Measuring esophageal anastomotic stricture index as a predictor of dilatation following esophageal atresia surgical repair

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ABSTRACT

Introduction. Anastomotic stricture is the most common complication following esophageal atresia (EA) surgical repair. The objective of this study was to evaluate Anastomotic Stricture Index (ASI: relationship between pouch and stricture diameters in the postoperative esophagram) as a predictor of the need for esophageal dilatation.

Methods. A retrospective review of all patients undergoing EA repair in our healthcare facility from 2009 to 2017 was designed. Proximal pouch ASI (proximal ASI) and distal pouch ASI (distal ASI) in the first and second postoperative esophagram were calculated, and correlation with the number of esophageal dilatations required was studied. For statistical analysis purposes, Spearman's correlation test and ROC curves were used.

Results. Of the 31 patients included, 21 (67.7%) required esophageal dilatation, and 11 (35.5%) required 3 or more dilatations. The relationship between ASIs in the first esophagram and the need for esophageal dilatation was not statistically significant (p >0.05). The relationship between proximal ASI (RHO = 0.84, p <0.05) and the number of dilatations in the second esophagram was statistically significant. None of the patients with <0.55 proximal ASI required dilatation; patients with 0.55-0.79 proximal ASI required less than 3 dilatations; and patients with >0.79 proximal ASI had a high risk of requiring 3 or more dilatations.

Conclusion. According to our study, measuring ASI in the second esophagram proves useful in predicting EA patients' postoperative management, especially when it comes to identifying patients with lower risk of undergoing multiple dilatations.

KEY WORDS: Esophageal atresia; Anastomotic stricture; Esophageal dilatation; Stricture index; Esophagram.

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MEDICIÓN DEL ÍNDICE DE ESTENOSIS DE LA ANASTOMOSIS ESOFÁGICA COMO PREDICTOR DE DILATACIÓN TRAS LA CORRECCIÓN QUIRÚRGICA DE LA ATRESIA ESOFÁGICA

RESUMEN

Introducción. La estenosis esofágica es la complicación más frecuente tras la corrección de la atresia esofágica (AE). El objetivo de este estudio es el análisis de los Índices de estenosis de la anastomosis (IEA: relación entre los diámetros de los bolsones y de la estenosis en el esofagograma postoperatorio) como predictores de la necesidad de dilatación esofágica.

Métodos. Se diseña un estudio retrospectivo incluyendo los pacientes con AE y anastomosis esofágica en nuestro centro entre 2009-2017, calculando los IEA del bolsón proximal (IEA-proximal) y distal (IEA-distal) en el primer y segundo esofagograma postoperatorio, analizando su correlación con el número de dilataciones esofágicas que necesitaron. Para el análisis estadístico, se ha empleado el test de correlación de Spearman y las curvas ROC.

Resultados. Se incluyeron 31 pacientes: 21 precisaron dilatación esofágica (67%), y 11 de ellos (35%) 3 o más dilataciones. No se demostró relación estadísticamente significativa entre los IEA del primer esofagograma con la necesidad de dilatación esofágica (p >0,05). Se observó una relación entre el IEA-proximal (rho = 0,84, p <0,05) y el número de dilataciones en el segundo esofagograma. Ningún paciente con ASI-proximal <0,55 necesitó dilatación; los pacientes con ASI-proximal entre 0,55-0,79 precisaron menos de 3 dilataciones y los pacientes con ASI-proximal >0,79 presentaron alto riesgo de necesitar 3 o más dilataciones.

Conclusión. Según los resultados de nuestro estudio, la medición de IEA en el segundo esofagograma constituye una herramienta útil para predecir el manejo postoperatorio en pacientes con AE, especialmente en la identificación de aquellos con menor riesgo de someterse a múltiples dilataciones.

PALABRAS CLAVE: Atresia esófago; Estenosis; Dilatación esofágica; Índice estenosis; Esofagograma.

INTRODUCTION

Esophageal atresia (EA) with or without tracheoesophageal fistula (TEF) is a congenital malformation occurring in 1.25-4.55 out of 10,000 live newborns[1,2]. Overall sur-

vival rate has increased up to 90% in specialist healthcare facilities[3], and up to nearly 100% in the absence of associated abnormalities or low weight at birth[1]. Despite perioperative patient care improvements, postoperative complications remain a source of morbidity impacting both short-term evolution and long-term quality of life.

The most frequent postoperative complication is anastomotic stricture (AS). According to the current literature, it has a frequency of 32-80%[4,5], with esophageal dilatations being required for treatment[6]. Various factors associated with AS occurrence have been described[7,8], but there is no objective tool allowing us to predict which patients will develop AS. Recent studies suggest measuring anastomotic stricture index[9,10] (ASI) as predictor of AS. ASI measures the relationship between various esophageal diameters (stricture diameter and pre-stenotic pouch diameter) in different postoperative images (esophagram, endoscopy) in order to predict the need for postoperative esophageal dilatation.

The objective of this study was to develop and analyze an index based on postoperative esophagram measurements which may help establish the risk of developing AS.

METHODS

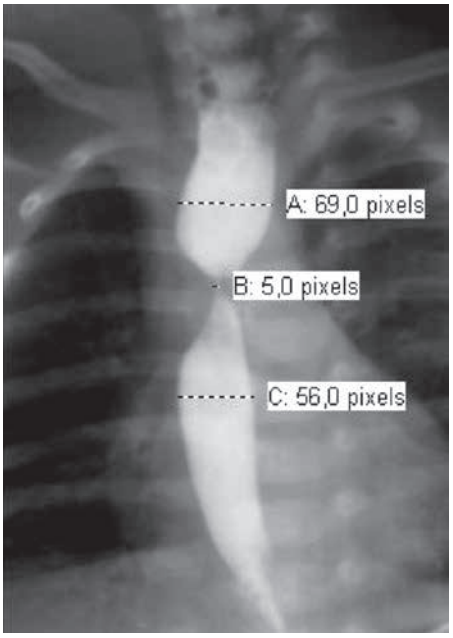
A retrospective study of all EA patients undergoing esophageal anastomosis in a tertiary healthcare facility from March 2009 to September 2017 was carried out. Exclusion criteria were absence of digitized esophagram images, early death, <12-month follow-up period, complications requiring re-intervention, and presence of H-type fistula. The following data were collected: sex, gestational age and weight at birth, type of esophageal atresia according to Gross' classification, associated abnormalities, age (days) at surgery, control esophagrams, postoperative complications, AS, number of dilatations, survival, and follow-up period.

A thoracotomy was carried out. The TEF (if present) and the esophageal anastomosis were located and ligated using interrupted stitches. A transanastomotic tube (TAT) was left in place in all cases. All patients received gastroesophageal reflux medication postoperatively (proton pump inhibitors (PPI) or H2 antagonists).

Postoperative esophagrams were the main tool used in this study. The "first esophagram" was carried out on the first postoperative days to rule out anastomotic dehiscence and initiate enteral feeding (once the patient had been extubated and the move was safe). The next esophagrams were performed during follow-up for complication control purposes, especially AS complications. At mid- and long-term controls, esophagram indication was established according to the patient's clinical situation (feeding difficulty, regurgitation, vomit, insufficient weight gain, etc.). In this study, the "second esophagram" was the first conducted following TAT removal, at least 7 days after full enteral feeding initiation.

AS was treated using high-pressure balloon dilatation under fluoroscopic or endoscopic control.

$$\text{Proximal ASI} = \frac{\text{proximal pouch diameter (A)} - \text{stricture diameter (B)}}{\text{proximal pouch diameter (A)}}$$



$$\text{Distal ASI} = \frac{\text{distal pouch diameter (C)} - \text{stricture diameter (B)}}{\text{distal pouch diameter (C)}}$$

Figure 1. Stricture indexes. ASI: A: superior pouch diameter, B: stricture diameter, C: inferior pouch diameter. In this case, proximal ASI = 0.93 and inferior ASI = 0.91, which reflects a great stricture.

ANASTOMOTIC STRICTURE INDEXES (ASIS)

Postoperative esophagrams were studied to calculate ASIs. Two indexes were analyzed: relationship between proximal pouch and stricture diameters in an anteroposterior projection (proximal ASI), and relationship between distal pouch and stricture diameters in an anteroposterior projection (distal ASI) (Fig. 1). Values ranged from 0 to 1, with lower values being closer to normal esophagus and higher values indicating greater stricture severity (Fig. 1).

ASIs were calculated in the "first esophagram" and the "second esophagram" by the same surgeon, looking for the maximum proximal and distal pouch diameters and the minimum stricture diameter in the anteroposterior projection.

ASIs were associated with the number of dilatations. Risk groups were created according to the need for dilata-

Table 1. Patient demographic characteristics.

Sex (male)	51.6%
Gestational age (median, range)	38 weeks (29-40)
Weight at birth (mean ± SD)	2.51 kg ± 0.77
Diagnosis: • Type III EA • Type I EA	 n = 27 (87.1%) n = 4 (12.9%)
Age at surgery (median, range)	1 day (0-103 days)
Long gap (≥3 vertebral bodies)	n = 2
Associated malformations • None • Down's syndrome • VACTERL • Cardiac malformations	 n = 23 n = 1 n = 2 n = 5

Table 2.

	No need for dilatation (mean ± SD)	*1-2 dilatations required (mean ± SD)*	*Recurrent AS (>3 dilatations) (mean ± SD)*
Distal ASI 1	0.50 (±0.25)	0.46 (±0.12)	0.51 (±0.17)
Proximal ASI 1	0.63 (±0.14)	0.67 (±0.09)	0.70 (±0.16)
Distal ASI 2	0.0 (±0.20)	0.61 (±0.13)	0.77 (±0.10)
Proximal ASI 2	0.51 (±0.20)	0.76 (±0.10)	0.88 (±0.05)

IEA proximal y distal en el "primer esofagograma" (IEA-distal 1 y IEA-proximal 1) e IE proximal y distal en el "segundo esofagograma" (IEA-distal 2 y IEA-proximal 2).

Table 3.

	Need for dilatation	*Number of dilatations required*
Distal ASI 1	RHO = -0.07, p = 0.71	RHO = -0.06, p = 0.77
Proximal ASI 1	RHO = 0.16, p = 0.39	RHO = 0.21, p = 0.27

Correlation between ASI and the need for dilatation and number of dilatations (Spearman's RHO) in the ''first esophagram". >0.7 RHO is considered as a high correlation.

tion (following ESPGHAN/NASPGHAN's clinical guides definition [11]): no dilatation, low AS recurrence risk (1 or 2 dilatations), and recurrent AS (3 or more dilatations).

Statistical analysis was carried out using the IBM SPSS Statistics Version 21 (IBM Corporation©) software. To study the relationship between ASIs and need for dilatation or number of dilatations, Spearman's correlation coefficient was used. Comparisons were carried out using Student's T-test. Cutoff values for each risk group were calculated using ROC (Receiver Operating Characteristic) curves. Statistical significance was established at $p < 0.05$.

RESULTS

From March 2009 to September 2017, 43 patients were diagnosed with esophageal atresia, 31 of whom met the inclusion criteria. The most frequent cause of exclusion was early death (n = 6), followed by absence of digitized images (n = 5) and complications requiring re-intervention (n = 1). Patient demographic characteristics are featured in table 1. Median follow-up was 4.1 years (1-8.6 years). Regarding postoperative complications, 7 patients (22.6%) had conservatively treated anastomotic leak, and none of the patients had recurrent TEF. All patients were discharged with anti-reflux treatment (H2 antagonists or proton pump inhibitors), and 6 patients with medical treatment failure required anti-reflux surgery (Nissen fundoplication).

The "first esophagram" was carried out within the first 10 days post-surgery in 78.6% of patients, with a median of 8 days. The "second esophagram" was performed within the first 60 days post-surgery in 77.4% of patients, with a median of 35 days.

21 patients (67.7%) were diagnosed with AS requiring one esophageal dilatation at least. 11 of them (35.5%) had recurrent AS requiring a median of 6 esophageal dilatations (3-22 dilatations). In total, 100 dilatations were performed in these patients, with no intra-operative complications. Median time to the first dilatation was 40 days (21-750 days).

ASIs were calculated in the "first esophagram" and in the "second esophagram". Mean and standard deviation were calculated for each esophageal dilatation risk group, as demonstrated in table 2.

ASIs in the "first esophagram" were analyzed, comparing ASI results in the group of patients not requiring dilatation with ASI results in the group of patients requiring 1-2 dilatations, without statistically significant differences ($p = 0.78$). This was also the case when comparing the first group with the AS group ($p = 0.33$). No correlation was found between ASIs and the need for dilatation or the number of dilatations (Table 3).

ASIs in the "second esophagram" were compared. Statistically significant differences ($p < 0.001$) were found between ASIs and the need or no need for dilatation. A positive correlation was also found between distal ASI and number of dilatations, and between proximal ASI, need for dilatations, and number of dilatations required (Table 4).

Proximal ASI in the "second esophagram" was used to predict the need for esophageal dilatation and the number of dilatations using ROC curves. Regarding the need for esophageal dilatation, patients with <0.55 proximal ASI (sensitivity = 100%, specificity = 60%) did not require dilatation, whereas all patients with >0.79 proximal ASI (sensitivity = 66.7%, specificity = 100%) required one dil-

Table 4.

	Need for dilatation	*Number of dilatations required*
Distal ASI 2	RHO = 0.64, p = 0.00	RHO = 0.74, p = 0.00
Proximal ASI 2	RHO = 0.72, p = 0.00	RHO = 0.84, p = 0.00

Correlation between ASI and the need for dilatation and number of dilatations (Spearman's RHO) in the "second esophagram". >0.7 RHO is considered as a high correlation.

atation at least and had a high risk of developing recurrent AS (sensitivity = 100%, specificity = 85%) (Fig. 2).

The same statistical analysis was carried out for distal ASI. None of the patients with >0.39 distal ASI required dilatation (sensitivity = 100%, specificity = 60%), and all patients with >0.72 distal ASI required one dilatation at least (sensitivity = 52%, specificity = 100%). The same >0.72 distal ASI cutoff value (sensitivity = 82%, specificity = 90%) was achieved as a risk marker of developing recurrent AS.

DISCUSSION

Even though EA mortality has significantly decreased in the last years, more than half of the patients have postoperative complications, with AS being the most frequent one. In our series, 67.7% of patients required one esophageal dilatation at least, consistent with the 32-80% frequency ranges currently described in the literature[4-6]. Various risk factors of developing AS have been described, such as anastomotic tension, gastroesophageal reflux, a long distance between ends, and anastomotic dehiscence[7,8]. In addition, recent publications consider the use of transanastomotic tube as a new risk factor[13]. The latest version of the ESPGHAN/NASPGHAN's EA guidelines includes recommendations such as proton pump inhibitor (PPI) treatment and AS management[11].

Identifying patients potentially developing AS is one of the great challenges in the mid- and long-term follow-up. Landish et al.[9] suggest that proximal pouch dilatation is the most important mechanism in symptom occurrence – food might get stuck at the AS of the dilated pouch, progressively causing feeding difficulty, regurgitation, aspiration, coughing, food impaction, etc. However, those symptoms are not specific and are similar to those caused by other disorders also frequent in EA patients, such as gastroesophageal reflux, suction-swallowing incoordination, or tracheomalacia. The most accepted management of suspected AS is to conduct a diagnostic test (esophagram or endoscopy) when the patient has symptoms, but not routinely, so as to avoid an excess of radiation[14]. In our study, no AS was demonstrated and therefore no esophageal dilatation was required in 32% of patients with any of these unspecific symptoms where esophagram was indicated.

Currently, there is no objective tool allowing patients with higher risk of developing AS or recurrent AS to be identified[11]. This is why measuring ASIs has been proposed in various publications. Said et al.[15] proposed an index based on the distal pouch, but index validation was not the main objective of the study. Parolini et al.[16] proposed an index based on endoscopic measurements (a routine endoscopy was performed in the first month post-surgery) and classified patients according to the risk of developing AS. In this study, the authors found that the first esophagram was not associated with the need for posterior dilatation. They also suggested that the presence of mild or moderate AS in the esophagram in the first week post-surgery could be a normal finding as a result of the edema occurring secondary to healing, and not a complication as such. These findings are consistent with

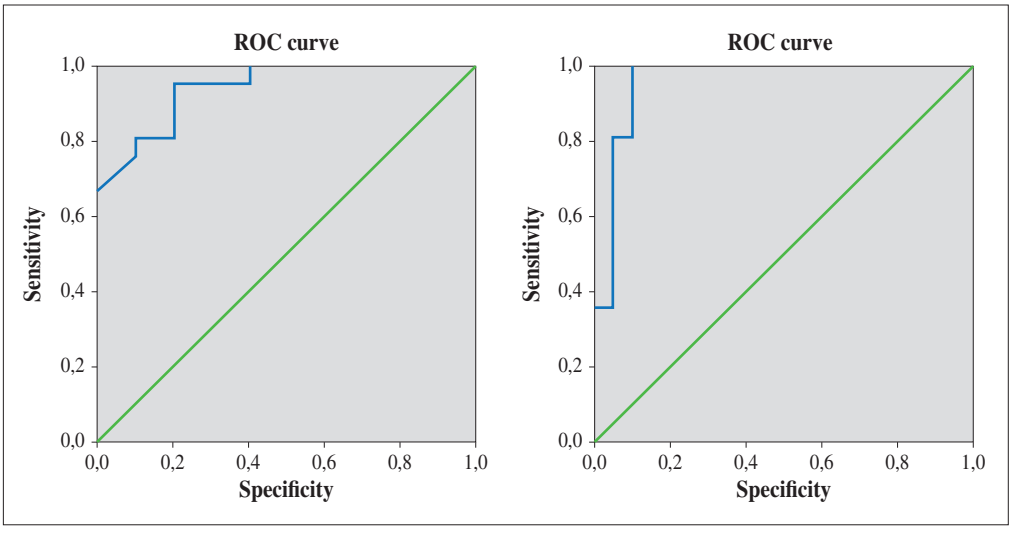


Figure 2. ROC curve for proximal ASI and need for dilatation (right: AUC = 0.943, 95% CI: 0.87-1.00) and need for ≥3 dilatations (left: AUC = 0.959, 95% CI: 0.891-1.00).

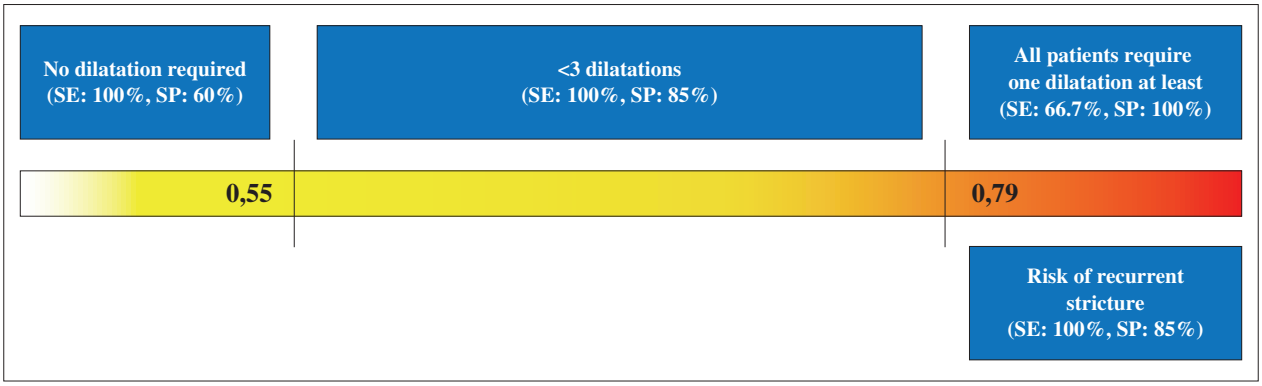


Figure 3. Association of proximal ASI in the "second esophagram" with the need for esophageal dilatation and the number of dilatations.

our results, where ASIs in the first esophagram were not associated with subsequent evolution. However, Sun et al.[10] measured ASIs in the proximal and distal pouch in the first esophagram using anteroposterior and lateral projection, and they concluded that the inferior pouch index was a good predictor of AS and recurrent AS. Landisch et al.[9] compared similar indexes and found that the best predictor was proximal pouch ASI in the late esophagram, which is similar to what we found in our study.

Consistent with other studies[9], our results demonstrate that proximal ASI has a higher correlation with the risk of developing AS or recurrent AS (AUC = 0.94 and 0.96, respectively) than distal ASI (AUC = 0.89 for AS, and AUC = 0.90 for recurrent AS). In the "second esophagram", none of the patients with a <0.55 proximal ASI required esophageal dilatation. This cutoff value has a high sensitivity (SE: 100%) to identify patients with a good prognosis. On the other hand, we found that all patients with a >0.79 proximal ASI (SP: 100%) required one esophageal dilatation at least. This cutoff value allows the presence of recurrent AS to be predicted with high sensitivity (SE: 100%, SP: 85%). Last, patients with a 0.55-0.79 proximal ASI had an intermediate risk of developing AS: 66% (8 out of 12) of these patients required one or two dilatations, but none of them developed recurrent AS (Fig. 3). Therefore, proximal ASI in the control esophagram can help identify patients with a high risk of developing recurrent AS, who will require a closer control.

Based on these results, we believe this tool can prove useful in EA patient follow-up, not so much in order to establish an indication for esophageal dilatation, but to determine the type of follow-up and inform parents of patient prognosis regarding AS. This would allow asymptomatic patients with a low proximal ASI to benefit from a more sparse follow-up. In patients with symptoms similar to AS, other causes should be ruled out as a first option. Parents of patients with intermediate risk proximal ASI should be trained in the early detection of these symptoms so that their children can be treated as soon as possible. Last, patients with a proximal ASI demonstrating a high risk of developing recurrent AS should have a closer follow-up, with higher vigilance and gastroesophageal reflux treatment. In the future, proximal ASI can be considered as an objective tool to compare and validate various therapeutic options in these patients (use of corticoids and mitomycin C, early dilatation, etc.).

This study has one limitation – it is a retrospective study including patients from one healthcare facility only. Multicenter and prospective studies are required to confirm these results.

CONCLUSIONS

According to our study results, there is a correlation between proximal ASI in the "second esophagram" and the presence of AS. Therefore, proximal ASI stands as a useful and reproducible tool to identify patients with risk of requiring esophageal dilatation. In addition, no correlation was found between ASIs in the "first esophagram" and development of AS.

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