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Morbidity and Mortality in Patients with Esophageal Atresia

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Abstract

Background—This study reports national estimates of population characteristics and outcomes for patients with EA/TEF and evaluates relationships between hospital volume and outcomes.

Methods—Patients admitted within 30 days of life who had ICD-9-CM diagnosis and procedure codes relevant to EA/TEF during 1999–2012 were identified using the Pediatric Health Information System database. Baseline demographics, comorbidities, and post-operative outcomes, including predictors of in-hospital mortality, were examined up to 2 years following EA/TEF repair.

Results—We identified 3479 patients with EA/TEF treated at 43 children's hospitals; 37% were premature and 83.5% had 1 additional congenital anomaly, with cardiac anomalies (69.6%) being the most prevalent. Within two years of discharge, 54.7% were readmitted, 5.2% had a repeat TEF ligation, 11.4% had a repeat operation for their esophageal reconstruction, and 11.7% underwent fundoplication. In-hospital mortality was 5.4%. Independent predictors of mortality included lower birth weight, congenital heart disease, other congenital anomalies, and preoperative mechanical ventilation. There was no significant relationship between hospital volume and mortality or repeat TEF ligation.

Conclusions—This study describes population characteristics and outcomes, including predictors of in-hospital mortality, in EA/TEF patients treated at children's hospitals across the United States. Across these hospitals, rates of mortality or repeat TEF ligation were not dependent on hospital volume.

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Introduction

Esophageal atresia with or without tracheoesophageal fistula (EA/TEF) is a rare congenital anomaly that mandates surgical intervention and is frequently associated with other anomalies. Patients with EA/TEF often have complicated medical courses due to both the esophageal anomaly and related comorbidities.(1, 2) Complications associated with EA/TEF repair include anastomotic leaks, strictures, and recurrence of TEF.(2–5) In addition, many patients experience gastroesophageal reflux disease (GERD) and recurrent pulmonary aspiration, both of which can result in hospitalizations or additional surgical intervention.(6, 7) Furthermore, despite substantial improvements in neonatal care and surgical techniques, some infants with EA/TEF will not survive.(8–10)

With an incidence of 2–4 cases per 10,000 births, many children's hospitals will treat only a few patients with EA/TEF each year.(11) This low incidence has limited the types of published reports on EA/TEF to mainly single-institution experiences. In addition, due to its rarity and complexity, the number of EA/TEF cases treated per year at an individual center may affect outcomes. Many surgical specialties, including pediatric surgery, have investigated the effect of hospital volume of a specific procedure on outcomes with mixed results.(12–16) In particular to EA/TEF, a system of regionalized subspecialization for treating EA/TEF patients in the United Kingdom has been described and has demonstrated modest improvements in outcomes.(17) No study to date has investigated the relationship between hospital volume and outcomes for EA/TEF in the United States.

Administrative databases represent data sources that can be used to compile large multiinstitutional cohorts of patients with rare diseases to perform descriptive studies and to examine interhospital differences in patient populations, treatments, and outcomes.(12, 18) Utilizing a multiinstitutional administrative database of freestanding pediatric hospitals, the objectives of this study were to describe national estimates of baseline characteristics and clinical outcomes for patients with EA/TEF and to determine if higher hospital volume was associated with improved outcomes, specifically lower rates of in-hospital mortality and repeat TEF ligations.

Methods

Cohort Identification and Validation

We conducted a retrospective multi-institutional cohort study of neonates with a diagnosis of EA/TEF who underwent at least one related surgical procedure and were treated between 1999 and 2012. This study utilized the Pediatric Health Information System (PHIS), a multi-institutional administrative database that contains inpatient, observation, emergency department, and ambulatory surgery discharge/encounter data from freestanding children's hospitals that are part of the Children's Hospital Association. Data elements were collected from 43 PHIS hospitals including demographics, diagnosis and procedure codes (International Classification of Diseases 9th Edition Clinical Modification, ICD-9-CM). Since 1999, resource utilization data has been collected in the PHIS as date-stamped billing codes for radiology, laboratory, pharmacy, and other hospital level charges; therefore, we initiated our cohort to coincide with the availability of this data to allow for a more detailed

characterization of the procedures and treatments administered. Encrypted medical record numbers allow for longitudinal tracking of patients across multiple hospital encounters.

The methodology to identify the cohort of neonates with EA/TEF has been previously published.⁽¹⁸⁾ Briefly, all patients with an ICD-9-CM diagnosis code for either congenital EA/TEF (750.3) or acquired TEF (530.84) who were admitted by 30 days of life and also had at least one EA or TEF related procedure during the index encounter were included in the cohort. This methodology has a sensitivity of 96% and positive predictive value of 96% for correctly identifying patients with EA/TEF. Patients with the diagnosis code for EA or TEF, but who underwent only a gastrostomy with no subsequent reparative EA/TEF procedure code identified within the PHIS were excluded. No other exclusion criteria were applied.

Data abstracted from the PHIS were validated by reviewing medical records of all patients with EA/TEF treated at two PHIS institutions (Nationwide Children's Hospital, Columbus, OH and Children's Hospital of Philadelphia, Philadelphia, PA). The Institutional Review Boards of both institutions approved this study.

Data Elements and Statistical Analysis

Preoperative variables examined included demographic and clinical characteristics at the initial admission during which the first EA/TEF related procedure was performed. Post-operative outcomes that occurred during the index admission and within 2 years of the first EA/TEF related procedure were also examined. Sequelae of EA/TEF often persist for many years, so we chose to assess outcomes for a duration of 2 years in order to balance the competing goals of achieving a large sample size and having a substantially long follow-up period to capture delayed EA/TEF related outcomes such as recurrent TEF, or undergoing a fundoplication or a repeat esophageal reconstruction. Comorbidities were based on ICD-9-CM procedure codes or hospital billing codes whenever possible, and ICD-9-CM diagnosis codes in other cases. For example, a diagnosis of recurrent TEF was determined by the surrogate of an additional TEF ligation procedure, while for comorbid congenital anomalies, such as congenital heart disease (CHD), diagnoses were grouped into broad categories that included all relevant diagnosis codes. All characteristics were reported as frequencies and percentages for categorical variables and as medians and interquartile ranges (IQR) for continuous variables. The associations between hospital volume and in-hospital mortality or repeat TEF ligation were evaluated using hierarchical logistic regression models, with volume first examined as a continuous variable then as a categorical variable.

To determine associations between individual pre-operative characteristics and mortality, chi-square and Fisher exact tests were performed for categorical pre-operative variables and Wilcoxon rank sum tests were performed for continuous variables. A multivariable logistic regression model for in-hospital mortality was fit after performing multiple imputation, starting with pre-operative characteristics associated with mortality at $p < 0.15$ in bivariate analyses then individually removing variables in order of decreasing statistical significance until only variables significant at $p < 0.10$ remained. Clinically significant first order interactions were also included if significant at $p < 0.05$. Hospital volume was also added to the final multivariable model in order to determine whether a relationship existed between

volume and mortality and repeat TEF ligation after adjustment for patient risk factors. Also, a sensitivity analysis was performed to quantify any potential biases caused by misclassification/measurement error in the model for in-hospital mortality.⁽¹⁹⁾ Each logistic regression model was fit using generalized estimating equations to account for the clustering of patients within hospitals. Odds ratios (OR) with 95% confidence intervals (CI) were presented for all variables in the final model. Lastly, to assess for changes over time, baseline characteristics and outcomes of the study cohort were compared between patients treated in earlier (1999–2005) and more recent (2006–2012) halves of the study period. Wilcoxon rank sum tests, chi-square tests, and Fisher exact tests were used to compare baseline characteristics, and marginal logistic and linear regression models were used to compare outcomes between time periods. All statistical analyses were performed using SAS version 9.3 (SAS Institute, Cary, NC). P values <0.05 were considered statistically significant.

Results

Cohort Identification and Characteristics

A total of 3,479 patients were identified with EA/TEF at 43 freestanding children's hospitals. Baseline characteristics and associated congenital anomalies are listed in Table 1. Of note, 1286 (37%) patients were born premature and 2905 (83.5%) patients had a diagnosis of an associated congenital anomaly with almost 70% of patients having some form of congenital heart disease (CHD). Nearly half (1665, 47.9%) of all patients were mechanically ventilated before their first procedure.

Outcomes

Following surgery, almost all patients were mechanically ventilated (3,220; 92.6%) and received total parenteral nutrition (TPN) (3,184; 91.5%) (Table 2). Seventy three percent of patients were treated with anti-reflux medications during the last two days of their admission and 57% on the day of discharge. The median post-operative length of stay (LOS) was 23 days (interquartile range (IQR) 13, 47), and 490 patients (17.0%) were readmitted within 30 days (Table 2). The percentage of patients who died in the hospital after their first procedure was 5.4%.

Table 3 shows outcomes within 2 years following the initial EA/TEF surgery for the 2,887 patients with 2 years of follow-up data. Approximately 55% of patients were readmitted at least once during the 2 year post-operative period. A diagnosis of pneumonia was present at a readmission in 12.7%; nearly half of these patients had multiple readmissions and 6.8% had five or more. Eleven percent of patients underwent reoperation related to their EA/TEF; 5.2% of patients with an initial TEF ligation had a second TEF ligation, and 0.7% had an esophageal replacement procedure. Additionally, 11.7% underwent a fundoplication.

Factors associated with In-Hospital Mortality

Characteristics significantly associated with an increased risk of in-hospital mortality in bivariate analyses included non-white race, lower birth weight, prematurity, lower gestational age, slow fetal growth/fetal malnutrition, certain congenital anomalies (CHD,

respiratory, palate, musculoskeletal, genetic, eye, and GI anomalies other than EA/TEF), and the use of pre-operative mechanical ventilation (Table 1). Independent factors associated with in-hospital mortality included lower birth weight, the use of preoperative mechanical ventilation or ECMO, and the presence of congenital heart disease or one of several other congenital anomalies (Table 4). Of note, there was a significant quantitative interaction between birth weight and race ($p < 0.05$) (Figure 1). In infants less than 2000 grams, black patients showed a greater decrease in their mortality risk for every 100 gram increase in birth weight (OR (95% CI); 0.82 (0.76, 0.88), $p = 0.02$) than white patients (0.89 (0.87, 0.92), $p < .0001$) or patients of other or unknown race (0.88 (0.84, 0.93), $p = 0.04$). In infants over 2,000 grams, these racial differences did not persist.

Effect of Hospital Volume on Outcomes

The relationships between hospital volume and in-hospital mortality and repeat TEF ligation were also examined. There were 14 hospitals that treated an average of 5 or fewer EA/TEF patients each year, 19 that treated 6–9, and 10 that treated 10 or more; the mortality rates for each group were 7.0%, 5.3%, and 4.8%, ($p = 0.15$), and the rates of repeat TEF ligation were 5.3%, 5.2%, and 6.1% ($p = 0.73$), respectively. Results were similar when volume was evaluated as a continuous variable. After adjusting for all variables in the final multivariable model (Table 4), there was no association between average annual hospital EA/TEF volume and in-hospital mortality ($p = 0.64$). Similarly, hospital volume did not show an association with the rate of recurrent TEF ligation in a multivariable model for that outcome ($p = 0.53$; data not shown).

Data Validation and Sensitivity Analyses

The misclassification rates between the PHIS and the institutional medical records varied by the type of data element (Table 5). For predominantly objective characteristics such as gender, date of birth, length of stay, and in-hospital mortality, the average misclassification rate was 1.5%. For post-operative outcomes that were based on date-stamped procedure codes such as rates of additional surgical procedures, the average misclassification rate was 7.8%. For comorbidities, which are based on discharge ICD-9-CM diagnosis codes, the average misclassification rate was 12.7%.

Results of the sensitivity analysis to account for misclassification and measurement error in the PHIS data support the conclusions drawn from the original mortality analysis, though several factors were no longer statistically significant predictors of mortality (Table 4). Based on the sensitivity analysis, factors that remain significantly associated with in-hospital mortality include congenital heart disease, genetic, musculoskeletal, and respiratory anomalies and preoperative mechanical ventilation.

To assess for time-related confounding of our results, outcomes were compared between the first and second halves of the study period. Differences in baseline variables and outcomes between the groups of patients treated during each time period are shown in Table 6. Thirty nine hospitals treated 1397 patients during 1999–2005 and 43 hospitals treated 2082 patients from 2006–2012. Compared to 2006–2012, patients treated in the earlier period were less likely to have another congenital anomaly besides EA/TEF, had a shorter post-operative

LOS,, and were less likely to have post-operative blood transfusions, and to be on anti-reflux medications at discharge. The in-hospital mortality rates were similar. At 2 years, all outcomes were similar between the two time periods.

Discussion

Utilizing a previously defined and validated algorithm to identify patients with EA/TEF in the PHIS, we have performed a longitudinal cohort study of patients with EA/TEF across 43 children's hospitals in the United States.(18) This study provides national estimates of demographic characteristics, comorbid conditions, and clinical outcomes for this rare disease. In addition, we were able to identify factors significantly associated with in-hospital mortality and to examine the relationship between hospital volume and outcomes.

Comorbid conditions are common in patients with EA/TEF. Previously, most reports of outcomes following EA/TEF repair had come from single center retrospective reviews, which are limited in their generalizability. By compiling this large cohort of patients with EA/TEF from over forty children's hospitals, our results represent national estimates of both baseline characteristics and post-operative outcomes. In addition, we identified several risk factors for mortality including lower birth weight, congenital heart disease, the presence of respiratory, musculoskeletal, genetic or eye anomalies, and preoperative mechanical ventilation or ECMO. These results are consistent with those previously reported in smaller studies. (8–10) Interestingly, the effect of birth weight on survival differed by race in our study; as birth weight increased, black patients showed a larger decrease in mortality risk than non-black patients. Potential causes for this interaction between birth weight and race on mortality range from issues related to access to care or health-system based treatment bias to differences in underlying pathophysiology or comorbid conditions. Additional investigation is warranted but is beyond the scope of this study.

An association between higher surgeon or hospital volume and improved outcomes has been demonstrated for a wide variety of adult surgical procedures including esophagectomy and lung resection.(20) The relationship between volume and outcomes is also being explored within pediatric surgery. For example, centralization of care of biliary atresia has occurred in the United Kingdom with early results suggesting an impact of surgeon and center experience on survival.(21) Increased hospital volume has also been associated with modest improvements in management of congenital diaphragmatic hernia.(13) Specific to EA/TEF, a recent report by Jawaid, *et al.* described incremental improvements in outcomes for patients with EA/TEF, including hospital length of stay and mortality, after institution of a subspecialization program.(17) Collecting data from 43 freestanding children's hospitals allowed us to explore the impact of hospital volume on several outcomes. We focused on mortality and repeat TEF ligation as potential surrogates for overall care and disease-specific care. As mortality will be affected by numerous factors including comorbid conditions and other congenital anomalies, it may be more reflective of a center's overall neonatal care rather than the surgical management of EA/TEF. However, repeat TEF ligation represents a disease related process that may be related to the surgical management of the patient. Repeat TEF ligation was chosen over other surgical procedures, such as

repeat esophageal procedures for leaks or strictures, because the indication for operation is more objective as detection of a repeat TEF requires intervention.

Overall, we found that 5.2% of patients underwent a repeat TEF ligation within 2 years. This rate is slightly less than previously reported rates for TEF recurrence of 6–10% (7); this is likely because we are reporting rates within 2 years of repair, while other studies have reported rates into adulthood. Similarly, we found an in-hospital mortality rate of 5.4%, which is likely an underestimate when one considers that patients not surviving to surgical repair were specifically excluded from our cohort. However, this rate is consistent with previously published rates.(10, 11) In terms of the effects of hospital volume, this analysis did not demonstrate a significant relationship between a hospital's average annual number of patients treated with EA/TEF and either mortality or repeat TEF ligation. The absence of an effect of volume on outcomes may be explained by the fact that all of the hospitals participating in the PHIS are freestanding pediatric tertiary care referral centers; these centers reflect an area of concentrated expertise for complex pediatric surgical diseases and may be akin to “centralized” or “subspecialization” programs instituted in other health care systems. Therefore, it remains possible that outcomes for patients with EA/TEF treated at smaller hospitals or at non-pediatric tertiary care referral centers may be related to volume. It is important to note that our data only allows for the association between volume and outcome to be analyzed at the hospital level; variation based on specific surgeon volume was not evaluated using this cohort because of concerns about the high rate of missing data on surgeons.

Several significant differences were found when patients' baseline characteristics and outcomes were contrasted between the early and latter halves of the study period. Compared to patients treated between 1999–2005, patients treated between 2006–2012 had higher rates of a number of other congenital anomalies, suggesting that the cohort of patients undergoing repair of EA/TEF has become more severely ill over time. This may, in part, explain why some post-operative outcomes, such as post-operative LOS and transfusions were gotten worse in the more recent time period. In addition, the increase in the number of hospitals contributing to PHIS over time may have also contributed to changes in pre and postoperative characteristics of the cohort over time. Importantly, in-hospital mortality, along with all outcomes measured at 2 years following repair, were similar between the two time periods. Taken together, these findings suggest an overall improvement in care over time allowing for more severely ill and complex neonates with EA/TEF to survive and undergo repair.

Although the PHIS database has been used to perform numerous descriptive and comparative effectiveness studies, it has several limitations.(22, 23) First, ICD-9-CM diagnosis codes in the PHIS are assigned to an entire hospital encounter, so it is not possible to determine exactly when during the course of an encounter a new diagnosis (e.g. a post-operative wound infection) is made. In contrast, codes for billable procedures, tests, and medications have an associated date stamp, which allows for determining the chronology of events during a patient's hospital encounter; therefore, whenever possible, we used procedure codes or billing codes to define variables and outcomes. Also, diagnosis codes for diseases that a child is evaluated for but does not truly have are sometimes included in their

list of discharge diagnoses in the PHIS. We have successfully excluded these cases in this cohort by using search criteria that include a combination of diagnosis and procedure codes to ensure the presence of the actual disease, although this situation might still exist for comorbid diagnoses, particularly other congenital anomalies.(18) Furthermore, for simplicity congenital anomalies were grouped into anatomic categories which in some cases, particularly CHD, have a wide range of severity and clinical relevance. Second, despite substantial quality control measures, there is always a concern for potential misclassification bias in studies using administrative databases. To determine the rates of misclassification and miscoding, we performed medical record reviews at two separate institutions. This chart review validation demonstrated high levels of accuracy in contrast with previous studies that have compared administrative databases to clinical registries.(24) Variables based on objective information (e.g. gender, gestational age) or procedure codes were very accurate, but there were increased rates of mismatches for comorbid diagnoses. We performed a sensitivity analysis to quantify the systematic error caused by misclassification in the PHIS and found similar results in the multivariable model for in-hospital mortality, though all associations were stronger in the original analysis. This analysis provides more useful estimates of the effects of misclassification on our findings than the qualitative assessments typically made about such biases. Another limitation is that administrative codes do not allow for differentiation among the anatomic variations of EA/TEF which may affect post-operative outcomes.(25) Also, data on esophageal dilations, which are one of the most commonly performed procedures on patients with EA/TEF following repair, was not reported because many of these procedures are performed as outpatients and by interventional radiologists, making accurate counting of dilations difficult and unreliable. Lastly, the PHIS database does not allow for the tracking of patients across hospitals, thus patients who did not continue to receive care at the same PHIS institution were lost to follow up.

Conclusions

This study provides longitudinal estimates of population characteristics, associated comorbidities, and outcomes for a large cohort of EA/TEF patients from 43 children's hospital in the United States. In addition, across these children's hospitals, there was no significant relationship between hospital volume and mortality or repeat TEF ligations. EA/TEF remains a complicated, potentially fatal, congenital anomaly that is associated with a number of significant long-term sequelae resulting in continued health care utilization.

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Figure 1. Effects of birth weight and race on mortality

There was a significant quantitative interaction between birth weight and race ($p < 0.05$). In infants less than 2000 grams, black patients showed a greater decrease in their mortality risk for every 100 gram increase in birth weight (OR (95% CI); 0.82 (0.76, 0.88), $p = 0.02$) than white patients (0.89 (0.87, 0.92), $p < .0001$) or patients of other or unknown race (0.88 (0.84, 0.93), $p = 0.04$). In infants over 2,000 grams, these racial differences do not persist.

Table 1

Baseline demographic and clinical characteristics of neonates with EA/TEF overall and grouped by survival to hospital discharge after the first EA/TEF related procedure.

	Total cohort (N=3479)	Died (N=189)	Survived (N=3290)	P
	N (%) or median (IQR)			
Male	1934 (55.6)	101 (53.4)	1833 (55.7)	0.54
Race				
White	2373 (68.2)	106 (56.1)	2267 (68.9)	0.0003
Black	327 (9.4)	30 (15.9)	297 (9.0)	
Other/Unknown	779 (22.4)	53 (28.0)	726 (22.1)	
Birth weight ^a	2580 (2020, 3050)	1868 (1280, 2370)	2604 (2070, 3075)	<.0001
Gestational age in weeks ^b	37 (35, 39)	34 (32, 36)	37 (35, 39)	<.0001
Prematurity	1286 (37.0)	113 (60.0)	1173 (35.7)	<.0001
Associated Congenital Conditions (N, %)				
Any other congenital anomaly	2905 (83.5)	183 (96.8)	2722 (82.7)	<.0001
Congenital heart disease	2420 (69.6)	174 (92.1)	2246 (68.3)	<.0001
Gastrointestinal anomaly	707 (20.3)	54 (28.6)	653 (19.9)	0.004
Eye anomaly	109 (3.1)	15 (7.9)	94 (2.9)	<.0001
Coloboma	39 (1.1)	8 (4.2)	31 (0.9)	<.0001
Head or Neck anomaly	27 (0.8)	4 (2.1)	23 (0.7)	0.06
Respiratory anomaly	564 (16.2)	54 (28.6)	510 (15.5)	<.0001
Palate anomaly	82 (2.4)	11 (5.8)	71 (2.2)	0.004
Musculoskeletal anomaly	919 (26.4)	75 (39.7)	844 (25.7)	<.0001
Genetic anomaly	212 (6.1)	37 (19.6)	175 (5.3)	<.0001
Slow fetal growth/malnutrition	265 (7.6)	28 (14.8)	237 (7.2)	0.0001
Pre-operative ventilation (N, %) ^c	1665 (47.9)	133 (70.4)	1532 (46.6)	<.0001
Pre-operative TPN (N, %) ^c	1517 (43.6)	93 (49.2)	1424 (43.3)	0.11
Pre-operative ECMO (N, %) ^c	7 (0.2)	2 (1.1)	5 (0.2)	0.051

* The first non-gastrostomy procedure listed in Figure 1 was treated as the first EA/TEF procedure.

^a N=3310.

^b N=2189.

^c For 72 patients this includes all encounters prior to the first non-gastrostomy procedure related to EA/TEF.

EA, esophageal atresia; TEF, tracheoesophageal fistula; TPN, total parenteral nutrition; ECMO, extra-corporeal membrane oxygenation.

Table 2

Post-operative outcomes and other occurrences at the index admission or within 30 days in 3479 patients with EA/TEF

Outcome	N (%) or median (IQR)
Total Length-of-stay	27 (15, 58)
Post-operative Length-of-stay	23 (13, 47)
Post-operative Mechanical ventilation	3220 (92.6)
Post-operative TPN	3184 (91.5)
Post-operative ECMO	29 (0.8)
Post-operative Blood transfusion	578 (16.6)
Anti-reflux meds during the last day of admission	1998 (57.4)
Tracheomalacia during index admission	65 (1.9)
Gastroesophageal reflux disease during index admission	992 (28.5)
30-day readmission	490 (17.0)
Death in-hospital	189 (5.4)

EA, esophageal atresia; TEF, tracheoesophageal fistula; IQR, interquartile range; TPN, total parenteral nutrition; ECMO, extracorporeal membrane oxygenation

Table 3

Post-operative outcomes within 2 years of initial EA/TEF surgery in 2887 patients with EA/TEF

Outcome	N (%)
Readmitted	1579 (54.7)
Additional surgery for TEF ligation ^a	133 (5.2)
Repeat operation for their esophageal reconstruction	329 (11.4)
Esophageal replacement procedure	19 (0.7)
Fundoplication	338 (11.7)
Gastrostomy tube placement (after EA/TEF repair)	511 (17.7)
Tracheostomy	176 (6.1)
Readmitted with a pneumonia diagnosis	366 (12.7)
Number of readmissions for patients with at least one pneumonia-related readmission	
1	190 (51.9)
2	82 (22.4)
3	50 (13.7)
4	19 (5.2)
5 or more	25 (6.8)

^aN = 2548, the number of patients who had an initial TEF ligation.

EA, esophageal atresia; TEF, tracheoesophageal fistula

Table 4

Independent predictors of in-hospital mortality during the initial admission for patients with EA/TEF, including results of sensitivity analysis (SA) accounting for data misclassification/measurement error.

Variable	Odds Ratio (95% CI)	P	Odds Ratio (95% CI) after Sensitivity Analysis
Birth weight (per 100 gram increase) ^a	0.88 (0.87, 0.90)	<.0001	0.88 (0.65, 1.19)
Congenital heart disease	3.67 (2.02, 6.68)	<.0001	1.74 (1.19, 2.57)
Eye anomaly	2.51 (1.3, 4.87)	0.01	1.43 (0.79, 2.35)
Genetic anomaly	3.76 (2.49, 5.65)	<.0001	2.04 (1.31, 3.07)
Musculoskeletal anomaly	1.62 (1.17, 2.25)	0.004	1.47 (1.03, 2.06)
Respiratory anomaly	1.85 (1.29, 2.65)	0.0008	1.61 (1.09, 2.33)
Pre-op ECMO	17.58 (1.92, 161.06)	0.01	1.12 (0.43, 2.25)
Pre-op TPN	0.57 (0.41, 0.8)	0.001	0.84 (0.58, 1.19)
Pre-op mechanical ventilation	1.93 (1.3, 2.86)	0.001	1.47 (1.03, 2.08)

^aThis model also included race ($p>0.10$), and there was a significant interaction between birth weight and race; please see the text of the results section for further details.

EA, esophageal atresia; TEF, tracheoesophageal fistula; SA, sensitivity analysis; ECMO, extra-corporeal membrane oxygenation; TPN, total parenteral nutrition

Table 5

Results of institutional chart review validation.

Variable	Misclassification Rate (%), CH1 (N = 78)	Misclassification Rate (%), CH2 (N = 95)	Overall Misclassification (%)
<i>Baseline Characteristics</i>			
Date of birth	0	6.3	3.5
Gender	0	1.1	0.6
Race	18.2	14.8	16.3
Birth weight	15.6	11.4 ^a	13.6
Gestational Age	3.8	0 ^b	1.7
Age at first surgery	10.3	6.3	8.1
Length of Stay	1.3	2.3 ^c	1.8
<i>Comorbid Diagnoses</i>			
Prematurity	10.3	10.5	10.4
Cardiac Anomalies	25.6	36.8	31.8
Renal Anomalies	10.3	5.3	7.6
Genitourinary Anomalies	3.8	8.4	6.3
Musculoskeletal Anomalies	5.1	9.5	7.5
<i>Outcomes (Procedures)</i>			
Readmission	11	5.7 ^c	8.2
Recurrent TEF (2 years)	6.4	5.7 ^c	6.0
Esophageal Replacement (2 years)	2.6	0 ^c	1.2
Fundoplication (2 years)	5.1	3.4 ^c	4.3
Gastrostomy Placement (2 years)	23.1	8 ^c	15.1
In-hospital Mortality	0	0	0

Due to missing data from PHIS, records were only validated for ^aN=70, ^bN=38, ^cN=88 patients. Continuous variables were defined as matching if their values in PHIS and the medical record were within 100 grams for birth weight, within 1 week for gestational age, and within 1 day for date of birth and length of stay.

EA, esophageal atresia; TEF, tracheoesophageal fistula; CH, children's hospital

Table 6

Comparisons of characteristics of patients treated between 1999–2005 to those treated between 2006–2012.

Variable	Treated in 1999–2005 (N=1397)	Treated in 2006–2012 (N=2082)	P
Age in days at first EA/TEF repair (median, IQR)	2 (1, 4)	2 (1, 4)	0.31
Birth weight (median, IQR) ^a	2565 (2000, 3062)	2582 (2030, 3035)	0.77
Gestational age in completed weeks (median, IQR) ^b	37 (34, 39)	37 (35, 39)	0.57
Associated diagnoses at or before admission with first EA/TEF repair (N, %)			
Prematurity	506 (36.2)	780 (37.5)	0.46
Slow fetal growth or fetal malnutrition	68 (4.9)	197 (9.5)	<.001
Any congenital anomaly (other than EA/TEF)	1097 (78.5)	1808 (86.8)	<.001
Congenital heart disease	852 (61.0)	1568 (75.3)	<.001
GI anomaly (other than EA/TEF)	261 (18.7)	446 (21.4)	0.049
Neurologic anomaly	81 (5.8)	209 (10.0)	<.001
Respiratory anomaly	197 (14.1)	367 (17.6)	0.006
Renal anomaly	242 (17.3)	437 (21.0)	0.007
Musculoskeletal anomaly	330 (23.6)	589 (28.3)	0.002
Genetic anomaly	70 (5.0)	142 (6.8)	0.03
Pre-op mechanical ventilation (N, %) ^c	686 (49.1)	979 (47.0)	0.23
Pre-op TPN (N, %) ^c	476 (34.1)	1041 (50.0)	<.001
Total Length-of-stay	23 (14, 52)	29 (16, 63)	<.001
Post-operative Length-of-stay	20 (12, 41)	26 (14, 49)	<.001
Post-operative Blood transfusion	186 (13.3)	392 (18.8)	0.005
Anti-reflux meds during the last day of admission	730 (52.3)	1268 (60.9)	0.03
Tracheomalacia during index admission	0 (0)	65 (3.1)	<.001
30-day readmission	232 (17.6)	258 (18.3)	0.68
Death in-hospital	81 (5.8)	108 (5.2)	0.55
Readmitted within 2 years	761 (54.5)	818 (54.9)	0.99
Additional surgery for TEF ligation	59 (4.7)	74 (5.7)	0.21
Repeat operation for their esophageal reconstruction	148 (10.6)	181 (12.2)	0.28
Esophageal replacement procedure	13 (0.9)	6 (0.4)	0.10
Fundoplication	181 (13.0)	157 (10.5)	0.11
Gastrostomy tube placement (after EA/TEF repair)	244 (17.5)	267 (17.9)	0.65