had a delayed repair developed strictures compared to 35.5% (n=22) who had a primary repair (P=0.48). Children that had a delayed repair developed significantly more anastomotic leaks compared to children that had a primary repair (40% vs 11.3%; P=0.04; Figure 1)

There was no statistical difference in the mean BW of children who developed strictures compared to those with no strictures (2.74kg vs 2.63Kg; P =0.548). Similarly, there was no difference in their mean GA respectively (37.4 weeks vs 37.3 weeks; P=0.9).

Table 1: Children with Gross Type C anomaly (n = 72) with comorbidities, complications, and related further procedures

Cardiac requiring operative correction	**n**	**Gastrointestinal**	**n**	**Genitourinary**	**n**	**Complications/Further related procedures**	**n**
[a]VSD+ASD+PDA	1	Anorectal malformation	4	Solitary Kidney	4	Nissen's Fundoplication	7
Tetralogy of Fallot	3	Cloaca	2	[b]PUJ/VUJ obstruction	2	Surgical Jejunostomy or Radiological Gastro-Jejunostomy tube	2
Pulmonary atresia + VSD + ASD	1	Duodenal atresia	2	Horseshoe Kidney	1	Common wall oesophagus and Trachea, subsequent trachea stenosis requiring tracheoplasty	1
ASD + PDA	2	Pyloric stenosis	1			Postoperative Pneumothorax	3
						Decortication for empyema post dilatation perforation	1
Airway	**n**	**Other**	**n**	**Limb/Facial/ Vertebra**	**n**	Redo surgery for a significant leak	2
Laryngeal Cleft	5	Tethered Spinal Cord	1	Finger deformity	1	Recurrent tracheoesophageal fistula	2
Choanal atresia/stenosis	2	Intraventricular haemorrhage	1	Dysplastic radius	1	Oesophageal stricture excision	2
Subglottic stenosis	1	**Genetic Syndromes**	**n**	Cranio-costo-facial syndrome	1	Tracheal Diverticulum	1
Tracheomalacia	17	Wenstrup syndrome	1	Hemifacial hypoplasia	1	Stomach perforation Pre-Op	1
Absent/Hypoplastic lung	1	Trisomy 21	1	Vertebral fusion anomaly	1	[c]OGD and foreign body/food bolus obstruction	4
				Cleft Palate/Lip	1	Long term central access (Port-A-Cath or Hickmann line)	4
				Craniosynostosis	1	Operative closure persistent gastrocutaneous fistula	2

aVSD ventricular septal defect; ASD Atrial septal defect; PDA patent ductus arteriosus; bPUJ/VUJ pelviureteric junction/vesicoureteric junction; cOGD Oesophago-Gastro-Duodenoscopy

Several treatment modalities were employed for strictures and frequently different treatment options were combined in the same child (Table 2). Six episodes (5%) of oesophageal perforation occurred after 120 dilatation sessions.

Table 2: Type of Stricture treatment employed per child (120 sessions)

Dilatation type employed	**Number of Children (n =27)**
Balloon only	13
Maloney only	4
Balloon + Maloney	1
Maloney + Tuckers	1
Balloon + Filiform + Maloney	1
Filiform + Maloney	2
Filiform + Maloney + balloon + [a]stricture resection	1
Balloon + Mitomycin/Balloon + Maloney	1
Tuckers + Balloon	1
Balloon + Maloney + [b]stricture resection	1
Balloon + filiform + Maloney + stent	1

aThis child had a delayed repair. Stricture resection was performed after 5 dilatation sessions. One further dilatation was required after stricture resection. bThis child had a primary repair, developed a leak and later a recurrent tracheo-oesophageal fistula identified at the first dilatation session. Stricture resection and recurrent fistula ligation were performed. One further dilatation session was required.

Overall a median of 3 dilatation sessions were required per child. Those who suffered leaks compared to those without leaks did not require significantly more dilatation sessions respectively (6.5 vs 3 median sessions; P= 0.2). However, those that underwent a delayed repair required significantly more dilatation sessions (12 vs 2 median sessions; P =0.001) (Table 3).

Table 3: Dilatation sessions required.

Type C oesophageal atresia	**Total**	**Median**	**Range**
Number of dilatations required (n= 27)	120	3	1-16
Number of dilatations required in children with significant leaks (n=4)	30	6.5	2-15
Number of dilatations required in children with small contained leaks (n=2)	17	8.5	1-16
Number of dilatations required in all children with anastomotic leaks (n=6)	47	6.5	1-16
Number of dilatations required in all children with NO anastomotic leaks (n=21)	73	3	1-12
Number of dilatations required in children that had delayed repair (n= 5)	60	12	6-16
Number of dilatations required in children that had early repair (n=22)	60	2	1-8

Children with anastomotic leaks compared to those without leaks respectively did not have a significantly earlier onset of initiation of dilatations (62.5 vs 179 median days; P = 0.58) or a significantly more prolonged duration of treatment (580 vs 121 median

days; P = 0.3) and their symptom-free period post-dilatation was not significantly shorter (37 vs 33 median months; P=0.73). Likewise, children that had a delayed repair compared to those with a primary repair respectively did not have a significantly earlier onset of initiation of dilatations (59 vs 229 median days; P=0.11) and their symptom-free period was not significantly shorter (22 vs 38 median months; P= 0.6). However, they had a significantly prolonged duration of treatment (610 vs 63 median days; P = 0.013) corresponding to the significantly more dilatation sessions required (Table 4).

Table 4: Median number of days till initiation of dilatation, duration of dilatation treatments, and the symptom-free period from last dilatation

Type C	All children with strictures	All children with anastomotic leaks	Children with no anastomotic leaks	Children with Early repair	Children with Delayed repair
Days from surgery to first dilatation Median (range)	122 (28 – 1038)	62.5 (44 – 449)	179 (28 – 1038)	229 (28 – 1038)	59 (44 – 63)
Days from first to last dilatation. Median (range)	121 (0 - 2434)	580 (0 – 2232)	76 (0 – 2434)	63 (0 – 2008)	610 (551 - 2434)
The symptom-free period from last dilatation till the end of the study in months. Median (range)	33 (0 - 124)	37 (0 – 67)	33 (0 – 124)	38 (0 - 122)	22 (19 - 124)

Furthermore, there was no correlation between the GA and time to onset of dilatations (P=0.50), duration of dilatations (P=0.05), and symptom-free period (P=0.10). However, there was a significant negative correlation between the GA and the number of dilatation sessions required (P=0.03). Similarly, there was no correlation between the BW and time to onset of dilatations (P=0.30), duration of dilatations (P=0.06), and symptom-free period (P=0.74). The BW also showed a statistically significant negative correlation with the number of dilatation sessions required (P=0.02). As expected, the GA and BW had a positive correlation (P = 0.003).

The linear regression model revealed that delayed repair increased the number of dilatations by an average of 7 sessions compared to primary repair. For every 1 week increase in GA, the number of dilatations reduced by 0.4 sessions. Finally, for every 333 days from primary surgery to first dilatation, the number of dilatation sessions reduced by 1. The delayed repair was the most important factor related to the number of dilatation sessions required (p <0.001); this was followed by lower GA or BW (p = 0.0265) and early onset of dilatations (p=0.0471).s

DISCUSSION

After a successful OA repair, understanding the factors that predispose to recurrent and refractory strictures facilitates counselling information provided to families and helps anticipate this complication to prevent ongoing morbidity from aspiration, feeding difficulties, failure to thrive, dysphagia, and food bolus obstruction. Several reports have described factors that predispose to the development of strictures and leaks after OA repair.[3-7,10-12] Few reports have correlated these factors with the onset or intensity of dilatations required to manage strictures.[3,9] Vergouwe et al [9] looked at factors that predisposed to refractory strictures and defined these as an anastomotic stricture requiring ≥5 dilatations at a maximum of 4-week intervals; strictures occurring after 4-week intervals were considered recurrent. The authors included Gross Type C and A variants, end-to-end, oesophagojejunal, and oesophagogastric anastomosis and concluded that isolated OA, anastomotic leak, and the need for oesophageal dilatation ≤28 days after anastomosis were risk factors for refractory strictures.

In this report, we focused on Type C variant with end-to-end anastomosis only and found that children that underwent a delayed repair were more likely to develop recurrent or refractory strictures based on their need for significantly more dilatation sessions over a longer period. Delayed repair in our cohort represents those whose gaps were too long to be closed at the primary operation, and so initially underwent fistula ligation only. Their oesophageal anastomoses were deferred and reattempted after gap studies showed improved gap length (no oesophageal elongation techniques used). It has been reported that if tension exists between the oesophageal ends leaks and strictures are more likely.[6,11] However, Thakkar et al [12] showed that as long as the primary repair is possible, measured gap length at the time of surgery was not a risk factor for anastomotic leak or stricture. We theorize that the scarring of the distal oesophagus that occurs after the fistula has been previously ligated and the subsequent mobilisation required results in compromised tissues that are not ideal for suturing.[3] These technical difficulties faced at delayed repair, rather than the actual gap length, maybe the more significant cause for difficult to manage strictures.[13] Furthermore, children who had delayed repair developed significantly more anastomotic leaks. Although anastomotic leaks alone were not associated with difficult strictures, when coupled with a long gap and a delayed repair, it may

have resulted in more aggressive scarring that was difficult to dilate. Children with long gap atresia and anastomotic leaks have been reported to suffer more severe strictures.[3,5,6]

Premature children also required more dilatation sessions. These smaller children with a smaller calibre oesophagus may have been more technically challenging and more prone to symptomatic luminal narrowing. The initial dilatation sessions may also have been milder and thus requiring more sessions over time.

Interestingly, like another report, leaks alone were not predictive of difficult strictures for this cohort.[5] This differed from the finding by Vergouwe et al., although they included jejunal and gastric anastomosis in their cohort.[9]

The development of symptomatic strictures early was also indicative for difficult strictures that required more dilatation sessions. This suggests that early dilatation had a negative impact on the anastomosis or that these strictures had a more aggressive aetiology; this finding was also noted in the report by Vergouwe et al. and Chittmittrapap et al.[9,14] In the latter study they observed that children who developed strictures within 6 months of surgery required five or more dilatations or surgical intervention. This was an independent finding because children who had a delayed repair or developed leaks or were premature respectively were not at more risk for early strictures.

The findings of this report are limited by our inability to adjust for the impact of GOR [3,5] anti-reflux medications [6,10,11] and anti-reflux surgery [11,12] as well as jejunal feeding. Other studies have highlighted the difficulties analysing the GOR variable.[9] Furthermore, several surgeons performed these operations with variable techniques and suture preference.[4] Several different dilatation devices [6,11] were used with some sessions complicated by perforation, while a few subsequent dilatation sessions were scheduled routinely as part of a stricture management regimen.[11]

CONCLUSION

The development of strictures after OA repair is multifactorial. When strictures occur in the early postoperative period, in premature babies, or after a delayed repair for long gap atresia, recurrent/refractory strictures that require several more dilatation sessions should be anticipated. Where possible, every reasonable attempt at a primary repair should be made and a more frequent clinical review of these subsets of children is recommended, so prompt diagnosis can be made to prevent ongoing morbidity from strictures. The occurrence of an anastomotic leak does not predict a difficult to manage stricture.

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REFERENCES

1. Engum SA, Grosfeld JL, West KW, Rescorla FJ, Scherer LRT. Analysis of morbidity and mortality in 227 cases of esophageal atresia and/or tracheoesophageal fistula over two decades. Arch Surg. 1995; 130:502-8.
2. Fusco JC, Calisto JL, Gaines BA, Malek MM. A large single-institution review of tracheoesophageal fistulae with evaluation of the use of transanastomotic feeding tubes. J Pediatr Surg. 2018; 53:118-20.
3. Tambucci R, Angelino G, De Angelis P, Torroni F, Caldaro T, Balassone V, et al. Anastomotic strictures after esophageal atresia repair: Incidence, investigations, and management, including treatment of refractory and recurrent strictures. Front Pediatr. 2017; 5:120.
4. Catalano P, Di Pace MR, Caruso AM, Salerno S, Cimador M, De Grazia E. A simple technique of oblique anastomosis can prevent stricture formation in primary repair of esophageal atresia. J Pediatr Surg. 2012; 47:1767-71.
5. Zhao R, Li K, Shen C, Zheng S. The outcome of conservative treatment for anastomotic leakage after surgical repair of esophageal atresia. J Pediatr Surg. 2011; 46:2274-8.
6. Serhal L, Gottrand F, Sfeir R, Guimber D, Devos P, Bonnevalle M, et al. Anastomotic stricture after surgical repair of esophageal atresia : frequency, risk factors, and efficacy of esophageal bougie dilatations. J Pediatr Surg. 2010; 45:1459-62.
7. Chittmittrapap S, Spitz L, Kiely EM, Brereton RJ. Anastomotic leakage following surgery for esophageal atresia. J Pediatr Surg. 1992; 27:29-32.
8. Thyoka M, Timmis A, Mhango T, Roebuck DJ. Balloon dilatation of anastomotic strictures secondary to surgical repair of oesophageal atresia: a systematic review. Pediatr Radiol. 2013; 43:898-901.
9. Vergouwe FW, Vlot J, IJsselstijn H, Spaander MC, van Rosmalen J, Oomen MW, et al. Risk factors for refractory anastomotic strictures after oesophageal atresia repair: A multicentre study. Arch Dis Child. 2019; 104:152-7.
10. Murase N, Uchida H, Kaneko K, Ono Y, Makita S, Yokota K. Prophylactic effect of H2 blocker for anastomotic stricture after esophageal atresia repair. Pediatr Int. 2015; 57:461-4.

11. Baird R, Laberge JM, Lévesque D. Anastomotic stricture after esophageal atresia repair: A critical review of recent literature. Eur J Pediatr Surg. 2013; 23:204-13.
12. Thakkar HS, Cooney J, Kumar N, Kiely E. Measured gap length and outcomes in oesophageal atresia. J Pediatr Surg. 2014; 49:1343-6.
13. Conforti A, Morini F, Bagolan P. Difficult esophageal atresia: Trick and treat. Semin Pediatr Surg. 2014; 23:261-9.
14. Chittmittrapap S, Spitz L, Kiely EM, Brereton RJ. Anastomotic stricture following repair of esophageal atresia. J Pediatr Surg. 1990; 25:508-11.