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Physical growth and social prognosis of esophageal atresia after 15 years of age

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Abstract

Background: The mortality rate of esophageal atresia (EA) has significantly improved, but late complications remain problematic. We evaluated the physical growth, late complications, and social prognosis of postoperative patients with EA who have reached 15 years of age.

Methods: EA patients who were treated at our institution from 1984 to 2003 were enrolled. The follow-up, physical growth at the last visit, late complications and treatment, academic status, and employment situation were evaluated.

Results: Twenty-nine EA patients were registered, and the 23 surviving patients (79.3%) were followed. Anthropometry at the latest visit tended to be below the standard values. Fundoplication was performed in 6 (26.1%) of 9 (39.1%) patients with gastroesophageal reflux. Anastomotic stenosis was found in 12 patients (52.2%), and 2 (8.7%) were treated with re-anastomosis. Thirteen patients were attending a regular school, and one was attending a school for disabled children. Four had jobs from 18 years of age. Follow-up was aborted during early childhood in nine patients.

Conclusions: The physical size of EA was smaller than in the healthy population of the same age. Late complications had not affected the physical growth but were sometimes recognized in adolescence. The social prognosis of the patients was largely favorable.

Keywords: Esophageal atresia, Long-term outcome, Physical growth, Social prognosis, Late complications

Background

Advances in perinatal intensive care and techniques in pediatric surgery have led to an improvement in the survival rate of patients with esophageal atresia (EA) [1]. However, control of gastroesophageal reflux (GER) disease and stenosis of the anastomotic site as a late complication after surgery remain important problems. Recently, our group summarized and published the predictive factors affecting the prognosis and late complications of 73 consecutive cases of EA at 2 centers in Kagoshima prefecture [2]. In that article, we clarified that associated cardiac and chromosomal anomalies significantly affected the prognosis based on our experience. In addition, GER and anastomotic stenosis were the most common late complications, and the growth of the surviving cases was insufficient. Now that a long-term survival has been achieved, we must analyze the effects of late complications on the social prognosis, including physical development, school attendance, and employment status.

The aim of the present study was to clarify the physical development status, effects of late complications on physical growth, social prognosis, and follow-up situation of postoperative patients with congenital EA treated at our institution who had reached 15 years of age.

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Methods

Study design

We retrospectively reviewed the medical records of patients with EA who had been treated from April 1984 to March 2003 at our institution. The patient characteristics that were analyzed included the birth weight, gestational age, gross classification, and associated anomalies. GER and anastomotic stenosis were assessed as late postoperative complications. We evaluated the growth of patients based on the body height (BH), body weight (BW), and body mass index (BMI) on the day of the last hospital visit and determined the standard deviation (SD) score for the normal population for every anthropometric factor using a software program developed by the Japanese Society for Pediatric Endocrinology (http://jspe.umin.jp/eng/index.html).

Statistical analyses

Regarding the statistical analyses, we performed a comparative study between the patients with and without late complications for the anthropometrics obtained at the latest visit using the Mann-Whitney *U*-test. We also analyzed the correlation between the anthropometrics and the age at the latest visit using Pearson's correlation test. We used R as the statistical software program.

Ethical approval

This study was performed according to the Ethical Guidelines for Medical and Health Research Involving Human Subjects by the Ministry of Health, Labour and Welfare of Japan in 2014, complied with the 1964 Declaration of Helsinki (revised in 2013), and was approved by the local ethics committee of our institution (registration number: 27–119).

Results

Patient characteristics

Patient characteristics are shown in Table 1. A total of 29 patients with EA (males, $n = 19$ [52.0%]; females, $n = 10$ [48.0%]) were registered in the present study. The mean gestational age was 38 weeks and 4.5 days (± 16.6 days). The mean birth weight was 2573.9 ± 509.6 g, and infants weighing < 2500 g accounted for 44% of the population (infants weighing < 1500 g were not included). With regard to the gross classifications of EA, type C was the most common ($n = 25$; 86.2%). Associated anomalies were detected in 15 patients (51.7%); cardiovascular anomalies and anorectal malformations, which occurred in 7 of these patients (24.1%), were the most common type of associated anomaly. The 7 patients with cardiovascular anomalies included 2 (6.9%) with atrial septal defect, 1 (3.4%) with ventricular septal defect, 2 (6.9%) with patent ductus arteriosus (PDA), 2 (6.9%) with Fallot's tetralogy, and 1 with other vascular anomalies (with some overlap). The 5 patients (17.2%) with other gastrointestinal anomalies included 2 (6.9%) with duodenal atresia, 2 (6.9%) with Meckel's diverticulum, and 1 (3.4%) with aberrant pancreas. The patients with other anomalies included 2 (6.9%) with genitourinary malformation, 2 (6.9%) with malformation of the extremity, 2 (6.9%) with vertebral malformation, and 1 (3.5%) with tracheal anomaly.

Table 1 Characteristics of 29 patients with esophageal atresia

Sex [M/F]	19/10	
Mean birth weight [g]	2573.9 ± 509.6	
Mean gestational age [weeks + days]	38 + 4.5 ± 16.6 days	
Gross classification [*n* (%)]		
A	2	(6.9)
C	25	(86.2)
D	1	(3.5)
E	1	(3.5)
Associated anomalies [*n* (%)]		
Total	15	(51.7)
Cardiovascular	7	(24.1)
Anorectal	7	(24.1)
Other gastrointestinal	5	(17.2)
Genitourinary	2	(6.9)
Extremities	2	(6.9)
Vertebral	2	(6.9)
Omphalocele	2	(6.9)
Tracheal	1	(3.5)

The overall survival rate in the present study was 79.3%. Five patients (17.2%) died in infancy, and 1 patient (3.4%) died at 4 years old. The causes of death in infancy were as follows: respiratory failure in 2 (6.9%) and heart failure due to associated cardiac anomaly, renal failure, and sepsis in 1 each (3.4%). The cause of death in the patient at 4 years of age was aspiration pneumonia associated with GER. The yearly breakdown of dead cases was 3 in the 1980s, 2 in the 1990s, and 1 in the 2000s.

Physical development status

Table 2 shows the standard deviations (SDs) of the BH, BW, and BMI at the time of the last hospital visit in patients > 6 years of age. The median age at this visit was 15 years and 5 months of age (range 7 years and 8 months to 24 years and 4 months). The median SD of the BH was −0.67 (range −2.99 to + 0.99), and the number of patients with −2SDs was 2 (14.3%). The median SD of the BW was −1.43 (range −3.15 to + 1.16), and the number of patients with −2SDs was 4 (28.6%). The median SD of the BMI was −1.22 (range −2.03 to + 0.73), and

Table 2 Anthropometric values of the 14 surviving patients older than 6 years of age

Median age of the latest hospital visit	**15 years and 5 months (7 years and 8 months to 24 years and 4 months)**
Anthropometry	**Median (range)**
Body height (SD score)	− 0.67 (− 2.99 to + 0.99)
Body weight (SD score)	− 1.43 (− 3.15 to + 1.16)
Body mass index (SD score)	− 1.22 (− 2.03 to + 0.73)

SD standard deviation

Table 3 Late complications and anthropometrics. Statistical analyses were performed by the Mann-Whitney *U*-test

	With late complications ($n = 12$)		**Without late complications ($n = 9$)**		***p* value**
	Median	**(Range)**	**Median**	**(Range)**	
Body height (SD score)	− 0.64	(− 2.99 to + 0.99)	− 0.48	(− 1.42 to + 1.62)	0.1
Body weight (SD score)	− 0.70	(− 3.15 to + 0.42)	− 1.09	(− 2.05 to + 1.16)	0.7
Body mass index (SD score)	− 0.75	(− 1.79 to + 1.94)	− 1.08	(− 2.03 to + 0.73)	0.5

the number of patients with −2SDs was 1 (7.1%). Both the BH and BW were lower than the standard value, and the BMI tended to be lower than the standard value. The ratios with ≤ −2SDs for each item tended to be over 2.3%, which is the ratio for the Japanese SD.

All patients with a stature under −2SDs were evaluated endocrinologically at the Department of Pediatrics in our institution, but none required endocrinologic intervention. There was no significant correlation between the SDs of the anthropometrics and the age at the latest visit.

Late complications

The late postoperative complications that were observed included GER ($n = 9$; 39.1%) and anastomotic stenosis ($n = 12$; 52.2%). GER was evaluated based on subjective symptoms, upper gastrointestinal (GI) findings, and 24-h pH monitoring. A reflux index (% time pH < 4 in the distal esophagus) of > 4% was considered to indicate GER. The period when the GER symptoms appeared ranged from 3 months to 17 years of age. Six patients required fundoplication based on their reflux index.

Anastomotic stenosis and dysphagia were evaluated based on upper GI findings and subjective symptoms. These symptoms appeared around 2 years of age. Eleven patients required balloon dilation, and two of them further required surgical resection of the stenotic site.

Evaluating the effects of late complications on EA patients' growth

To clarify the effects of late complications on growth in EA patients, the BH, BW, and BMI were compared by the presence of late complications. The presence of late complications and anthropometrics are shown in Table 3.

Table 4 Schooling and employment status

School	Senior high school	Attending	1
	School for disabled children	Attending	1
	Senior high school	Graduated	1
	Vocational school	Graduated	3
	Graduate school	Graduated	1
Employment	Employed		4
	Unconfirmed		1

There were no significant differences in the anthropometrics by late complications (BH: $p = 0.1$; BW: $p = 0.5$; BMI: $p = 0.7$).

Schooling and employment status

Table 4 shows the schooling and employment status. Six of the 7 patients (85.7%) who continued follow-up until graduation from junior high school continued to senior high school. Only one patient entered a school for disabled children.

Four of the 5 patients who graduated from high school were confirmed to be employed (the employment status was unconfirmed in the remaining patient).

Follow-up status

The age at the time of follow-up interruption in the surviving cases is shown in Table 5. Nine patients stopped follow-up by early childhood and four due to moving to a remote area after being discharged following curative surgery. Three patients (13.0%) were able to continue follow-up until at least 16 years of age, and follow-up is ongoing in 4 patients (17.4%).

Table 5 Age at the time of follow-up interruption

5 years of age or younger	9	(39.1%)
6–15 years old	7	(30.4%)
16 years of age or older	3	(13.0%)
Follow-up ongoing	4	(17.4%)

Discussion

The present study revealed the following findings: (1) the SD values of the BH, BW, and BMI were lower than in the normal population in Japan; (2) as late complications, GER and anastomotic stenosis were frequent; (3) as far as confirmed, the social prognosis (including the schooling and employment status) was relatively good; and (4) the follow-up was stopped early in a considerable number of cases.

Little et al. reported that the BH and BW of patients with EA tended to approach the norm as their age increased [3]. Similarly, in a 5-year follow-up study by Gischler et al., the BH, BW, and BMI of EA patients seemed to approach the norm with age as well [4]. Deurloo et al. reported that the BH and BW were below the 5th percentile for age in 7% of surviving patients with EA [5]. In the present study, the percentages of patients showing BH, BW, and BMI values of < -2SDs were 13.2%, 20.8%, and 9.4%, respectively. The SD values of BH, BW, and BMI were all lower than in the general Japanese population. We should carefully monitor patient growth and consider performing an active intervention with nutritional support during growth spurts of patients with EA.

GER, which occurs in up to 75% of EA patients, is the most common late postoperative complication in this patient group [6]. Excessive tension at the anastomotic site and abnormal esophageal motility have been identified as factors associated with GER. The experimental study by Montedonico et al. showed that a decrease in the lower esophageal sphincter tone and the shortening of the intra-abdominal esophageal segment due to excessive anastomotic tension were responsible for GER [7]. Kawahara et al. described a lack of contraction of the lower esophagus as the cause of postoperative GER in EA patients [8]. Based on these previous reports—when possible—we must take care to decrease the tension at the site of anastomosis in the esophagus and avoid injuring the vagal nerve. We have recently started to perform thoracoscopic surgery, which provides a wide and clear view of the esophagus and vagal nerve, for EA; thus, the incidence of GER can be expected to improve.

Baird et al. reported that anastomotic stricture occurred in 24–79% of open repair cases and 9–32% of thoracoscopic repair cases [9]. The impairment of the blood flow at the tips of both the upper and lower esophagus is reported to be one of the reasons for anastomotic stenosis. Vukadin et al. stated that an inadequate surgical technique during anastomosis (i.e., the use of too few or too many sutures) was strongly associated with stenosis [10]. In most cases, postoperative anastomotic stenosis can be treated by balloon dilatation. However, in patients with anastomotic stenosis associated with severe GER, the anastomotic region is exposed to acid due to GER, and anti-reflux surgery should be performed. In the current study, 11 patients with anastomotic stenosis underwent balloon dilatation, and 4 with refractory anastomotic stenosis caused by acid exposure underwent anti-reflux surgery.

In the present study, the presence or absence of late complications (i.e., GER and anastomotic stenosis) had no significant effect on the patients' growth. Presse et al. reported that postprandial fullness, slow eating, and dysphagia were associated with growth failure in EA patients [11]. As children tend to experience difficulty in precisely describing their symptoms, complications—especially GER—may be overlooked. In addition to a careful interview of the families and patients, the regular evaluation of the esophageal function using modalities such as upper GI and esophagoscopy may lead to the early detection of GER. Furthermore, the regular measurement of anthropometric factors may help monitor the development and growth of EA patients.

In the present study, the social prognosis, including the schooling and employment status, was favorable in most cases who continued follow-up until graduation from junior high school. A good social prognosis can be expected in surviving cases of EA, aside from those with episodes that cause neurological abnormalities, such as hypoxic encephalopathy in the neonatal period, and those with chromosomal abnormalities.

However, in many cases in the present study, follow-up was stopped relatively early. One patient in our study required fundoplication because the subjective symptoms of GER worsened during senior high school. Since some complications may manifest after puberty, as in this patient, regular follow-up should be continued when possible, even in cases showing good progress.

Conclusions

In postoperative patients with EA, anthropometrics tended to be low over the long-term follow-up compared with standard values. Although the social prognosis of the surviving cases was largely favorable, many patients suffered from late complications, such as GER and stenosis of the anastomosis. There are a considerable number of patients whose follow-up was stopped early after the definitive operation. In order to maintain a favorable

long-term quality of life and ensure adequate social adaptation, regular follow-up observation should be continued after puberty, regardless of the presence of late complications.

Abbreviations
EA: Esophageal atresia; GER: Gastroesophageal reflux; BH: Body height; BW: Body weight; BMI: Body mass index; SD: Standard deviation; PDA: Patent ductus arteriosus; GI: Gastrointestinal.

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Authors' contributions
M.R., M.M., K.S., and N.K. contributed to the conception and design of this study. M.M., Y.K. H.T., O.S., and K.Y. collected and analyzed the data. Y.W., M.M., K.T., M.S., and T.M. performed the statistical analysis. M.R. drafted the manuscript. M.M., K.T., and I.S. critically reviewed the manuscript and supervised the whole study process. The authors read and approved the final manuscript.

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Availability of data and materials
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the local ethics committee of Kagoshima University Hospital (registration number: 27–119). Written informed consent was obtained from the parents of the patients for the participation in the study and publication of the manuscript.

Consent for publication
Not applicable

Competing interests
The authors declare that they have no competing interests.

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References

1. Yagi M, Kohno M, Asagiri K, et al. Twenty-year trends in neonatal surgery based on a nationwide Japanese surveillance program. Pediatr Surg In. 2015;31:955–62.
2. Masuya R, Kaji T, Mukai M, et al. Predictive factors affecting the prognosis and late complications of 73 consecutive cases of esophageal atresia at 2 centers. Pediatr Surg Int. 2018;34:1027–33.
3. Little DC, Rescorla FJ, Grosfeld JL, et al. Long-term analysis of children with esophageal atresia and tracheoesophageal fistula. J Pediatr Surg. 2003;38:852–6.
4. Gischler SJ, van der Cammen-van Zijp MHM, Mazer P, et al. A prospective comparative evaluation of persistent respiratory morbidity in esophageal atresia and congenital diaphragmatic hernia survivors. J Pediatr Surg. 2009;44:1683–90.
5. Deurloo JA, Ekkelkamp S, Schoorl M, et al. Esophageal atresia: historical evolution of management and results in 371 patients. Ann Thorac Surg. 2002;73:267–72.
6. Shawyer AC, Pemberton J, Kanters D, et al. Quality of reporting of the literature on gastrointestinal reflux after repair of esophageal atresia-tracheoesophageal fistula. J Pediatr Surg. 2015;50:1099–103.
7. Montedonico S, Diez-Pardo JA, Possogel AK, et al. Effects of esophageal shortening on the gastroesophageal barrier: an experimental study on the causes of reflux in esophageal atresia. J Pediatr Surg. 1999;34:300–3.
8. Kawahara H, Kubota A, Hasegawa T, et al. Lack of distal esophageal contractions is a key determinant of gastroesophageal reflux disease after repair of esophageal atresia. J Pediatr Surg. 2007;42:2017–21.
9. Baird R, Laberge JM, Levesque D. Anastomotic stricture after esophageal atresia repair: a critical review of recent literature. Eur J Pediatr Surg. 2013;23:204–13.
10. Vukadin M, Savic D, Malikovic A, et al. Analysis of prognostic factors and mortality in children with esophageal atresia. Indian J Pediatr. 2015;82:586–90.
11. Presse N, Taillefer J, Maynard S, et al. Insufficient body weight of adults born with esophageal atresia. J Pediatr Gastr Nutr. 2016;62:469–73.

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