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# Review of Complications of Operated Esophageal Atresia and Tracheoesophageal Fistula Patients

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## What is already known on this topic?

- *Esophageal atresia (EA) and tracheoesophageal fistula (TEF) are the most common congenital esophageal anomalies.*
- *Patients who have been operated on for EA and TEF in childhood face problems with their gastrointestinal, respiratory, and skeletal systems, and growth retardation during follow-up.*

## What this study adds on this topic?

- *The most common complication in patients operated on for EA and TEF is recurrent pneumonia.*
- *Gastroesophageal reflux (GER) increases the risk of recurrent pneumonia, development of stricture in the esophagus, and growth retardation.*
- *Patients should be closely monitored for scoliosis due to its predisposition to frequent hospitalizations and recurrent pneumonia.*

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## ABSTRACT

**Objective:** This study was aimed to investigate the complications arising during follow-up and the reasons for hospitalization in pediatric patients who were operated on for esophageal atresia (EA) and tracheoesophageal fistula (TEF).

**Materials and Methods:** Between 2007 and 2019, all patients operated for EA and TEF were evaluated in terms of age, gender, age at diagnosis, post-op, and complications in follow-up.

**Results:** In the study, 28 of 50 patients were operated on for EA and TEF, 14 for isolated EA, and 8 for isolated TEF. The mean age of the patients was 4.9 ± 4.4 years, and 18 (36%) of them were female. The median age of diagnosis was 1 (IQR: 1–3) day and the mean follow-up duration was 4.6 ± 4.1 years. During follow-up, 84% of patients had recurrent pneumonia, 60% gastroesophageal reflux (GER), 34% growth retardation, 30% restrictive lung disease, and 18% scoliosis. Postoperative pneumonia, hospitalization, development of stricture and growth retardation were more frequent in patients with GER ($P < .05$). Patients with scoliosis had more frequent pneumonia and hospitalization rates ($P < .05$).

**Conclusion:** Hospital admissions of the patients with EA and TEF were higher due to GER, recurrent pneumonia, restrictive lung disease, and scoliosis in the follow-up. Pneumonia, hospitalization, stricture in the esophagus, and growth retardation were observed more frequently in patients with GER. Patients should be followed up by the pediatric pulmonology, gastroenterology, and orthopedic departments.

**Keywords:** Complications, esophageal atresia, tracheoesophageal fistula

## INTRODUCTION

Esophageal atresia (EA) is a congenital anomaly characterized by interruption of the continuity of the esophagus and sometimes accompanied by tracheoesophageal fistula (TEF). Although the incidence of EA and TEF is approximately 1/2500–3500, they are the most common congenital esophageal anomalies and their etiology is generally unknown.[1,2] Approximately 50% of EA and TEF cases may have an isolated malformation; trisomy 13, trisomy 18, VACTERL (vertebral anomaly, anal atresia, cardiac anomaly, tracheoesophageal anomaly, renal anomaly, and upper extremity anomalies), or CHARGE syndrome (coloboma, heart defect, choanal atresia, developmental delay and growth retardation, genital hypoplasia, ear anomaly, or deafness) may accompany.[2,3] In the study it was found that 39–56% of EA and TEF cases are diagnosed in the prenatal period due to polyhydramnios. Most cases are diagnosed with clinical findings such as vomiting, regurgitation, and saliva accumulation in the mouth after birth.[4] Inability to advance a nasogastric catheter more than 10–15 cm in the neonatal period may suggest EA. This finding can be demonstrated by a

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chest radiograph showing the bending of catheter in the upper esophageal pouch. In the presence of a suspicious diagnosis or a suspected proximal TEF, the diagnosis can be confirmed fluoroscopically with water-soluble contrast material.[5] Surgical repair of atresia and fistula, if any, is usually performed in the first days of life.[4]

Five-year survival rates are generally not affected in babies with isolated EA or TEF, but if there are concomitant cardiac anomalies or chromosomal abnormalities, this rate decreases to approximately 20%. Patients who are followed up with EA and TEF in childhood face gastrointestinal and respiratory system complaints as well as growth retardation and some orthopedic problems.[4] There are few studies about the follow-up of patients operated for EA and TEF. We aimed to evaluate the complications, the frequency of hospitalization, and the reasons for hospitalization in the follow-up of patients with EA and TEF.

## METHODS

The files of all patients who were followed up in the Pediatric Chest Diseases Department between 2007 and 2019 after an operation for EA and TEF were reviewed.

Patients' diagnoses, gender, comorbidities, admission complaints, age of diagnosis, diagnostic methods, age of surgery, duration of postoperative hospitalization, and complications in the early postoperative period were recorded.

In the follow-up, the current ages of the patients at the last follow-up, body mass index (BMI), BMI z-scores, number of hospitalizations, the recurrence of pneumonia, chest X-ray findings, pulmonary function tests (PFT) (in compliant patients), and complications observed during the follow-up were recorded. Patients who had 2 attacks of pneumonia in 1 year or had at least 3 attacks of pneumonia in their lifetime and who were clinically and radiographically normal between the attacks were accepted as recurrent pneumonia.[6] $FEV_1$ (forced expiratory volume in the first second), FVC (forced vital capacity), $FEF_{25-75}$ (25-75% of forced expiratory flow) percent predicted by age in the patients' PFTs, and $FEV_1$/FVC values were recorded. BMI z-scores were calculated according to age. Patients with BMI z-score ≥+2SD for age were considered as obese, patients with ≥+1SD to <+2SD as overweight, patients with ≥−2SD to <+1SD as normal weight, patients with ≥−3SD to <−2SD as weak (low weight), and patients with <−3SD were classified as very thin (very low weight).[7-9] Patients' age at diagnosis, concomitant disease, postoperative hospitalization, the recurrence of pneumonia, GER, stricture development in the esophagus, restrictive lung disease, tracheomalacia, scoliosis, thoracotomy due to rib fusion, and growth retardation (BMI z-score for age (BMI z-score for age <-2SD)) were recorded. The frequency of complications such as and their effects on the number of hospitalizations were evaluated. The number of hospitalizations of patients under and over 2 years of age was compared. Restrictive lung disease was defined as a decrease in lung parenchyma expansion and total lung capacity, low vital capacity and FVC in PFTs, and normal $FEV_1$/FVC ratio in patients.[10] The lateral curvature of the patients' spines, of above 10 degrees to the right or left, detected radiologically in the coronal plane, was evaluated as scoliosis.[11]

The study was conducted following the principles of the Helsinki Declaration (2008). It was conducted with the approval of the Ethics Committee of the Gazi University Faculty of Medicine (May 11, 2020, Decision number 303) Since the study was conducted retrospectively, patient consent was not obtained.

### Statistical Analysis

After collecting all the obtained data, Statistical Package for the Social Sciences (SPSS) version 22.0 (IBM SPSS Corp.; Armonk, NY, USA) was used for statistical analysis. Descriptive data are presented as frequency, percentage, mean ± standard deviation, median, and 25th, and 75th percentile [interquartile range (IQR)]. Since parametric assumptions are not met in the analysis of continuous variables, the Mann–Whitney *U*-test was used. Nominal variables were analyzed with the chi-square test, and in the analysis of nominal variables, when the distribution was not compatible with the chi-square test, Fisher exact test was used. Spearman correlation analysis was conducted to examine the interaction of variables with other parameters and the relationship between these parameters. A value of $P < .05$ was considered significant for all tests.

## RESULTS

Of the 50 patients operated for esophageal anomalies and followed up in the Pediatric Chest Diseases Polyclinic for a period of 12 years, 14 had isolated EA, 8 had isolated TEF, 28 had EA and TEF. There were 32 (64%) male and 18 (36%) female patients in total. In the study, 2 (4%) patients had Down syndrome, 2 (4%) had VACTERL syndrome, 6 (12%) had congenital heart disease (ventricular septal defect, atrial septal defect), and 1 (2%) had neurofibromatosis. The diagnoses and demographic characteristics of the patients are shown in Table 1. The most common presenting complaints were increased saliva, cough after feeding, respiratory distress, wheezing, bruising, and recurrent lung infection. The median age of diagnosis was 1 (IQR: 1-3) days. The mean age at diagnosis of patients with EA and H-type TEF (a subtype of TEF) was 90 ± 42.4 days, while the median age of diagnosis of the other patients was 1 (IQR: 1-3). In the study, 2% of the patients were diagnosed by antenatal ultrasonography,

**Table 1.** Patients' Demographic Characteristics and EA[a]/TEF[b] Operation Information

| | |
|---|---|
| Average age (years) (mean ± SD), median age at diagnosis (days) (IQR) | 4.9 ± 4.4 1 (1-3) |
| | *n* (%) |
| Gender | |
| Female | 18 (36) |
| Male | 32 (64) |
| Diagnoses | *n* (%) |
| EA[a] | 14 (28) |
| TEF[b] | 8 (16) |
| H-Type TEF[b] | 2 (2) |
| EA[a]+TEF[b] | |
| EA[a] and distal TEF[b] | 26 (52) |
| EA[a] and proximal TEF[b] | 1 (2) |
| EA[a] proximal and distal TEF[b] | 1 (2) |
| Median age at surgery (days) (IQR) | 2 (1-4) |

[a]Esophageal atresia; [b]Tracheoesophageal fistula.
SD, standard deviation; IQR, Interquartile Range.

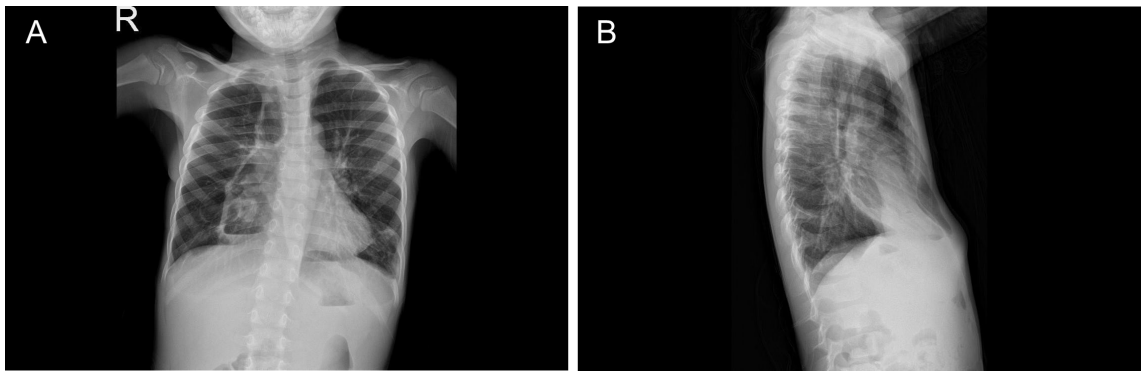


**Figure 1. a,b.** Chest radiograph images of the patient who underwent colon interposition.

8% by endoscopy, 38% by chest radiograph after nasogastric catheter insertion, and 52% by fluoroscopic examination. Six of the patients (12%) were referred to suitable centers for surgery after diagnosis. The median age at surgery was 2 (IQR: 1-4) days, and the mean postoperative hospital stay was 47.4 ± 38.9 days. Anastomotic leak (4%), refistulization (12%), and thrombosis (2%) were complications seen in the early postoperative period. Colon interposition was performed in a patient who developed circulatory disturbance at the anastomotic site after thrombus development in the left external iliac vein. The chest radiograph of this patient is given in Figure 1.

The current mean age of the patients at their last controls was 4.9 ± 4.4 years, and the mean BMI was 15.5 ± 3.7. Body mass index z-scores of the patients according to age are given in Table 2. The median number of hospitalizations in the follow-up was 4 (IQR: 2-7). The median number of hospitalizations of patients in the first 2 years of age was 10 (IQR: 7-12), and it was statistically significantly different from hospitalizations over the age of 2 years ($P = .036$). The comparison of the number of hospitalizations by age is given in Table 3. The most common reason for hospitalization was pneumonia and the median number of recurrences of pneumonia in follow-up was 3 (IQR: 1-6). The mean follow-up period of the patients was 4.6 ± 4.1 years. Other reasons for hospitalizations were respiratory distress, feeding difficulty, and stricture development in the esophagus. Chest radiographs of the patients were found to be normal in 16%, showed interstitial thickening in 48%, atelectasis in 24%, pleural thickening in 8%, and infiltration in 12%. Chest radiograph findings of the patients are given in Table 4. The average $FEV_1$ of 17 patients who could perform pulmonary function test (PFT) was 62.8 ± 18.7%, FVC 67.2 ± 17.4%, $FEV_1$/FVC 90.2 ± 12.7, $FEF_{25-75}$ 54.6 ± 18.7%.

During the follow-up, 84% of the patients had recurrent pneumonia, 60% GER, 28% growth retardation, 30% restrictive lung disease, 8% tracheomalacia, 18% scoliosis, and 48% rib fusion. Esophageal dilatation was performed in 20 (40%) patients due to stricture development during follow-up. Growth retardation was present in all patients with concomitant diseases. The diagnosis of GER was made by fluoroscopic examination in 11 patients and by pH monitoring in 6 patients. In 13 patients with symptoms such as vomiting, refusal of food, weight loss, bitter water in the mouth, burning sensation in stomach and esophagus, early satiety, abdominal pain, and bad breath, the diagnosis was made with a response to GER treatment. Early and late complications of the patients are shown in Table 5. Late complications were most common in patients with EA and distal TEF, and least in patients with H-type TEF. It was observed that there was a moderate ($r = 0.594$, $P = .014$,) positive correlation between the age of diagnosis and the number of hospitalizations, and a high positive correlation ($r = 0.816$, $P = .003$) between the number of the recurrence of pneumonia and hospitalizations during follow-up. Correlations regarding the number of hospitalizations are given in Table 6. Hospitalization was found to be more frequent in the presence of concomitant disease, GER, stricture development, growth retardation, restrictive lung disease, scoliosis, and rib fusion ($P < .05$). The evaluation of the factors affecting the frequency of hospitalization is given in Table 7. Recurrent pneumonia was found to be the most common complication in the follow-up.

**Table 2.** Body Mass Index Z-Score for Age in the Last Controls of the Patients

| ***z*-score** | ***n* (%)** |
|---|---|
| <−3SD | 5 (16) |
| ≥−3SD to <−2SD | 9 (18) |
| ≥−2SD to <−1SD | 5 (10) |
| ≥−1SD to <+1SD | 12 (46) |
| ≥+1SD to <+2SD | 2 (6) |
| ≥+2SD | 1 (4) |

**Table 3.** Comparison of the Number of Hospitalizations by Age

| | **0-2 Year(s)** | **>2 Years** | ***P*** |
|---|---|---|---|
| Number of hospitalizations, median (IQR) | 10 (7-12) | 4 (2-6) | .036[a]* |

[a]Mann–Whitney *U*-test, *Statistically significant.
IQR, interquartile range.

**Table 4.** Chest Radiograph Findings of the Patients in Their Last Controls

| | ***n* (%)** |
|---|---|
| Normal | 8 (16) |
| Interstitial thickening | 24 (48) |
| Atelectasis | 12 (24) |
| Pleural thickening | 4 (8) |
| Infiltration | 6 (12) |

**Table 5.** Postoperative Early and Late Complications of the Patients

| | *n* (%) |
|---|---|
| Early complications | |
| Refistulization | 6 (12) |
| Anastomotic leak | 4 (8) |
| Thrombosis | 1 (2) |
| Late complications | |
| Recurrent pneumonia | 42 (84) |
| Gastroesophageal reflux | 30 (60) |
| Rib fusion | 24 (48) |
| Stricture development in the esophagus | 20 (40) |
| Restrictive lung disease | 15 (30) |
| Growth retardation | 14 (28) |
| Scoliosis | 9 (18) |

**Table 6.** Correlation with the Number of Hospitalizations

| | Number of Hospitalizations | |
|---|---|---|
| | *R* | *P* |
| Age at diagnosis | 0.594 | .014[a*] |
| Number of recurrences of pneumonia | 0.816 | .003[a*] |

[a]Spearman correlation analysis, *Statistically significant.

It was found that patients with GER had more frequent pneumonia, more stricture development, and growth retardation ($P < .05$). The comparison of complications in patients according to the presence of GER is given in Table 8. It was observed that patients with scoliosis had pneumonia more frequently ($P = .046$). Growth retardation was also found at a higher rate in patients with frequent pneumonia ($P = .047$). The comparison of the frequency of having pneumonia according to the presence of complications is given in Table 9.

## DISCUSSION

The number of hospital admissions of patients who have undergone surgery due to EA and TEF, which are the most common esophageal anomalies, are also increasing due to complications observed during follow-up.[4] In our study, it was observed that the frequency of hospitalization was higher in the presence of accompanying disease, GER, stricture development, growth retardation, restrictive lung disease, scoliosis, and rib fusion. Awareness of the complications associated with the gastrointestinal, respiratory, and skeletal systems can reduce the frequency of these admissions. In our study, it was determined that the most common complication in patients followed up for EA and TEF was recurrent pneumonia, and other complications such as esophageal stricture and growth retardation were found to be more common in patients with GER. In the follow-up, it was observed that patients who developed scoliosis had pneumonia and were hospitalized more frequently.

Esophageal atresia and TEF can be recognized in 39-56% of patients by detecting polyhydramnios in ultrasonography performed during the antenatal period, and by observing a smaller fetal stomach and a larger upper part of the esophagus.[12,13] In our study, only 1 (2%) of the patients was diagnosed by antenatal ultrasonography. In the study, 8% of our patients were diagnosed by endoscopy, 38% by chest radiograph, and 52% by fluoroscopic examination. Unlike the literature, our patients were diagnosed mostly with examinations performed for EA and/or TEF-related findings in the postnatal period. Regular follow-up of prenatal pregnancies and detailed evaluation by ultrasonography may increase the frequency of diagnosis in this period. In a study by Zani et al.,[14] it was observed that the

**Table 7.** Comparison of the Number of Hospitalizations by the Presence of Complications

| Complication | Number of Hospitalizations, Median (IQR) | *P* |
|---|---|---|
| Accompanying disease ($n = 11$) | | .042[a*] |
| Yes | 10 (7-12) | |
| No | 3 (2-5) | |
| Gastroesophageal reflux ($n = 30$) | | .003[a*] |
| Yes | 6 (4-8,5) | |
| No | 2 (2-3) | |
| Stricture development ($n = 20$) | | .016[a*] |
| Yes | 8 (5-10) | |
| No | 3 (2-4) | |
| Growth retardation ($n = 14$) | | .022[a*] |
| Yes | 9 (7-12) | |
| No | 3 (2-4) | |
| Tracheomalacia ($n = 4$) | | .168[a] |
| Yes | 2,5 (1,25-3,75) | |
| No | 4 (2-6) | |
| Restrictive lung disease ($n = 15$) | | .026[a*] |
| Yes | 8 (7-12) | |
| No | 2 (1-5) | |
| Scoliosis ($n = 9$) | | .042[a*] |
| Yes | 10 (7-13) | |
| No | 3 (2-5) | |
| Rib fusion ($n = 24$) | | .012[a*] |
| Yes | 6,5 (5-10) | |
| No | 2 (2-3) | |

[a]Mann–Whitney *U*-test; *Statistically significant.
IQR, interquartile range.

**Table 8.** Comparison of Complications in Patients by the Presence of Gastroesophageal Reflux

| Complication | Gastroesophageal Reflux, *n* (%) | | *P* |
|---|---|---|---|
| | Yes | No | |
| Pneumonia | 30 (71.5) | 12 (28.5) | .012[a*] |
| Stricture development | 15 (75) | 5 (25) | .008[a*] |
| Growth retardation | 10 (71.4) | 4 (28.6) | .034[b*] |
| Restrictive lung disease | 9 (60) | 6 (40) | .312[a] |
| Scoliosis | 5 (55.5) | 4 (44.5) | .854[b] |
| Tracheomalacia | 2 (50) | 2 (50) | 1.000[b] |
| Rib fusion | 14 (58.3) | 10 (41.7) | .098[a] |

[a]Chi-square test; [b]Fisher's exact test, *Statistically significant.

**Table 9.** Comparison of the Frequency of Pneumonia by the Presence of Complications

| Complication | Number of Recurrences of Pneumonia, Median (IQR) | *P* |
|---|---|---|
| Scoliosis ($n = 9$) | | .046[a*] |
| Yes | 8 (8-11) | |
| No | 2 (1-4) | |
| Growth retardation ($n = 14$) | | .047[a*] |
| Yes | 8 (5.75-9.25) | |
| No | 2 (1-3) | |

[a]Mann–Whitney *U*-test, *Statistically significant.
IQR, interquartile range.

mean age of diagnosis in patients with H-type TEF was 8 days (1 day-36 months), and it was found that patients with H-type TEF in our study were also diagnosed late, consistent with the literature. In the study conducted by Acher et al.,[15] it was stated that 62% of 445 patients who were followed up for EA and TEF were operated on within the first 7 days of life. In our study, it was observed that 88% of the patients were operated on within the first week. It has been observed that patients with a later time of surgery are patients with H-type TEF and patients who are referred to suitable centers for surgery.

VACTERL syndrome, CHARGE syndrome, chromosomal abnormalities, growth retardation, genitourinary anomalies, and congenital heart diseases may accompany approximately half of the patients who are followed up for EA and TEF.[16] In our study, in addition to EA and/or TEF, 22% of the patients had an accompanying disease. Growth retardation was observed in all of the patients with concomitant diseases. It was observed that the frequency of hospitalization was more frequent in those with concomitant diseases. Therefore, patients who are followed up for EA and TEF should be screened for concomitant anomalies and should be closely monitored.

In the study conducted by Leibovitch et al.,[4] it was shown that the hospitalization rate of patients who were operated on due to EA and TEF was 87% in the first 2 years of life and decreased to 10% between the ages of 16 and 21. It was found that the main reasons for hospitalization were anastomotic stenosis and respiratory tract diseases.[4] In our study, it was observed that hospitalization of patients under the age of 2 was more common and the most common reason for hospitalization was pneumonia. It was found that 28% of our patients had BMI z-scores below −2 SD for age. It was observed that 74.6% of low and very low-weight patients had frequent pneumonia before the age of 2.

In the study conducted by Cartabuke et al.,[17] it was reported that 44.2% of 43 patients who were followed up due to EA and TEF had recurrent respiratory tract infection, 86.7% tracheomalacia, and 54.5% restrictive pulmonary disease in the follow-up. Tracheomalacia was found in 8% of our patients, and restrictive lung disease was found in 30%. It was observed that the patients had frequent postoperative pneumonia. Recurrent pneumonia can cause obstructive and/or restrictive pulmonary disease, bronchiectasis, and chronic respiratory failure in patients.[6] It was observed that the number of hospitalizations was higher in patients with restrictive lung disease.

Gastroesophageal reflux is an important clinical problem seen in patients after surgical repair of EA and TEF, and impaired esophageal motility may occur as a result of delayed gastric emptying with the displacement of the gastroesophageal junction. The incidence of GER varies between 35 and 60% in these patients.[18,19] GER was detected in 60% of our patients during follow-up. Due to the increase in the frequency of GER in the first year after surgery, it is recommended that patients with EA and/or TEF should be given proton pump inhibitor treatment. Discontinuation of treatment should be decided by pH monitoring, and annual control is recommended.[20]

Anastomotic stricture is a common complication after EA and TEF surgery. Studies have shown that approximately half of the operated patients require esophageal dilatation, especially in the first 2 years of age.[15] Esophageal dilatation was applied to 40% of the patients in our study during follow-up. In retrospective studies, it was shown that the frequency of GER increased in patients who underwent dilatation due to the development of stricture in the esophagus, and patients operated at younger ages more commonly needed dilatation, especially in the first 2 years of age.[4,16,21] In our study, it was observed that patients who required dilatation were younger at diagnosis and the frequency of GER was higher than other patients. It has been found that GER is associated with recurrent pneumonia, esophageal stricture, and growth retardation. With the treatment and follow-up of these patients for GER, the frequency of pneumonia and hospitalization can be reduced and growth retardation can be prevented.

Prevalence of scoliosis varies between 6 and 50% in patients after EA and TEF repair. Scoliosis can develop as a result of congenital spinal anomaly or secondary to rib fusions and pleural scars caused by thoracotomy. The lateral vertebral deformity is more likely to occur in patients after repeated thoracotomy.[22] In the study of Sistenone et al.,[23] rib fusion was found to be associated with scoliosis in 30% of the patients who were operated on due to EA and TEF. In our study, rib fusion was detected in 48% of the patients, and scoliosis was found in 18% of the patients. Rib fusion was detected in all patients with scoliosis. Since the average age of the patients participating in our study was small, it was thought that our patients with rib fusion may develop scoliosis during follow-up, and the patients are followed up by the orthopedics department in this respect. Scoliosis decreases lung expansion, drainage of secretions, causes bronchial obstruction, atelectasis, and a predisposition to recurrent pneumonia by causing a decrease in total lung capacity.[24] In our study, it was observed that patients with scoliosis were hospitalized more frequently and had pneumonia.

The limitation of our study was that it was single-center and retrospective. In order to generalize these findings, it will be useful to confirm the results with multi-center prospective studies with more patients.

In conclusion, EA and TEF are common esophageal anomalies. Complications related to the gastrointestinal, respiratory, and skeletal systems may occur during follow-up, and growth retardation is observed. The most common postoperative complication is recurrent pneumonia. The frequency of pneumonia, stricture development in the esophagus, and growth

retardation are increased in patients with GER. Close follow-up and treatment of these patients in terms of GER is necessary to reduce the frequency of pneumonia, hospitalization, the need for dilatation and to prevent growth retardation. Patients with rib fusion should be followed up in terms of the development of scoliosis which is another cause of frequent hospitalization. For this reason, patients must be closely monitored with a multidisciplinary approach after EA and TEF repair by the pediatric chest diseases, pediatric gastroenterology, pediatric surgery, and orthopedic departments.

**Ethical Committee Approval:** Ethics committee approval was received from the ethics committee of Gazi University School of Medicine (11/05/2020, Decision number: 303).

**Informed Consent:** Informed consent was not obtained due to the nature of this study.

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