Impact of digestive-surgical cross-disciplinary management in patients with esophageal atresia

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ABSTRACT

Objective. The objective of this study was to analyze whether patients undergoing esophageal atresia (EA) surgery benefit from a cross-disciplinary follow-up program, based on current clinical guidelines, implemented in our institution.

Materials and methods. An observational, analytical, retrospective study of patients undergoing EA surgery from 2012 to 2022 was carried out. The results of a joint pediatric surgery and gastroenterology consultation program –which was implemented in 2018 and applies a protocol based on the new ESPGHAN-NASPGHAN guidelines– were analyzed. Patients were divided according to whether they had been treated before or after 2018. Quantitative variables –follow-up losses, anti-reflux treatment initiation and duration, and enteral nutrition initiation– and qualitative variables –prevalence of gastroesophageal reflux, anti-reflux surgery, respiratory infections, anastomotic stenosis, re-fistulizations, dysphagia, impaction episodes, need for gastrostomy, and endoscopic results– were compared.

Results. 38 patients were included. 63.2% had gastroesophageal reflux. 97.4% received anti-reflux treatment in the first year of life, with treatment being subsequently discontinued in 47.4%. Discontinuation time decreased by a mean of 24 months following program implementation ($p<0.05$). A 4.6-fold increase in the frequency of pH-metries was noted following program implementation. The protocol standardized endoscopies in asymptomatic patients when they turn 5 and 10 years old. 25 endoscopies with biopsy were carried out after 2018, with histological disorders being detected in 28% of them. The number of follow-up losses significantly decreased following protocol implementation ($p<0.05$).

Conclusions. Digestive-surgical cross-disciplinary follow-up of EA patients has a positive impact on patient progression. Applying the guidelines helps optimize treatment and early diagnosis of complications.

KEY WORDS: Esophageal atresia; Cross-disciplinary patient care team; Advance care planning.

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IMPACTO DEL MANEJO MULTIDISCIPLINAR DIGESTIVO-QUIRÚRGICO EN LOS PACIENTES CON ATRESIA DE ESÓFAGO

RESUMEN

Objetivos. El objetivo de este estudio es analizar si los pacientes intervenidos de atresia de esófago (AE) se benefician de un programa de seguimiento multidisciplinar, basado en las guías clínicas actuales, implantado en nuestro centro.

Material y métodos. Estudio retrospectivo, observacional y analítico incluyendo los pacientes intervenidos de AE entre 2012 y 2022. Se analizaron los resultados de la implantación en 2018 de un programa de consultas conjuntas de gastroenterología y cirugía pediátrica aplicando un protocolo basado en las nuevas guías ESPGHAN-NASPGHAN. Se dividieron a los pacientes tratados antes y después de 2018 y se compararon las variables cuantitativas: pérdidas de seguimiento, inicio y duración del tratamiento antirreflujo e inicio de nutrición enteral, y cualitativas: prevalencia de reflujo gastroesfoágico, realización de cirugía antirreflujo, infecciones respiratorias, estenosis de la anastomosis, refistulizaciones, disfagia, episodios de impactación, necesidad de gastrostomía y resultados de las endoscopias.

Resultados. Se incluyeron 38 pacientes. Un 63,2% presentaron reflujo gastroesofágico. El 97,4% tomaron tratamiento antirreflujo el primer año de vida que posteriormente se retiró en el 47,4%. El tiempo de retirada se redujo una media de 24 meses tras la aplicación del programa ($p<0,05$). Se realizaron 4,6 veces más pHmetrías tras la implantación del programa. El protocolo estandarizó la realización de endoscopias en pacientes asintomáticos al cumplir 5 y 10 años. Se realizaron 25 endoscopias con tomas de biopsia después de 2018, detectando alteraciones histológicas en un 28%. El número de pérdidas de seguimiento se redujo de forma significativa tras la implantación del protocolo ($p<0,05$).

Conclusiones. El seguimiento multidisciplinar digestivo-quirúrgico de los pacientes con AE genera un impacto positivo en su evolución. La aplicación de las guías facilita la optimización del tratamiento y el diagnóstico precoz de las complicaciones.

PALABRAS CLAVE: Atresia de esófago; Equipo multidisciplinar; Previsión de cuidados.

INTRODUCTION

Esophageal atresia (EA) is a congenital malformation that occurs in 1 out of 2,500-4,500 live newborns[1-4].

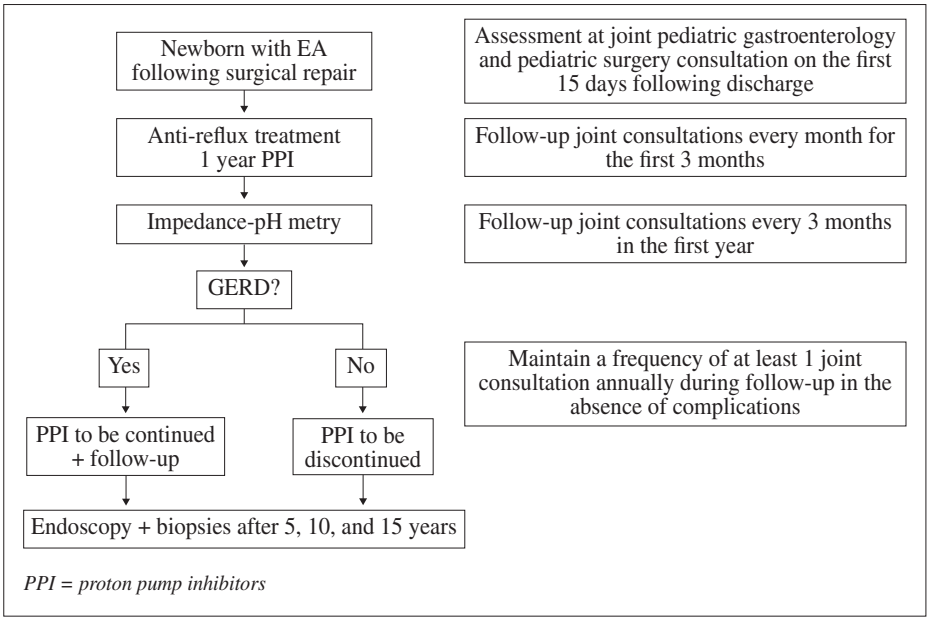

Figure 1. Follow-up protocol of esophageal atresia patients used in our institution after 2018, adapted from the 2016 ESPGHAN-NASPGHAN guidelines[1].

Postnatal survival rate has increased up to over 90% in specialist centers[5,6]. However, the morbidity associated with the anatomical alteration of the esophagus, airway involvement, and postoperative complications are present in the long-term follow-up of these patients, with a strong impact on quality of life.

The presence of long-term gastrointestinal and respiratory symptoms is highly frequent (22-45% have gastroesophageal reflux and 21-84% dysphagia, 8.7% have persistent cough, and 4.3% have recurrent respiratory infections)[1,6], with these patients having a worse perceived quality of life[5-9].

The lack of systematization regarding postoperative treatment and follow-up in the growth period, as well as the absence of transition programs for adults[1,5,6], remain an issue. In response to this need, the ESPGHAN-NASPGHAN guidelines were published in November 2016 in an attempt to standardize the long-term treatment and follow-up of EA patients from a cross-disciplinary standpoint in a consensual manner[1,4].

The objective of this work was to analyze the results of the application of a standardized cross-disciplinary follow-up program based on the ESPGHAN-NASPGHAN guidelines in a third-level pediatric institution, as well as to assess its long-term impact on EA patients.

MATERIALS AND METHODS

An analytical, observational, retrospective study of all patients undergoing EA surgery in a third-level institution from January 2012 to January 2022 was carried out. Exclusion criteria were early death, follow-up period < 6 months, and lack of follow-up data.

The variables analyzed included sex, date of birth, type of esophageal atresia according to Gross classification, associated abnormalities, age at surgery, surgical technique, follow-up time, follow-up losses, survival, prevalence of gastroesophageal reflux (GERD), anti-reflux treatment initiation and duration, impedance-pH metries, anti-reflux surgery, prevalence of respiratory infections requiring hospital stay, anastomotic stenosis, re-fistulizations, dysphagia, impaction episodes, nasogastric probe (NGP) enteral nutrition initiation, liquid and solid tolerance initiation, need for gastrostomy, endoscopies, biopsies, and disorders noted at pathological examination.

Since January 2018, patient follow-up and treatment were carried out according to the ESPGHAN-NASPGHAN guidelines published in 2016. With this goal in mind, a new program was created in our institution to guide the joint management and treatment of patients undergoing EA surgery by the Pediatric Gastroenterology Unit and the Pediatric Surgery Department. To receive cross-disciplinary treatment, patients attended a joint consultation program with specialists from both areas simultaneously, thus reducing the number of annual consultations required during follow-up. The program is detailed in figure 1.

Clinical progression, treatment, and follow-up data before and after program implementation in 2018 was compared. Data was collected in tables, and the IBM SPSS Statistics software, version 26 (IBM Corporation©), was used for statistical purposes. Descriptive data was expressed as frequencies and means. The analysis of quantitative variables was carried out using Student's t-test, while calculating the standard error of the mean (SE) and confidence interval (CI) of the difference. The analysis of qualitative variables was conducted by means of the Chi-squared test, with results being expressed in numbers. Statistical significance was established at $p < 0.05$.

Table 1. Epidemiologic data and distribution by study groups.

	Before 2018	*After 2018*
Sex	10 (45.5%) male 11 (54.5%) female	11 (68.8%) male 5 (31.2%) female
Surgical technique: – Thoracotomy – Thoracoscopy	 21 (95.5%) 1 (4.5%)	 0 16 (100%)
Diagnosis: – Type A – Type C	 3 (13.6%) 19 (86.4%)	 3 (18.8%) 13 (81.3%)
Long gap (≥3 vertebral bodies)	5 (22.7%)	6 (37.5%)
Associated malformations: – None – Cardiac – Other	 11 (50%) 6 (27.3%) 5 (22.3%)	 9 (56.3%) 3 (18.8%) 4 (25%)

RESULTS

From January 2012 to October 2022, 46 patients were diagnosed with EA. 38 of them were included, whereas early deaths due to polymalformative syndromes (n=5) and patients with a <6-month follow-up (n=3) were excluded. Demographic characteristics are featured in table 1.

Of the 38 patients, 16 received standardized management and follow-up based on the ESPGHAN-NASPGHAN protocol –patients born after January 2018–, and 22 underwent non-standardized management and follow-up at the surgeon's discretion –patients born before January 2018.

Median follow-up was 57-5 months (range: 15-131 months). 5 follow-up losses occurred in the pre-program implementation group –three of them before 1 year of life– and 0 occurred in the post-program implementation group. The reduction in the number of follow-up losses was statistically significant (p=0.03).

97.4% of the patients received anti-reflux treatment – H2 antagonists or proton pump inhibitors– in the first year of life. Treatment was initiated before leaving the Neonatal Care Unit. Following program implementation, mean days to treatment initiation decreased from 16.8 (SE=3.34) to 8 (SE=1.89), with a difference of 8.8 days (CI) (0.93-16.66); (p=0.03).

Before 2014, gastroesophageal reflux (GERD) was diagnosed based on symptoms and using a gastroesophageal transit test as a complementary means. After 2014, GERD was diagnosed through impedance-pH metry, with timing not being standardized until the program was implemented in 2018, after which it was routinely performed at 1 year of life.

A 4.6-fold increase in the number of impedance-pH metries was noted following program implementation. 63.2% of the patients had GERD –68.2% in the pre-program implementation group and 56.3% in the in the post-program implementation group–, without significant differences between groups in spite of using different diagnostic strategies.

Of the GERD patients, 25% had no symptoms, 45.8% had digestive symptoms, and 29.2% had extra-digestive symptoms. 50% of the patients diagnosed with GERD had anastomotic stenosis (AS). The association was statistically significant (p=0.02).

The anti-reflux treatment was discontinued during follow-up in 47.4% of the patients. Mean discontinuation time decreased by 24 months following program implementation (CI) (6.75-42.54), from 42.2 months (SE=7.16) to 17.75 months (SE=2.85); (p=0.01).

Nissen anti-reflux surgery was conducted in 21.05% of the patients, without statistically significant differences between groups.

No differences were found in terms of patients with respiratory infections requiring hospital stay (47.4%), percentage of AS (68.4%), or re-fistulization rate (8.8%).

50% of the patients had dysphagia, which was more frequent in the post-program implementation group (17/22 vs. 12/16) (p=0.009). However, no differences in terms of impaction episodes were noted between groups (27.8%).

The frequencies of the main complications calculated by groups are featured in table 2.

Mean NGP enteral nutrition initiation time was 14 days in both groups (SE=4.37 before program implementation; SE=3.56 after program implementation). Oral feeding started earlier following program implementation, both in terms of liquids –40.68 days (mean) (SE=14.45) vs. 20.25 days (SE=4.02); (p=0.24)– and solids –16 months (SE=1.79) vs. 13 months (SE=0.87); (p=0.16).

18.4% of the patients required gastrostomy for feeding purposes during follow-up –4 before program implementation and 3 after program implementation.

Table 2. Frequency of complications in each patient group.

Complications	*Before 2018*	*After 2018*	*P value*
GERD	63.6%	56.3%	0.64
AS	68.2%	68.8%	0.97
Dysphagia	31.8%	75%	0.01
Impactions	25%	31.3%	0.68
Respiratory infections requiring hospital stay	50%	43.8%	0.70
Re-fistulizations	5%	14.3%	0.35

GERD = gastroesophageal reflux; AS = anastomotic stenosis.

The program standardized the performance of endoscopies in asymptomatic patients when they turned 5 and 10 years old. Given that patients born after 2013 turned 5 when the program was implemented, the study of endoscopic results in this series is a descriptive one –there was no control group. 25 endoscopies with biopsy were conducted after 2018 (16 patients), with mild histological disorders being found in 28% of the samples (25% of the patients). No case of dysplasia was noted. Histological disorder types are featured in table 3. Of the patients with histological disorders at biopsy, 25% had no GERD symptoms, 50% had digestive symptoms, and 25% had extra-digestive symptoms.

Table 3. Histological disorders in endoscopic biopsies.

Histological outcome	*Frequency*
Esophagitis	3 (12%)
Gastritis	2 (8%)
Ectopic gastric mucosa	2 (8%)
Total	7 (28%)

DISCUSSION

The advances made in the fields of surgery and intensive neonatal care have allowed for an increase in the survival of patients with congenital abnormalities such as EA. This poses new challenges in terms of follow-up during growth and transition to adulthood[5,6,8].

The need for cross-disciplinary consultation stems from EA's most frequently related morbidities –digestive and respiratory symptoms[1,4-12].

Before this cross-disciplinary program was implemented, patient management and treatment were not standardized and used to depend on patient progression and the physician's professional criteria. In addition, patients had to go to hospital more often, since they had separate pediatric gastroenterology and pediatric surgery appointments. Implementing a cross-disciplinary program has allowed for a significant reduction in follow-up losses.

This demonstrates that the management of patients with pathologies requiring chronic follow-up should be standardized. It also shows that advances should be made in the creation of adulthood transition programs[6,9,10].

In our series, GERD was present in 63.2% of the cases. Before 2014, GERD confirmation was less standardized, and it was carried out based on symptoms and a gastroesophageal transit test with lower sensitivity and specificity. In spite of this limitation, the percentage of GERD before and after the standardization of impedance-pH metries is similar between the groups and higher than that described in the previous literature (20-45%)[1,6]. In our institution, 25% of the patients diagnosed with GERD had no symptoms, which means protocolized diagnostic tests and a close follow-up could favor GERD detection in little symptomatic and even asymptomatic patients.

Protocol implementation allowed the specialists involved in patient follow-up to establish consensual treatment patterns. It also reduced time to anti-reflux treatment initiation.

This study confirms the association of GERD with EA in our series, consistent with the ESPGHAN-NASPGHAN guidelines, and it highlights the importance of establishing an early preventive anti-reflux treatment.

The standardization of impedance-pH metry at 1 year of life allows the anti-reflux treatment to be discontinued, thus avoiding excessive treatment of patients without GERD and favoring clinical consensus among specialists, which otherwise could prove complex as there is no correlation between symptoms and GERD as measured through pH metry[1,12].

50% of the study patients had dysphagia, similar to the incidence reported in other articles (20-80%)[1,3,5,8,11,12]. This symptomatology significantly increased following program implementation. We believe this may be due to the fact patients in the post-2018 group were younger, and

therefore, questions were addressed to parents/guardians, whereas older patients might have got used to living with dysphagia and consequently might have not reported it as a symptom. It is also possible that ongoing follow-up allows for better detection. Further studies are required to confirm either of these two hypotheses.

Following the implementation of the cross-disciplinary follow-up program, patients initiated oral tolerance both to liquids and solids earlier. This could be due to the fact patients adapt to treatment earlier as a result of attending consultations regularly.

It should also be considered that, concomitantly to the implementation of the program in 2018, thoracotomy was gradually replaced by EA thoracoscopic repair, which could explain why oral feeding was initiated earlier[13]. However, the current literature only reports earlier oral tolerance initiation in the case of liquids, but it has not analyzed the impact on solid tolerance or explained the increase in the incidence of dysphagia.

An increasing number of studies show the impact of respiratory morbidity on EA patients and its long-term implications. A meta-analysis described a 33.3% prevalence of long-term respiratory sequelae[5]. Bronchial hyperreactivity is seemingly the most frequent symptom, since it has been reported in up to 45% of adult patients[5,7,8]. Distorted pulmonary function tests –with both restrictive and obstructive patterns–, greater frequency of asthma, and increased respiratory infections as compared to the general population have also been reported[5,7,8]. In our series, 47.4% of the patients had respiratory infections requiring hospital stay. This percentage is higher than that found in other series[1], but similar to that described by Lejeune et al.[8], who reported a 31% rate of respiratory re-admissions in the first year of life –mostly due to respiratory infections. It is also similar to other studies reporting a risk of pneumonia of 27-43% between years of life 2 and 5[8,14].

The last guidelines and consensuses support standardized endoscopic follow-up in asymptomatic patients due to the high prevalence of histological esophagitis, which ranges from 12.4% to 90% depending on the study[1,4,5,12]. In our study, esophagitis rate was 12%, with histological disorders being found in 28% of the patients. Endoscopic biopsies seemingly have an important role in the diagnosis of esophagitis, since there may be histological esophagitis without associated macroscopic findings[12]. In our series, no cases of dysplasia were noted, but the increased risk of Barrett's esophagus in these patients –up to 4 times higher than the general population when reaching adulthood– and the associated oncological risk seemingly support the performance of follow-up endoscopies after 5 and 10 years, and also when transitioning to adulthood[1,4].

Regarding study limitations, the 2018 change in the surgical technique may represent a confusion factor when comparing complications. In addition, the follow-up time assessed was longer in the pre-program implementation group, which could distort the difference in the data referring to the number of events occurred in the follow-up period.

In spite of these limitations, the study highlights the importance of standardizing treatment and follow-up of EA patients, responding to their needs during growth and transition to adulthood.

According to the study results, cross-disciplinary joint assessment of EA patients by pediatric surgery and gastroenterology specialists during follow-up reinforces the therapeutic decision-making process and favors treatment adaptation according to patient progression. Closely monitoring a program involving all specialists participating in the long-term treatment of EA may help reduce follow-up losses and the use of unnecessary treatments.

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